

NATIONAL SCIENTIFIC MEDICAL MEETING 1994 Abstracts

ANAESTHESIOLOGY

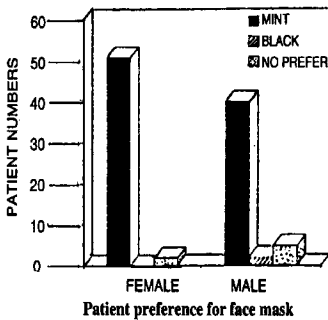
AN ALTERNATIVE FACE MASK FOR PRE-OXYGENATION - A STUDY OF PATIENT PREFERENCE

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Pre-operative stress is well documented and multifactorial in aetiology. Anxious patients often show further signs of stress immediately prior to induction of anaesthesia and during pre-oxygenation. In our hospital standard black rubber masks are used for preoxygenation. Several authors have reported the use of scented oils painted onto the rubber face masks facilitating inhalational induction in children¹. The objective of this study was to assess whether adult patients had a preference for the type of face mask used for pre-oxygenation prior to the induction of anaesthesia.

100 patients ASA class 1, 2 or 3 aged between 17 and 19 years were chosen at random from the theatre list for elective surgery to be included in the study. The patients were visited on the ward. It was explained that they would be brought directly into the operating room prior to surgery. An intravenous cannula would be sited and baseline monitoring established. They would then be given oxygen to breathe for 2 mins prior to the induction of anaesthesia through either an anatomical black rubber face mask or 'King System's Fresh Scent' (mint scented) face mask. A brief description of each mask was given, alternating the order between patients. The patients were allowed to handle and breathe through the masks and then express any preference for one or other mask.



47 men and 53 women were included in the study. Mean age 48.5 yrs \pm 1.98 SEM. 91 patients preferred the clear scented mask ($p < 0.001$), 2 patients the black rubber mask and 7 had no preference.

The majority of patients preferred the clear scented mask and volunteered that they found it less frightening. Use of this mask may help facilitate a smoother anaesthetic induction.

Reference

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RELATIVE MERITS OF PREANAESTHETIC MEDICATION IN PAEDIATRIC DAY-CASE DENTAL ANAESTHESIA

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Oral Trimeprazine tartrate has been used extensively in our

hospital as a premedication for children. In recent times oral Midazolam has been used. We sought to compare speed of onset and recovery of both agents in the day ward setting.

45 children between 3-10 years undergoing dental extractions were studied in a prospective randomised double-blind trial. 22 children received oral Trimeprazine 2mg/Kg and 23 children received oral Midazolam 0.5mg/Kg. An independent evaluator observed behavioural changes at 30 and 60 minutes post administration of premedication and also rate of recovery to alert state on return to the day ward and at proposed discharge time.

There was a significant difference in attainment of a calm and drowsy state in the Midazolam group by 30 minutes post administration. However, by 60 minutes this continuing trend ceased to show statistical significance. On return to the day ward behavioural patterns were similar in both groups. By proposed discharge time the Midazolam group reached suitability for discharge sooner ($p = 0.01$).

We propose oral Midazolam as a more efficient preanaesthetic.

EUROPEAN NOSOCOMIAL INFECTION SURVEY: ANALYSIS OF IRISH DATA

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

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

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

Organisms (Irish Group)

G Positive	16.6%
G Negative	38.8%
Fungus	2.7%
Polymicrobial	16.6%
Unidentified	25%

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

*European Nosocomial Infection Survey.

MORBIDITY AFTER DAY CASE ANAESTHESIA – PROPOFOL-OSOFLURANE vs. PROPOFOL-ENFLURANE

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Because of its physicochemical properties isoflurane has been proposed as the volatile agent of choice for day case anaesthesia. In a randomised controlled study we compare the clinical effects of isoflurane or enflurane anaesthesia. Following ethical approval and informed consent 100 day cases were randomised to receive enflurane (n=50) or isoflurane (n=50). Following induction with fentanyl 0.75 µg/kg, droperidol 0.5 mg and propofol a laryngeal mask was placed and anaesthesia maintained with 60% N₂O in O₂ and enflurane or isoflurane. Post operative sequelae were carefully recorded. Patients were given a questionnaire on post discharge sequelae and asked to return this after 1 week. Data were analysed statistically.

The groups were demographically similar. The incidence of pain and emesis was low (table). All patients were discharged home and discharge times were similar in both groups. 93% returned the questionnaire. 23% visited their GP for wound related problems. There was a low incidence of anaesthesia related malaise. Seven patients (7%) were dissatisfied.

We conclude 1) anaesthesia related morbidity is low after day case surgery; 2) isoflurane and enflurane do not differ with respect to discharge time, morbidity or patient satisfaction.

	Enflurane	Isoflurane
Pain	9 (18%)	11 (22%)
Nausea/vomiting	0	0
Post discharge malaise	4 (8%)	2 (4%)
GP visit necessary	10 (20%)	13 (26%)

INHALATION INDUCTION OF ANAESTHESIA WITH HALOTHANE AND SEVOFLURANE IN CHILDREN: A RANDOMIZED, CONTROLLED, COMPARISON

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Inhalation induction of anaesthesia remains popular in children. Halothane is widely used for this purpose. The search continues for alternatives. This study compared inhalation induction with halothane and sevoflurane in children with particular reference to speed and safety. Forty healthy children were randomly allocated to have anaesthesia induced with halothane or sevoflurane. Prior to and at one minute intervals during induction, heart rate, blood pressure and arterial oxygen saturation were recorded. Time taken to loss of eyelash reflex and to completion of induction was noted. Events of coughing, breathholding, laryngospasm or excitement during induction were recorded. Induction times for the two agents were similar. There were no episodes of coughing, breath-holding, laryngospasm or arterial desaturation in either group. The incidence of excitement during induction was higher for sevoflurane patients (the difference between groups was not statistically significant). Heart rate and mean blood pressure decreased during induction in both groups. Halothane patients exhibited greater decreases, the difference between groups being significant ($p < 0.01$ for heart rate, < 0.05 for blood pressure). We conclude that sevoflurane is an appropriate alternative to halothane for inhalation induction in children, offering similar induction times and lack of airway complications with greater cardiovascular stability.

PRE-EMPTIVE ROLE OF THE SPACE BLANKET IN SHIVERING AFTER GENERAL ANAESTHESIA

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We investigated the role of the space blanket (UN 320) used pre-emptively in post anaesthetic shivering and patients' subjective perception of cold after general anaesthesia. 68 ASA Class I and 2 patients undergoing surgery on the peripheries, were randomised into two groups: Group 1 were wrapped in the space blanket prior to induction of anaesthesia, group 2 had standard surgical draping. In all subjects, anaesthesia was induced with fentanyl and propofol, and maintained with nitrous oxide, oxygen and enflurane. Patients graded their perception of cold on a visual analogue scale, before induction and in recovery. Skin (dorsum of hand) and core (nasopharyngeal) temperatures were recorded at 15 minute intervals. Shivering and cold scores were recorded by blind observers. Groups were similar with respect to age, gender and duration of anaesthesia (41.6±4.8 vs. 47.5±3.3 minutes respectively, mean + SEM). Incidence of shivering were, respectively, 15% and 63% ($P < 0.001$). Cold scores were 2.4±0.4 and 5.7±0.5 respectively ($P < 0.001$). Skin temperatures rose with increasing duration of anaesthesia in both groups but were higher at 15, 30, and 45 minutes in group 1 (33.38±0.25 vs. 31.56±0.31, 34.46±0.25 vs. 32.45±0.31, and 35.22±0.36 vs. 33.13±0.34, respectively, $P < 0.001$, each comparison). Core temperature rose slightly in group 1 and fell in group 2, $P = 0.11$.

We conclude that in spontaneously breathing patients, the space blanket decreases post-anaesthetic shivering and patients' perception of cold, even after relatively short general anaesthetics.

THE EFFECT OF ORAL OMEPRAZOLE ON SERUM BUPIVACAINE LEVELS FOLLOWING EPIDURAL ANAESTHESIA

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The Histamine-2 receptor antagonists cimetidine and ranitidine have been given preoperatively as prophylaxis against acid aspiration. Both agents affect the elimination of bupivacaine, a local anaesthetic agent used to provide analgesia by the epidural route^{1,2}. Omeprazole reduces gastric acidity, and has been shown to be significantly more effective in preventing aspiration and lung damage than ranitidine³.

Ten patients undergoing elective epidural analgesia for chronic back pain were given omeprazole 40mg orally 2 hours prior to epidural insertion, while a further ten received no premedication. The total dose of bupivacaine administered was 80mg. Blood samples were taken at 0, 15, 30, 45, 60, and 120 minutes for assay of serum bupivacaine levels. Results showed no difference in values between the groups.

This demonstrates that pretreatment with omeprazole has no effect on serum bupivacaine level, and suggests that omeprazole is the most appropriate prophylactic antacid therapy for patients undergoing epidural anaesthesia.

References

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3. A comparison of the effects of omeprazole and ranitidine on gastric secretion in women undergoing elective Caesarean section. Ewart, M. C., Yau, G., Gin, T., Kotur, C. F., Oh, T. E. Anaesthesia 1990; 48: 527-530.

ONDANSETRON IN LAPAROSCOPIC SURGERY

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Postoperative nausea and vomiting (PONV) is common (40%) after laparoscopic surgery¹. We assessed the effect of ondansetron (5-HT₃ antagonist) on PONV.

40 patients received either ondansetron 4mg or placebo (random allocation, double blind) before laparoscopic surgery. A standard anaesthetic technique was used. Morphine and diclofenac provided postoperative analgesia. Anti-emetic therapy was provided by prochlorperazine if required

The number of postoperative emetic episodes and requirements for anti-emetic therapy were recorded. Nausea severity scores were assessed at 1, 2, 4 and 24 hours after surgery. Statistical analysis was performed by unpaired t test or Mann Whitney. $P < 0.05$ was considered statistically significant.

The 2 groups were comparable for age, sex, duration of surgery and recovery time. The number of emetic episodes after surgery did not differ significantly between the ondansetron (30%) and placebo groups (45%). Anti-emetic requirements did not differ significantly between the ondansetron (30%) and placebo (35%) groups. Nausea severity scores did not differ significantly at any time.

We were unable to demonstrate a statistically significant benefit from the use of ondansetron.

CARDIOVASCULAR

APPLICATION OF BODY SURFACE ELECTROCARDIOGRAPHIC MAPPING TO THE DETECTION OF ACUTE MYOCARDIAL INFARCTION

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In 194 controls and 101 patients, QRS and STT iso-integral maps, recorded using a newly developed 64-electrode mapping device, were analysed to determine the ability of the system to discriminate myocardial infarction (MI) from control. Controls, 194 (mean age=48yrs, 120 male) with no history of cardiac disease were selected randomly and mapped. Patients, 101 (mean age=62yrs, 77 male) were mapped as early as possible after onset of chest pain suggestive of first MI. The mean time delay between pain onset and map recording was 163 minutes. Of these 78 were mapped in the mobile coronary care unit, outside hospital. Forty six patients had anterior MI and 55 had inferior MI, all with standard ECG criteria. All patients had significant elevation of cardiac enzymes. Fisher's linear discriminant function (DF) was applied to the iso-integral measurements for both the controls and MIs, and achieved a correct classification of 97% of the controls (189/194), 72% of the anterior (33/46) and 76% of the inferior (42/55) MI groups.

This preliminary work suggests that DF analysis of iso-integral maps not only achieves a good separation of controls from MIs but can also differentiate between types of MI. Further work is required to improve the technique and extend it to assess both location and extent of MI.

A NATIONAL AUDIT OF ACUTE CORONARY CARE

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We performed a national seven day audit of mortality, delay times

and administration on thrombolysis in patients with acute myocardial infarction (A.M.I.) in the Republic of Ireland.

Twenty three coronary care units (CCU) and 17 combined intensive care/coronary care units (CCU/ICU), participated (100% participation). 109 patients had definite acute myocardial infarction. A.M.I. mortality was 11.9%.

Median delay time from onset of symptoms to CCU/ICU admission in patients with myocardial infarction was 4 hours, being greater in Dublin compared to the rest of the country (6 v. 4 hours, $P < 0.05$).

Thrombolysis in AMI related to Sex and Area n (%)

Area	Male	Female	Total
Dublin	13/24 (54.0)	4/11 (36.3)	17/35 (48.6)
Non Dublin	15/45 (33.0)	6/29 (20.7)	21/74 (28.4)
TOTAL	28/69 (40.6)	10/40 (25.0)	38/109 (34.9)

34.9% of patients with confirmed myocardial infarction received thrombolysis. Males and Dublin patients tended to receive thrombolysis more readily. None of the 38 MI patients receiving thrombolysis died compared with 13 (18.3%) of the 71 who did not receive it ($P < 0.01$).

Conclusions: This national audit highlights the need to reduce delay times and to increase the utilisation of thrombolysis in patients with acute MI in Ireland.

NON-ANTICOAGULATION IN ATRIAL FIBRILLATION

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Atrial Fibrillation (AF) is an important risk factor for embolic stroke. Recent clinical trials demonstrated that anticoagulation reduces the risk of stroke in such patients. However there is also evidence that many patients with AF are not anticoagulated for reasons that have not been systematically identified. In a prospective study we examined the reasons for nonanticoagulation in 94 consecutive hospital inpatients with AF from a variety of causes. They had a mean age of 75 ± 9 years, with a mental test score of 7.6 ± 2 (normal 10). 34 lived alone and they lived an average of 14 ± 12 miles from the hospital laboratory. Three categories of reasons for non-anticoagulation emerged: (1) Medical contraindications $n = 38$, commonest being limited life expectancy, liver disease, alcoholism, gastrointestinal haemorrhage and recent stroke, (2) Cognitive Impairment (mental test score < 8) $n = 33$, and Monitoring Problems (patients unwilling or unable to obtain regular thromboplastin time monitoring) $n = 48$. Thirty patients were classified in two or more of these categories. Anticoagulation in AF especially in the target population - the elderly - is a complex enterprise requiring review of social, cognitive and medical issues.

EARLY DIAGNOSIS OF MYOCARDIAL INFARCTION WITH BED-SIDE RAPITEX MYOGLOBIN KIT IN ACCIDENT AND EMERGENCY

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For maximum benefit from thrombolytic therapy, early diagnosis of myocardial infarction (MI) is imperative. Bed-side cardiac enzyme kit may have an advantage over standard laboratory assay for rapid diagnosis. Semi-quantitative bed-side latex agglutination (Rapitex) kit for myoglobin (Mgb-k) was compared with serum creatine phosphokinase (CPK), and correlated with standard

immunospectrophotometric assay of myoglobin (Mgb-IA). 37 patients presenting to Accident & Emergency department (A&E) with classical history of chest pain were enrolled. 23 patients had positive Mgb-k on admission. Of them, 13 had non diagnostic ECG (CPK normal in 9, diagnostic in 4) and 10 had diagnostic ECG (CPK normal in 6, diagnostic in 4). In positive Mgb-k group, 22 had evidence of MI by Day 2 (diagnostic ECG & CPK). Of 14 patients with negative Mgb-k, 12 had non-diagnostic ECG (CPK normal in 11, diagnostic in 2) and 2 had diagnostic ECG (CPK normal). In this group, 2 patients had evidence of MI by day 2. Mgb-k showed sensitivity, specificity and positive predictive value of 91.66%, 92.30% & 91.66% respectively; compared to those of CPK - 50%, 91.66% & 88%. Mgb-k correlated well with Mgb-IA ($r=0.60$).

Bed-side Mgb-k is a useful tool in rapid diagnosis of MI in A&E and could facilitate decision regarding thrombolysis.

in the 10th intercostal space in the midaxillary line. The ICG was recorded by passing a 64kHz constant AC current between the electrode on the right side of the neck and the electrode in the midaxillary line and measuring the voltage between the other 2 electrodes. VT was induced in 23 studies and recordings were made firstly during the initial rhythm and then during VT. Each recording was ensemble averaged over 5 beats and the peak of the ICG, $dz/dt(\max)$, was measured. There was a highly significant reduction in $dz/dt(\max)$ between the initial rhythm ($\text{mean}\pm\text{sd } 0.79\pm 0.30\Omega/\text{s}$) and VT ($\text{mean}\pm\text{sd } 0.30\pm 0.12\Omega/\text{s}$, $p<0.001$). In patients who lost consciousness during VT, $dz/dt(\max)$ was $\text{mean}\pm\text{sd } 0.27\pm 0.02\Omega/\text{s}$ ($n=3$) and where there was no loss of consciousness $dz/dt(\max)$ was $\text{mean}\pm\text{sd } 0.30\pm 0.13\Omega/\text{s}$ ($n=20$). In conclusion the onset of VT is associated with a significant reduction in the amplitude of the ICG. Thus the ICG would assist in the detection of potentially shockable VT.

ASSOCIATION OF PLASMA FIBRINOGEN AND OTHER RISK FACTOR PROFILE WITH EXTENT OF CORONARY ARTERY DISEASE

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To evaluate presence and severity of coronary artery disease (CAD) and its association with plasma fibrinogen (Fib) and other risk factors, we analysed 809 patients (638 males, 171 females) mean age of 55.89 years (SD 18.9), undergoing elective coronary angiogram. 215 patients had normal coronary arteries (NCA) and 594 patients had CAD. Patients with CAD, as opposed to NCA had significantly higher levels of Fib (3.31 vs 2.8, $p<0.00001$), cholesterol (6.35 vs 5.8, $p<0.0001$), triglycerides (1.9 vs 1.5, $p<0.0001$) cholesterol/HDL ratio (7.3 vs 6.03, $p<0.0001$). HDL was inversely related (0.92 vs 1.05, $p<0.0001$) to CAD. As compared to single vessel disease, patients with 3 vessel disease showed higher levels of cholesterol ($>8\text{mmol/l}$) and Fib ($>3.5\text{gm/l}$), and increased prevalence of diabetes smoking and positive family history for CAD. There was linear relationship between Fib and severity of CAD. Plasma fibrinogen level was significantly elevated in the presence of diabetes, hypertension and history of smoking. This cross-sectional study confirms that plasma fibrinogen and other risk factors can predict presence as well as severity of CAD.

DOBUTAMINE STRESS ECHOCARDIOGRAPHY: INITIAL EXPERIENCE IN 100 PATIENTS

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Stress induced myocardial ischaemia can be directly visualised as regional wall motion abnormalities during stress echocardiography. This study assessed the usefulness of dobutamine stress echocardiography (DSE) in the investigation of patients with coronary artery disease. 100 patients referred for coronary arteriography had DSE performed. Its diagnostic accuracy in the detection of ischaemic heart disease was: sensitivity 89%, specificity 82%, positive predictive value 0.92, negative predictive value 0.70. Corresponding results for exercise treadmill testing were 84%, 50%, 0.88, 0.43 respectively. 23 of the patients were subsequently treated by percutaneous coronary angioplasty (PTCA). Patients with angiographically and clinically successful angioplasty had a significant reduction in stress induced ischaemia ($p<0.0001$) demonstrated by repeat DSE after PTCA. Patients with an unsuccessful result showed no significant change ($p=0.65$). In conclusion dobutamine stress echocardiography is a more accurate diagnostic test for coronary artery disease than conventional treadmill testing. It identifies regional wall motion improvement after successful coronary angioplasty and is therefore a potential non invasive tool for guiding management strategies after coronary revascularisation.

USE OF IMPEDANCE CARDIOGRAPHY TO DETECT VENTRICULAR TACHYCARDIA DURING ELECTROPHYSIOLOGICAL STUDIES

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Ventricular tachycardia (VT) is a common cause of out-of-hospital cardiac arrest in patients with chronic ischaemic heart disease. Automated external defibrillators use ECG analysis algorithms to detect VT and determine the need for DC shock based on heart rate alone. Impedance cardiography is a non-invasive measure of cardiac output and the purpose of this study was to determine if the impedance cardiogram (ICG) could identify those patients in VT who require DC shock. During 56 electrophysiological studies the ICG was recorded through 4 spot electrodes. Two electrodes were placed on the back of the neck at the level of the 6th cervical spine separated by 6cm and 2 were placed on the left anterior chest wall, one in the 9th intercostal space in the midclavicular line and the other

ANALYSIS OF THE REGULATED EXPRESSION OF THE HUMAN THROMBOXANE RECEPTOR

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A number of whole animal studies indicate that TXA₂ receptor number is increased in response to androgens. The aim of this study is to investigate this at a cellular level in cultured cell lines. The regulation of TXA₂ receptor binding was studied in human erythroleukaemia (HEL) cells, HELB1 cells, and human embryonic kidney (HEK) cells. The latter two were stably and transiently transfected with the TXA₂ receptor respectively. Cells of each line were incubated with dihydrotestosterone (DHT) (control with vehicle) and a radioligand binding assay using a tritiated TXA₂ receptor was performed. The resulting data were subjected to scatchard analysis.

Expressing the increase in TXA₂ receptor number in the cells

incubated with DHT as a percentage of the control valve the following were obtained: HEL:48%, HELB1:26%, HEK:-31%, though not achieving statistical significance, these results agree with the hypothesis that DHT increases TXA2 receptor number in HEL cells and that this is mediated at the genomic level.

This work was supported by the HRB.

DOPPLER ECHOCARDIOGRAPHIC ASSESSMENT OF THE RESTING HEART IN ISCHAEMIA

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Traditionally, measurements of the systolic behaviour of the left ventricle have been used to estimate the recovery and function of the myocardium following reperfusion after an ischaemic episode. The techniques used have included Echocardiography, Nuclear Cardiology and Angiography. It has recently been shown, however, that diastolic dysfunction is an important contributor to cardiac symptoms and always occurs in cardiac disease even in the absence of systolic abnormalities.

We report on a study to evaluate the usefulness of Doppler Echocardiographic measurements of diastolic function for the non-invasive assessment of reperfusion during and following thrombolytic therapy for the treatment of coronary occlusion. Trans-mitral flow velocity profiles were obtained at regular intervals during thrombolysis on a number of patients admitted via the accident and emergency department with acute myocardial infarction. A number of parameters were derived from these profiles and were compared to those obtained for a human model of myocardial ischaemia created by balloon inflation during percutaneous transluminal coronary angioplasty.

Results demonstrate an impairment of diastolic function following acute myocardial infarction and a recovery over a period of several hours following thrombolytic treatment which could be consistent with the reported phenomenon of 'myocardial stunning'.

CONTRACTILE RESPONSES OF MESENTERIC ARTERIES FROM PORTAL HYPERTENSIVE RATS

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We have examined the effects of pre-hepatic portal hypertension on the responsiveness of rat mesenteric arteries. Rats were made portal hypertensive by creating a portal vein stenosis, or sham operated. Effectiveness of surgery was assessed by measuring the degree of portal-systemic shunting using the radioactive microsphere technique. Degree of shunting was $59.6 \pm 7.2\%$ ($n=5$) and $0.08 \pm 0.05\%$ ($n=5$) in 14 day portal hypertensive and 14 day sham rats, respectively. Mesenteric arteries of diameter 200-350 μm were mounted in small vessel myographs for the investigation of contractions to noradrenaline (NA) and relaxations to acetylcholine (ACh). Endothelium-dependent relaxations to ACh were not significantly altered by portal hypertension. Potency of NA was not significantly altered by portal hypertension, but the maximum contraction to NA was significantly greater in mesenteric arteries from portal hypertensive rats (1.66 ± 0.129 , $n=6$) than in vessels from sham rats (0.59 ± 0.079 , $n=6$, $P < 0.001$). Smooth muscle mass was not altered significantly. Hence, portal hypertension alters the responsiveness of rat mesenteric arteries to NA.

BLOOD PRESSURE SIMULATION IN A TUBULAR MODEL

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Simulation of blood pressure and flow has been used in cardiovascular research for many years. However, the use of working physical models is rare and research has chiefly relied on more convenient mathematical models. The testing of noninvasive blood pressure (NIBP) measurement devices has been identified as one application in which a working hydraulic model may be beneficially employed. A hydraulic simulator has been developed in which physiological blood pressure waves are reproduced in a system of tubes. The arterial vascular system is represented by an asymmetric T-tube, with two discrete reflecting sites. A tissue equivalent material is used to simulate the arm. Pressure waves of physiological characteristics were produced in the tubing system. An occlusive cuff technique was used to accurately identify systolic, diastolic and mean pressure in the collapsible tube. The results suggest that the system has potential for use in cardiovascular research, and as part of a test device for NIBP measurement techniques.

CAROTID ARTERY ATHEROSCLEROSIS; LIPOPROTEIN (a) AND RESTENOSIS AFTER ENDARTERECTOMY

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To investigate whether lipoprotein(a) [Lp(a)] is a risk factor for the development of carotid artery atheroma and restenosis after endarterectomy, 100 consecutive patients who had undergone endarterectomy were studied with repeat carotid doppler ultrasonic scans to assess restenosis. We recorded history of vascular disease, medications and smoking habits. Fasting samples were analysed for serum total cholesterol, HDL cholesterol, triglycerides, apolipoprotein A1 and B, urate, glucose and Lp(a). Carotid artery stenosis was associated with higher levels of Lp(a) (390 ± 40 vs 142 ± 30 mg/l for controls, mean \pm SEM, $p < 0.05$) and concentrations were 45% higher ($p < 0.05$) in the 39 patients who had concomitant peripheral vascular disease. During follow-up (24-168 months) 23% of patients restenosed and the median time to restenosis was 110 months. Cigarette smoking, hypertension and previous myocardial infarction were weakly associated ($p < 0.1$) with restenosis but no association was found between Lp(a) levels and restenosis after endarectomy.

Supported by the Irish Heart Foundation.

URINARY 8-EPI-PROSTAGLANDIN F2 EXCRETION AS A NON-INVASIVE MARKER OF FREE RADICAL INJURY IN HUMANS

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The isoprostanes are free radical-derived products of arachidonic acid. One of these isoprostanes, 8-epi prostaglandin F3 α has biological activity in that it is a potent renal vasoconstrictor and activates platelets. We have developed a highly sensitive gas chromatography/mass spectrometry assay to detect this compound in human urine,

using 0^{18} labelled 8-epi-prostaglandin $F2\alpha$ as the internal standard. We applied this assay to two situations thought to be associated with free radical injury, cigarette smoking and acetaminophen poisoning. Levels in healthy male and female non-smokers ($n=12$) were 18 ± 2 pg/umol creatinine (mean \pm SEM). Excretion was increased in young healthy smokers of greater than 15 cigarettes per day (38 ± 3 , $n=12$; $p<0.0005$). Excretion was also increased in patients following acetaminophen overdose (144 ± 46 , $n=8$; $p<0.05$). Levels were highest in two subjects with evidence of severe toxicity, a subject with acute renal failure (320 pg/umol creatinine), and a patient with 4.3-fold in increase in prothrombin time (378 pg/umol creatinine). Urinary excretion of 8-epi-prostaglandin 2α is increased in the setting of free radical generation. Measurement of this isoprostane may provide a non-invasive marker of free radical-induced tissue injury in vivo. Furthermore, it is possible that production of biologically active 8-epi-prostaglandin $F2$ plays a pathophysiological role in the setting of free radical generation.

5,6 EPOXY-EICOSATRIENOIC ACID; A NOVEL REGULATOR OF SODIUM HOMEOSTASIS?

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5,6 epoxy-eicosatrienic (EET) acid, a product of cytochrome P450 epoxygenase metabolism of arachidonic acid, is a potent renal vasoconstrictor and inhibitor of Na/L ATPase. There is preferential induction of 5,6-EET over its related isomers (8,9-, 11,12- and 14-15-EET) following salt loading in rats. We have developed a highly sensitive and specific gas chromatography, mass spectrometry assay to characterise the urinary excretion of 5,6 EET in normal subjects and in a clinically relevant setting i.e. patients with abnormal salt and water handling. In patients with congestive cardiac failure NYHA classes III and IV, urinary 5,6-EET was 22.3 ± 8.5 (mean SEM, $n=13$) pg/mg creatinine (cr). In contrast, levels in normal subjects were 5 ± 3.5 pg/mg cr ($n=12$, $p<0.05$) and in congestive cardiac failure NYHA classes I and II, 4.7 ± 3.2 pg/mg cr ($n=10$, $p<0.05$). Furthermore, levels were grossly elevated in patients with hepatic cirrhosis complicated by ascites, 57.8 ± 14.2 pg/mg cr ($n=7$) compared to cirrhosis without ascites 8.3 ± 12.1 pg/mg cr ($n=7$), $p<0.005$ and normal subjects ($p<0.0005$). Formation of 5,6-EET is increased in severe cardiac failure and in cirrhosis complicated by ascites, suggesting a role for this eicosanoid in the regulation of sodium and water homeostasis possibly as a counter-regulatory mechanism to the renin-angiotensin system.

INFECTIVE ENDOCARDITIS IN THE '90s: AN AUDIT OF THE EXPERIENCE IN ONE CENTRE: ST. JAMES'S HOSPITAL

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A retrospective survey was conducted of the medical records of 248 patients, who were referred for transthoracic echo (TTE), in whom a clinical diagnosis of infective endocarditis was considered. 31 episodes of endocarditis were diagnosed in 29 patients (M:F 18:11, age range 25-79 years) in the period 1990-93. TTE findings of vegetations supported the diagnosis in 23/31 episodes (74%). 5 episodes involved prosthetic valves, 13 episodes in diseased native

valves, 2 cases in congenital VSD. There were 11 episodes of native valve sepsis of which 4 were right-sided in drug abusers.

Blood cultures were positive in 18 episodes:- *S. aureus* (9); *S. epidermidis* (4), *Strep species* (4), *Endoterrcococcus* (1). *Coxiella burnetti* was identified in one case serologically and one case of *aspergillus* was cultured at autopsy.

7 (23%) patients required surgery (3 acutely):- AVR (5), AVR and MVR (1) and pulmonary valvectomy (1). Overall mortality in this series was 6/31 (19%).

Conclusion: total mortality remains high (19%) (despite positive identification of causative organisms in 4 of 6 deaths. Staphylococci were the most common organisms isolated representing 72% of positive cultures, suggesting the need for change in initial empirical antibiotic regimens.

Despite known limitations, TTE confirmed the clinical diagnosis in 74% of episodes in this series.

THE USE OF VASODILATOR AGENTS TO RESTORE CARDIAC OUTPUT FOLLOWING INHIBITION OF NITRIC OXIDE SYNTHESIS

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Nitric oxide (NO) synthase inhibitors including N^G -nitro-L-arginine methyl ester (L-NAME) restore arterial pressure in septic shock but can depress cardiac output (CO) in some subjects. We have previously shown that CO is restored by administration of nicardipine. The aim of this work was to assess the ability of different vasodilators to restore CO following L-NAME. In pentobarbitone-anaesthetised pigs, systemic and pulmonary vascular resistance (SVR, PVR) and CO were measured before and after administration of a bolus of L-NAME (10 mg/kg i.v.) alone ($n=8$) and followed by bolus doses of levromakalim (LCK 10-40 μ g/kg i.v.: $n=8$) or an infusion of sodium nitroprusside (SNP 14 μ g/kg/min i.v. for 15 minutes at each dose: $n=8$).

Results	SVR	PVR	CO
Pre-Rx	117 ± 12	18 ± 2	5.0 ± 0.5
L-NAME	$236 \pm 21^*$	$45 \pm 9^*$	$3.7 \pm 0.4^*$
LCK	$109 \pm 7^{\dagger\dagger}$	$22 \pm 2^{\dagger}$	4.6 ± 0.5
Pre-Rx	110 ± 8	19 ± 2	5.1 ± 0.4
L-NAME	$203 \pm 13^*$	$46 \pm 8^*$	$3.9 \pm 0.2^*$
SNP	$107 \pm 6^{\dagger\dagger}$	$17 \pm 1^{\dagger\dagger}$	$4.4 \pm 0.3^{\dagger}$

Mean \pm SEM. SVR, PVR in kPa sec/l. CO in l/min. Pre-Rx=pre-treatment. * $P<0.05$ vs Pre-Rx. $\dagger P<0.05$ vs L-NAME alone. $\dagger\dagger P<0.01$ vs L-NAME alone.

Both vasodilators significantly restored baseline haemodynamics but only SNP completely restored baseline PVR while LCK restored CO more potently. These findings may be of value to those using NO synthase inhibitors to treat septic shock.

FIVE YEAR FOLLOW UP AFTER CORONARY ARTERY BYPASS SURGERY; EXPERIENCE WITH INTERNAL MAMMARY ARTERY

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1006 patients underwent coronary artery bypass surgery (CABG)

in this hospital between 1986-92. Role of internal mammary artery (IMA) graft and five year follow up of patients operated between 1986 - June '88 was reviewed. 131 (13%) patients were females. The age of the patients was between 22-77 (average 56) years. 810(18%) had IMA graft. In 1986 47.6% had IMA graft, while in 1992 92.4% had IMA graft. The peri and immediate postoperative mortality was 0.5%.

353 patients had a five year follow up. Questionnaire was sent to the patient regarding present status. Preoperative risk factors, cardiac status, age, sex, type of graft were reviewed to predict mortality and morbidity. 35 patients (9.9) have died, 11 (3.1%) due to a cardiac cause. The youngest 39 years and the oldest 69 years (average 55.45). 8 of these patients had previous myocardial infarction. 7 had a low ejection fraction. 9 were smokers. IMA was used in 6 patients.

Majority of patients undergoing CABG are male. Most being in their fifth and sixth decade. There is increased trend to use IMA graft. Use of double IMA is still limited to selected cases. The pre operative evaluation and the type of graft may predict long term mortality and morbidity.

FIBRINOLYSIS IN THE MANAGEMENT OF ARTERIAL OCCLUSION

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This study presents the results of our use of recombinant tissue plasminogen activator (rtPA) in the lysis of acute arterial thromboses.

Lysis was performed in 21 patients (26 procedures). Of these 14 patients had occluded femoropopliteal grafts, and the remaining 7, occluded arteries.

TPA was infused into the thrombus using a low dose (0.5-4 mg/hr) method. Patients were managed in the vascular surgical unit. Routine coagulation studies were not carried out.

Of the graft group 17 procedures successfully lysed the occlusion. Only 6 patients required surgery. In the patients with occluded native arteries, 4 reperfused and 3 failed to lyse.

We then analysed parameters such as age, duration of symptoms, embolic triggers and pre-treatment distal run-off, to try to predict which patients were likely to respond favourably to local lysis. Our limited study suggests that low dose fibrinolysis can be accomplished safely without complex surveillance during treatment.

CRITICAL CARE MEDICINE

INTENSIVE CARE AND HIGH DEPENDENCY CARE IN A TERTIARY REFERRAL INTENSIVE CARE UNIT

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The Intensive Care Unit (ICU) is a finite and expensive resource. The study measured: (i) the workload in a busy ICU with 8 staffed and 3 unstaffed beds and no associated high dependency unit (HDU); (ii) the daily number of intensive care (I) and high dependency care (H) patients; (iii) the frequency of refused ICU admission due to lack of staffed beds.

A list of patient parameters which would require ICU treatment was agreed by 6 ICU consultants and these parameters were applied daily by the authors to designate ICU patients as I or H.

Over 10 months, of the 2432 bed-days available (based on 8 ICU beds), 2451 were used (bed occupancy of 101%). I and H patients accounted for 1823 (74%) and 628 (26%) bed-days respectively. 73% of the H bed-days (461/628) were required for former I patients who no longer needed I treatment but who were not suitable for general ward care. During the study 376 patients were admitted and 49 requests for admission were refused due to lack of staffed beds.

Thus, over-extended ICU facilities were being used to perform HDU activity. By allowing earlier discharge from ICU, an HDU would free staffed ICU beds and reduce the frequency of refused admissions.

APACHE II IN A MIXED MEDICAL AND SURGICAL INTENSIVE CARE UNIT

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APACHE II is a severity of disease classification based on age, chronic health history and an acute physiology score calculated from 12 physiological parameters⁽¹⁾. To evaluate APACHE II in a mixed medical and surgical intensive care unit (I.C.U) we studied 100 consecutive patients. Data were analysed using t-tests and logistic regression. Mean APACHE II score was higher for nonsurvivors (NS) than for survivors (S). (25.7±7.1 vs 16.5±5.3, p<0.0001). Increasing APACHE II score was associated with decreasing survival (odds ratio 0.81/unit, p<0.0001). Neither medical/surgical status nor emergency status added to the predictive power (p>0.04). With varying cut-off thresholds APACHE II tended to over-predict death in the higher ranges and to under-predict death in the lower ranges. In conclusion APACHE II provides useful group prognostication in a broad I.C.U population but has limited applicability to individual patients.

Reference

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PULSE OXIMETER PERFORMANCE ASSESSMENT

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Pulse oximetry has gained wide acceptance as a non-invasive method of monitoring oxygenation of arterial blood. Although pulse oximeters are widely used for this purpose, they are often used without being subjected to routine performance assessment to verify their accuracy. There is now a commercially available simulator which can be used to verify the operation of pulse oximeters in a variety of ways.

Four hospitals have been surveyed to determine practices in respect of performance assessment. In addition a Bio-Tek SpO₂ simulator has been used to assess the performance of 100 pulse oximeters in the four hospitals, over a range of patient conditions. The Bio-Tek instrument was used to simulate varying levels of SpO₂, pulse rate and pulse amplitude. The results of this evaluation have shown the value of routine performance assessment and the need to implement guidelines for users of pulse oximeters.

In addition, the performance of 6 different models of pulse oximeter has been compared over a wide range of SpO₂ values. As well as comparing the performance of different models, this evalu-

ation has highlighted the regions in which the different models are most reliable and also those areas where results need to be interpreted with caution.

ADULT CRITICAL CARE VENTILATORS: DEVELOPMENT OF END USER TEST PROTOCOLS FOR PERFORMANCE EVALUATION, USING A PHYSICAL LUNG MODEL

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Mechanical ventilators are of vital importance to respiratory life support. However, there is a need to develop more realistic performance verification procedures for lung ventilators. Test conditions specified by manufacturers in terms of simulated patient "load", i.e. total thoracic compliance (C_{tot}) and airway resistance (R_{aw}) combinations, do not reflect the range encountered clinically. Simple test lungs (rubber bags) are often used to represent the patient's lungs.

Protocols have been developed and applied to ventilators selected randomly from clinical use. A calibrated model lung capable of simulating the physiological range of C_{tot} and R_{aw} was used to represent patient "load" in health and disease.

Results highlight the inadequacy of testing ventilators under ideal conditions using test lungs. Lung simulations showed discrepancies in elected and measured ventilator parameters. As C_{tot} decreased and R_{aw} increased patient delivered minute volume and inspiratory flow decreased by up to 20% and 40% respectively over ventilator set values. With increased R_{aw}, at breathing rates above 20 BPM intrinsic PEEP was significant.

Ventilator testing under realistic patient conditions must be further developed. Procedures enabling ventilators of different manufacture to be compared and evaluated, will facilitate more informed decisions when purchasing and provide a sound basis for routine testing.

DERMATOLOGY

CRYOTHERAPY BY THE MULTI-DIP TECHNIQUE – NOT A SOURCE FOR HUMAN PAPILLOMA VIRUS (H.P.V.) INFECTION

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Objectives: To assess whether H.P.V. can be transmitted from a patient onto a cotton bud applicator and hence, into a central liquid nitrogen source during the treatment of viral warts.

Patients and Methods: 10 patients with viral warts were treated with liquid nitrogen applied by cotton bud applications repeatedly dipped into a central liquid nitrogen container. Washings were taken from the container pre and post use and further washings were taken from each of the cotton buds following use and one unused bud as a control. We used the polymerase chain reaction (PCR) to amplify any H.P.V. DNA present using a consensus H.P.V. primer.

Results: 13 separate samples were taken and despite using PCR to amplify any H.P.F. present all samples were negative for H.P.V. DNA.

We conclude, therefore, that H.P.V. does not contaminate the cotton bud.

A THERAPEUTIC STUDY OF NAIL PSORIASIS USING ELECTRON BEAMS

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Background: Involvement of the nails in psoriasis is common. Psoriatic nails that are dystrophic, are unsightly and are a source of social embarrassment and annoyance to the patient. Treatment is difficult and there is no consistently effective method of treatment.

Methods: The study aims to determine whether electron beam irradiation is effective in treating nail psoriasis, and the type of psoriatic nail disease which responds favourably to this treatment. The effect of electron beam therapy in the treatment of psoriatic nails was assessed in 12 patients with symmetrical nail psoriasis. Active treatment was randomly allocated to the affected nails of one hand while the other one served as a control. The nails and the beds were treated with an electron beam of 7 Mega electron volts. A total dose of 6 Gy was given in 8 fractions over 8 weeks, i.e. one fraction of 0.75 Gy per week. Assessment was done at 3 months, 6 months and 12 months after treatment.

Results: Three months after the electron beam therapy, one patient showed marked improvement of the treated nails when compared to baseline; 2 showed moderate improvement; 6 patients showed slight improvement; and 3 patients failed to respond. At 6 months, only one patient continued to show moderate improvement. In 2 patients, the slight improvement seen at 3 months was maintained. In 6 patients, the improvement noted at 3 months was not sustained. The patient with marked improvement of the treated nails at 3 months showed slight improvement at 6 months and 1 year. At one year, only one patient continued to show moderate improvement. In 2 patients, the slight improvement noted at 6 months was maintained. In 9 patients, the nails had reverted back to the pre-treatment state. Compared to the control hand, there was a statistically significant improvement at 3 months ($p < 0.05$) but not at 6 months ($p < 0.5$) and one year ($p < 0.5$) (Wilcoxon signed rank test). Compared to the baseline for the treated hands, there was a statistically significant improvement at 3 months ($p < 0.05$) and at 6 months ($p < 0.05$) but not at one year ($p < 0.5$) (Wilcoxon signed rank test). In 4 patients, the nails of the control hand showed improvement, 3 slightly improved and one moderately improved but this was not statistically significant ($p < 0.5$) (Wilcoxon signed rank test). A decrease in subungual hyperkeratosis was the main improvement noted, followed by pitting and onycholysis. The only local side effect was a temporary deep brownish-black discolouration of the electron beam treated nails.

Conclusions: Electron beam therapy appears to have a temporary beneficial effect on psoriatic nails at this dosage.

ANTIOXIDANT DEPLETION IN NON-MELANOMA SKIN CANCER

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Development of skin cancer results from a complex interplay of numerous factors. Ultraviolet irradiation of skin leads to formation of oxygen radicals. Superoxide dismutase (SOD) protects cells against free radicals by catalysing the dismutation of superoxide anion into O₂ and H₂O₂. Superoxide radical may also be formed in cancer cells. Different workers have shown a reduction in Mn SOD and a variable alteration in Cu-Zn SOD in malignancies. Renal transplant patients (RTP) are at high risk of recurrent skin cancer. This study examines expression of SOD in normal non-sun exposed

skin (N=8), squamous cell carcinoma (SCC) (N=115) and basal cell carcinoma (BCC) (N=12) of RTP and SCC in non-RTP (N=8), in both tumour and adjacent skin. Polyclonal antibodies to Mn SOD and Cu-Zn SOD (Biogenesis) were used for immunohistochemical detection. In normal skin, Mn SOD and Cu-Zn SOD was expressed in epidermis and adnexae, particularly in the basal cells, in endothelial cells and prominently in nerves. There was marked depletion of Mn SOD in: 97% of SCC in RTP, 75% of BCC in RTP and 88% of SCC in non-RTP. There was depletion of Cu-Zn SOD in 97% of SCC in RTP, 66% of BCC in RTP and 76% of SCC in non-RTP. Perilesional skin had reduced staining, especially of the basal cells. Reduced SOD activity may contribute to tumour growth. As retinoids are known to scavenge free radicals this provides support for their use in RTP with recurrent skin cancer.

OPTIC GLIOMAS IN NEUROFIBROMATOSIS TYPE 1

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Optic gliomas have been reported with variable frequency in Neurofibromatosis Type 1 (N.F.1) but appear to be the commonest tumour of the central nervous system diagnosed on imaging the anterior visual system by computed tomography (C.T.) with contrast enhancement. Recommendations for baseline CNS investigations also vary from C.T. or magnetic resonance imaging (M.R.I.) as a baseline in all patients to performing C.T. only on those with visual symptoms.

This study sought to define the prevalence and clinical significance of optic glioma in patients presenting to dermatology out-patient clinics.

New patients with N.F.1 presenting to dermatology clinics in 6 hospitals were recruited. Standard diagnostic criteria for N.F.1 were used for inclusion in the study. Assessment included symptoms, ophthalmological examination including visual acuity, fundoscopy, slit lamp examination for Lisch nodules and C.T. scan of orbits including views of the optic nerve. Patients who had doubtful C.T. results had an M.R.I.

30 patients (14 males, 16 females) with confirmed N.F.1 were studied, age range from 6 to 67 years. C.T. scans were abnormal in 5. Optic nerve gliomas were present in 4 patients and one patient had sphenoid wing dysplasia. Of these, all had normal visual acuity and fundoscopic examination. Lisch nodules were identified in all cases. One patient complained of headache.

The prevalence of optic gliomas was 13% in this study, in agreement with other studies. Ophthalmological examination was useful in confirming the presence of Lisch nodules but did not detect any of the gliomas present. C.T. or M.R.I. is the investigation of choice in making the diagnosis of optic glioma and as some of these progress to cause visual impairment or blindness, diagnosis with a view to careful follow up appears sensible.

PORPHYRIN ABNORMALITIES IN ACQUIRED IMMUNE DEFICIENCY SYNDROME

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An increasing number of HIV positive individuals with porphyria have been reported, suggesting an aetiological role for HIV in the

pathogenesis of this condition. Many HIV patients are also seropositive for hepatitis C. Recent data suggest an increased prevalence of hepatitis C in porphyria cutanea tarda of probable aetiological significance. A prospective study was undertaken of porphyria metabolism in HIV positive patients.

Thirty three patients were screened. Urinary 24 hour specimens were analysed spectrophotometrically. Plasma samples were analysed fluorometrically. Faeces were screened by solvent extraction and positive samples were further analysed by high performance liquid chromatography (HPLC). Each patient was assessed clinically. Full blood counts, liver function tests, T lymphocyte counts and serology for hepatitis C (Enzyme linked immunosorbent assay) were performed.

There were 28 males and 5 females with an age range 18-35 years. 13 patients (40%) had increased urinary porphyrin excretion ranging from 336-799 ug/24h (normal <200). 10 patients (30%) had elevated plasma porphyrins ranging from 9-55 nmol/l (normal range: 2.3-8.7). Faecal screens were positive in 3 of 9 (33%) available specimens. All patients with abnormal porphyrin metabolism had AIDS defining illnesses and were more immunosuppressed (mean CD4 count: 34/ul) than those with normal porphyrins (mean CD4 count: 145/ul). 8 of 9 patients (89%) with abnormal porphyrin screens tested for hepatitis C had positive serology compared to 7 of 12 patients (58%) with normal porphyrin screens. Mean aspartate aminotransferase in patients with porphyrin abnormalities was 80 IU/l (N: 7-40), mean alkaline phosphatase was 150 IU/l (N: 30/100) compared with 56 IU/l and 112 IU/l respectively in the group with normal porphyrins. No patient had clinically evident porphyria.

Porphyria metabolism is grossly abnormal in patients with established HIV infection. Hepatitis C however may also be an aetiological factor.

AN AUDIT OF MELANOMAS DIAGNOSED AT A PIGMENTED LESION CLINIC

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The incidence of melanoma is increasing worldwide. The number of deaths in Ireland has doubled from 1975-1985, it has been suggested that delay in presentation might be one of the major factors. A previous Irish study found a mean delay in presentation after onset of symptoms of 21 months with only 45% of melanomas being under 1.5 mm Breslow depth at presentation. To address this issue, a Pigmented Lesion Clinic (P.L.C.) was set up in the City of Dublin Skin and Cancer hospital in 1988. Its aims were to facilitate the rapid referral and treatment of early melanomas. A retrospective study of histologically proven cases of melanoma diagnosed at the P.L.C. from 1988-1993 was undertaken. Characteristics studied were age and sex distribution, skin type, duration and nature of symptoms, melanoma type, Breslow's depth, Clarke's level, treatment received and outcome. During the period studied, 1,600 new patients were seen at the P.L.C., 50 melanomas were diagnosed, 21 lentigo malignas were seen. Mean age was 49 years (range 14-87). 37 patients were female (74%) and 13 were male (26%). The female:male ratio was 2.85:1. 68% of recorded skin types were 1 or 2. 38% had a history of severe sunburn in childhood. 12% had used sun beds. The commonest melanoma site was the leg in females (33%) and the back in males (55%). 72% were superficial spreading melanomas, 18% lentigo maligna melanomas, 8% nodular, 2% acral lentiginous. The mean Breslow depth was 1.02mm in females and 1.33mm in males, median Clarke's level in both groups was 3. The mean duration of

symptoms was 10 months. Increasing size was noted in 78%, colour change in 68%, abnormal sensation in 40% and bleeding in 18%. All were stage 1 at presentation. 4 patients have progressed to stage 2 disease, 2 are clinically clear at present, the other 2 died from metastatic disease. It would appear that the P.L.C. is fulfilling its role in picking up early melanoma. These earlier presentations correlated with thinner lesions, and improved survival rates.

SUBUNGAL MELANOMA; A RELATIONSHIP TO TRAUMA?

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Hutchinson referred in 1886 to "melanotic whitlow" - a coal-black discolouration at the edge of an inflamed nail. He pointed out that it generally is attributed by the patient to injury, the diagnosis is subsequently often delayed and the prognosis poor. We present five cases of subungual melanoma that followed a significant penetrating or crush injury to the nail.

The mean age at presentation of the group was 55 years (range 23-74). The mean delay in diagnosis was 2.7 years. All the tumours presented with a Clark level of III to IV. The mean Breslow thickness was 2.4 mm (range 1.3-8 mm). Two of the five patients had lymph node involvement at diagnosis. The 2 year survival in the group was 60%.

Malignant melanoma has been described as arising de novo within an inoculation site, a tattoo and following a penetrating ocular injury. Since the 1930's papers concerning subungual melanoma do not mention trauma or only mention it to describe it as coincidental with one exception in which the type of injury was not documented.¹ In all our cases there was a clear history of significant and memorable injury which led to the patients and doctors attributing the non-healing nail lesion to the injury for a period of two years. Trauma may play an important aetiological role in the development of subungual melanoma.

Reference

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MALIGNANT MELANOMA - IT IS STILL PRESENTING LATE

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We conducted a retrospective review of 390 patients with invasive malignant melanoma diagnosed between 1976 and 1993 inclusive. The number of cases in the periods 1976-81, 1982-87, 1988-93 were 55, 148 and 187 respectively indicating a rise in the mid-eighties of over 100%. Up to 1985 the female to male ratio was 3:1. It is now 1.7:1.

The mean age at presentation was 44.4 years (range 7-88 years). 18 patients (5%) had multiple primary melanomas. In ten patients no primary lesion was found. There were 180 superficial spreading melanomas (47%), 120 nodular melanomas (31%), 37 lentigo maligna melanomas (10%) and 30 acral-lentiginous melanomas (8%). The mean Breslow thickness of the group was 2.7 mm. In the period 1976-81 37% of melanomas had a Breslow thickness of >3mm. This has reduced significantly to 22% in 1988-93. However in 1988-93 50% of the invasive malignant melanomas were Clark level IV-V. In the

same time period the percentage of patients with lesions <0.8 mm has increased from 23 to 30% of the total. These are mainly young and middle-aged women. This is reflected in a superior female 5 year survival of 75% compared to 45% for males.

Despite public education 50% of the malignant melanomas are Clark level IV-V and 31% are nodular poor prognostic lesions. These mainly occur in the elderly and in the young and middle-aged male. Education about the sun should be for life and commence at an early age i.e. in primary school.

Reference

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ACRAL MELANOMA - A CLINICOPATHOLOGICAL STUDY OF 34 CASES

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A retrospective review was conducted of 34 patients who presented with acral melanoma between 1978-1993. There were 19 men and 15 women. The mean age at presentation was 63 years (range 22-88 years). Five of the patients had Stage II disease at presentation. Histological details obtained included melanoma subtype. Clark level, Breslow thickness, mitotic activity, cell type, lymphocytic infiltrate, vascular ± lymphatic invasion, regression and desmoplasia. Twenty three patients had acral lentiginous melanomas, six were of superficial spreading type and five were of the nodular variant. Three of the patients had lesions that were Clark level II to III. The remainder (90%) were Clark level IV to V. The mean Breslow thickness was 4.76 mm (range 0.2-22 mm). The mitotic figures per 10 HPF ranged from 0-75 with a mean of 7.3. The commonest cell type was round (40%), followed by spindle cell (27%) and bizarre cell type (15%). Two patients were noted to have desmoplasia (5%).

The two and five year survival respectively were 60% and 45%. Clark level, Breslow thickness, mitotic activity bizarre cell type and vascular invasion correlated with a poor clinical outcome. Delay in presentation and the presence of advanced disease contribute to the poor prognosis in this group of patients.

Reference

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COMPARISON OF PUVA PROTOCOLS FOR CHRONIC PLAQUE PSORIASIS (CPP)

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The optimal PUVA protocol for CPP is still unclear. An uncontrolled study suggested that twice rather than 3 or 4 times weekly exposure, with starting dose based on minimal phototoxic dose (MPD) rather than skin typing, cleared patients with less exposures and a lower cumulative dose¹. We undertook a randomised controlled trial of twice-weekly/MPD versus 3 times weekly/skin typing. 83 patients were treated. MPD testing was carried out in 42 patients; 41 patients had doses based on skin type. Clearance rates were similar in each group (97.4% and 94.6%). There was no significant difference between groups though there was a trend towards a higher cumulative dose in the twice weekly/MPD group. For patients of skin type I and II, the cumulative dose of UVA was significantly

higher with the twice-weekly/MPD regimen (70J/cm² vs 55.8J/cm², p<0.35). Our findings do not confirm that twice-weekly/skin typing has a UVA-sparing effect compared to thrice-weekly/skin typing. In fair-skinned populations, like the Irish, a twice weekly/MPD regimen could predispose to the early emergence of non-melanoma skin cancer.

Reference

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RESULTS OF PATCH TESTING IN A DUBLIN CLINIC, 1979 - 1988

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Information about the epidemiology of contact dermatitis in much of Europe has been known since the 1970s. To compare results with those of our European colleagues, we carried out a retrospective study on patch test results combined with clinical information from hospital notes on 1,941 patients seen over a 9 year period. Patch testing was carried out with a European standard battery and two readings were made. 49% of patients were female and 41% male. Their ages ranged from 10 to 90 years. The duration of dermatitis was less than five years in 79%. The hand was the most frequently affected site at the time of presentation. Facial dermatitis was more common in females (20%) than in males (8%); The feet were most frequently affected in males (13%) compared to females (5%). 74% of positive results were present at 48 hours. Nickel was the overall most common sensitiser (16.5%) and this sensitivity was predominant in females. Potassium dichromate was the next most frequent sensitiser (7%) and this reaction was most commonly found in males. Fragrance mix, cobalt, Balsam of Peru and thiram mix were the next most frequent sensitisers. Overall, these results differ little from those of other European countries in spite of Ireland being largely an agricultural country with few large industries.

ENDOCRINOLOGY/METABOLISM/ LIPIDS

NEW BIOMARKERS IN PAGET'S DISEASE OF BONE

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Paget's disease of bone is a focal disorder that may affect one or multiple sites of the skeleton. The prevalence of the disease in the population over 55 years based on a survey of pelvic radiographs varies from 1.7% in Dublin to 0.7% in Galway. The disease is often asymptomatic but can be associated with chronic pain, deformity and enlargement of bones, neurological syndromes, fractures, and rarely sarcomatous change. Bone biomarkers quantify both the level of activity in bone and the response to therapy. We evaluated new markers of resorption (serum telopeptide and urine crosslinks) and formation (serum osteocalcin and serum procollagen I carboxy-extension peptide) in a small sample of patients (n=11). The biomarkers indicated a concurrent level of activity for resorption and formation that was consistent with coupling of resorption to formation. In conclusion, new biomarkers of bone activity assist the clinician in the assessment and management of Paget's disease of bone.

OSTEOPOROSIS: BIOCHEMICAL ASSESSMENT OF BONE TURNOVER

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Osteoporosis accounts for bone fracture in about 40 per cent of women over 80 years old. Bone loss implies a negative bone balance per bone remodelling cycle. The magnitude of the loss is influenced by the bone turnover rate. New biomarkers of bone resorption and formation have been described. These include assays for serum collagen telopeptide (ICTP) procollagen I carboxyterminal propeptide (PICP), serum osteocalcin (Oc) and urine pyridinium crosslinks (U-Pyr). Preliminary studies were done using these markers in premenopausal healthy women (n=30), post-menopausal osteoporotic (PM-OP) subjects (n=13), and in other bone disorders (20). Correlation of collagen markers with other bone indicators are shown in Table 1. Mean values for PICP, Oc, and serum ICTP/creatinine in PM-OP and pre-menopausal control subjects were 133.7±73 v 125.2±33 ug/l, Oc 18.5±7.6 v 12.8±3.8 ug/l, and Serum ICTP/cr 59.3±17.9 v 49±15.9 ug/mmol respectively. This may reflect increased bone turnover in PM-OP, but considerable overlap between groups was evident. Use of an index to assess the remodelling imbalance and turnover may be needed.

Table 1.
Correlation of Tests of Bone Resorption and Formation.

	n	r	p
Serum ICTP/creatinine v U-Pyr/cr	29	0.89	0.0001
Serum ICTP/cr v Ur. hydroxyproline/cr	32	0.39	0.032
Serum PICP v Serum Alk. Phos	34	0.44	0.009
Serum PICP v Serum Oc.	29	0.03	ns
Serum PICP v Serum Oc/cr	24	0.39	0.058

MICROALBUMINURIA IN NEWLY DIAGNOSED NIDDM HIGHLIGHTS NEUROPATHY BUT NOT MACROVASCULAR DISEASE

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We measured 24hr urine microalbuminuria (MicroA) in 183 consecutive newly diagnosed cases of NIDDM, after stabilisation of metabolic control, to determine its utility in identifying associated diabetic pathology. 38% had elevated MicroA (> 25ugs/24hrs). Those with normal MicroA - Group A (n = 114) were compared to those with elevated MicroA - Group B (n = 69). The 2 groups did not differ significantly regarding age, sex ratio, education, BMI or mean HbA1. Presence of neuropathy was evaluated by a symptom and clinical examination score system (derived from Lehtinen, Diabetes 1989). Neuropathy was also assessed by measurement of vibratory perception threshold -VPT- and heart rate variability with deep breathing -HRV- (both corrected for age). The prevalence of retinopathy was documented through fundoscopy of dilated pupil. The prevalence of clinical (and electrocardiographic) features of coronary, peripheral and cerebrovascular disease was documented. 33% of group A were hypertensive compared to 58% of group B (p=0.03). The prevalence of macrovascular disease or retinopathy did not differ significantly between the 2 groups. However neurological symptom score (p=0.03), neurological exam score (p = 0.03) and prevalence of impotence (p < 0.01) were higher in group B. VPT and HRV did not differ significantly between the groups. MicroA appears to highlight underlying neuropathy more than other problems in new cases of NIDDM.

THE IN VITRO EFFECT OF FLUORIDE AND OTHER BONE CELL EFFECTORS ON HUMAN OSTEOBLAST PROLIFERATION

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Sodium fluoride (NaF) is used clinically in the treatment of osteoporosis. To study the effect of fluoride on human osteoblast proliferation in vitro, we administered various (0 - 500 μ M) concentrations of NaF to cultured human osteogenic sarcoma cells (SaOS, LJOB, and MG-63 cell lines). We used the methylene blue assay for cell number and [³H]-thymidine incorporation as indices of cellular proliferation. We also investigated the role of other bone cell effectors on the mitogenic response.

NaF, in micromolar concentrations, is a biphasic stimulator of osteoblastic proliferation, with maximal stimulation occurring at 50 μ M. This effect is more evident in cells treated with 10^{-7} M dexamethasone, and is greatly potentiated in 1.0 mM phosphate-supplemented media. NaF influenced the effect of hormones such as insulin, insulin-like growth factor 1 (IGF-1), parathyroid hormone [1-84] (PTH [1-84]), PrH [53-84], and oestrogen, on bone cell proliferation.

LOOKING THIN BONES IN THE EYE

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The significance of scleral hue (SH) as an index of bone density was assessed, since Type I collagen forms the ground substance of bone and of sclera. The SH of a patient with severe osteogenesis imperfecta was reproduced and serially diluted X 50% until near white, giving 9 grades of blueness (Sillence 1993). 8 osteoporotic patients had S.H evaluated visually and by photography.

By visual analysis, intraobserver variation was ≤ 1 grade. Fluorescent lighting was one grade bluer than sunlight (which was unreliable) or 22 KW standard white lamp. Relating fracture frequency with visual SH gave an R value of 0.112 ($p = 0.79$ - not statistically significant). Photography, color slides and densitometry and computer screening of photographs had unavoidable variations due to the printing process.

To circumvent these problems a novel colorimeter was developed: A standard blue light source, transmitted by optical fibre and focused to a 5mm footprint on the sclera, is reflected to a portable imaging spectrometer. The reflectance spectra are analysed and quantitated numerically and studies are underway to compare them to bone density measurements.

RELATIVE HYPOMAGNESAEMIA IN DIABETIC PATIENTS

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With the relevant ethics approval, clinical data was collected from Mater Hospital diabetic patients on the severity of their diabetic complications. Venous blood was drawn with minimum stasis from patients and healthy controls. Plasma Magnesium concentration was determined in the hospital biochemistry laboratory by a colourimetric assay. Type I diabetics showed a significant ($p < 0.01$) decrease in plasma magnesium concentration ($[Mg] = 0.80 \pm 0.02$ mmol/l s.e.m,

$n=9$) compared to controls ($[Mg] = 0.86 \pm 0.01$ mmol/l, $n=23$). Type II diabetics ($[Mg] = 0.84 \pm 0.02$ mmol/l, $n=16$) showed an intermediate value, not significantly differing from controls or Type I diabetics. There was a significant ($p < 0.05$) decrease in plasma magnesium concentration between the diabetic group as a whole ($[Mg] = 0.83 \pm 0.01$ mmol/l, $n=25$) and control.

Control plasma magnesium values agreed well with a study performed in the same laboratory on 1000 normal samples taken from the blood bank. In each group the mean approximated the mean, indicating a normal distribution. No significant correlation was found between glycosylated haemoglobin, fasting blood glucose concentration or duration of diabetes and magnesium concentration.

AUDIT OF A LIPID CLINIC

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Hyperlipidaemia is common and contributes to our having a high incidence of ischaemic heart disease (IHD). To monitor practices with a view to improving efficiency and service, the first 402 patients registered at our lipid clinic were audited. We found that 30% had established atherosclerotic vascular disease at presentation; 25% had a family history of hyperlipidaemia; 62% had a family history of IHD and 7% had NIDDM. Investigations for secondary causes of hyperlipidaemia revealed 7.5% of patients to be hypothyroid. All received dietary advice. By the end of 2 years, 41% of patients required addition of lipid lowering drugs, 75% of these were commenced on HMG Co A reductase inhibitors. Approximately 30% were lost to follow-up, mainly males and asymptomatic patients but these also included heavy smokers and patients who had IHD. At the end of two years there was a mean weight loss of 2.5 ± 0.77 kg ($p=0.1$), mean (in mmol/l) cholesterol fell by 20% ($p < 0.01$) (8.1 ± 0.9 to 6.5 ± 0.1) and HDL rose by 20% ($p < 0.001$) (1.19 ± 0.07 to 1.43 ± 0.06). This produced a substantial change in the mean cholesterol / HDL ratio from 6.8 to 4.5 (- 34%) ($p < 0.01$) which is within the recommended range suggesting considerable beneficial changes in IHD risk. As high risk patients defaulted greater effort at follow-up and education, probably involving patients' general practitioners, is needed.

B-ENDORPHIN AND JOINING PEPTIDE STIMULATE ANDROSTENEDIONE PRODUCTION IN HUMAN ADRENAL CELLS *IN VITRO*

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This study examines the androgen stimulating properties of proopiomelanocortin derived peptides, ACTH, β -Endorphin (β -Endo) and Joining Peptide (JP). Human adrenal glands were obtained at resection of kidneys for transplantation: Cell suspensions were prepared and cortisol, androstenedione (A4) and dehydroepiandrosterone (DHEA) production was measured following incubation both with and without the addition of ACTH (10^{-2} - 10^{-11} M), β -Endo (10^{-6} - 10^{-10} M) and JP (10^{-6} - 10^{-10} M), alone and in combination. ACTH and JP stimulated cortisol, A4 and DHEA production but β -Endo stimulated only A4 and DHEA production. Although ACTH, 10^{-9} M, stimulated cortisol production, 120 ± 51.3 nmol/l (mean \pm SE, $n=10$), the addition of β -Endorphin, 10^{-10} M, significantly inhibited ACTH-stimulated cortisol production, $48 \pm$

28 nmol/l, $p < 0.025$. However, A4 production increased from 4.5 ± 2.3 nmol/l with ACTH alone to 6.2 ± 3.2 nmol/l with ACTH + β -Endo. ACTH-stimulated DHEA production was not affected by β -Endo. JP 10^{-10} M also inhibited cortisol production, 12 ± 28 nmol/l, $p < 0.025$, and stimulated A4 production, 5.5 ± 2.8 nmol/l. The data suggest that if the secretion of β -Endo/JP increases to herald adrenarche as previously reported, cortisol production would fall while A4 production increases. The predictable *in vivo* response is increased ACTH secretion returning cortisol production to basal while further increasing androgen production, a sequence which may explain the evolution of adrenarche.

THYROTOXICOSIS AND THYROID CANCER

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The co-existence of thyrotoxicosis and clinically significant thyroid cancer is deemed to be so rare that a generally applied clinical rule is that an active nodule is almost never malignant and coincidence is very unlikely. We report four cases which indicate that caution should be applied when following this maxim. Four women aged 29 to 76 years had a multinodular goitre and absent thyroid antibodies; 2 had been treated with 131 I, none had other history of irradiation to the head or neck. The tumours were classified as papillary (2), mixed anaplastic/papillary (1) and anaplastic (1). Two patients had cervical lymphadenopathy and one had pulmonary metastases. Both patients with anaplastic carcinoma succumbed to their disease within 6 months; neither of the patients with papillary carcinoma had evidence of tumour recurrence at follow-up 6 months and 4 years respectively. The interval between diagnosis of thyrotoxicosis and development of thyroid cancer varied from 6 months to 27 years. In one patient, at least, the tumour was directly contributing to the thyrotoxic state. Our experience is consistent with an increase in the concordance of thyrotoxicosis and clinically significant thyroid cancer and suggests that the working clinical concept that thyrotoxicosis insures against the possibility of life-threatening malignancy should be revised.

RARE SEVERE POSTMENOPAUSAL HYPERANDROGENEMIA OF BENIGN OVARIAN AETIOLOGY

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Severe hyperandrogenemia in postmenopausal women is rare and usually due to androgen-secreting tumours of the adrenal or ovary. We describe two cases of postmenopausal hyperandrogenemia secondary to benign ovarian lesions. Two women aged 62 and 68 years presented with hirsutism, alopecia and frontal balding. Both had significantly elevated total testosterone: 4.0 and 11.3 nmol/l (0.6-2.0) and testosterone/sex hormone binding globulin (T/SHBG): 21.4 and 55.9 (1.0-5.2); androstenedione was elevated in 1 patient: 13.8 nmol/l (3.3-9.9). Diagnosis was made following laparotomy, identifying hyperthecosis ovarii in one patient and a simple ovarian cyst in the other as the sources of the hyperandrogenemia. Proof that the cyst was functioning was provided by aspiration of the cyst fluid revealing a testosterone level of 344 nmol/l and an androstenedione level of 267 nmol/l. Post-operatively there was normalisation of

androgen levels. Our experience suggests that in the differential diagnosis of postmenopausal hyperandrogenemia, benign aetiologies such as hyperthecosis should be prominent. To our knowledge this is the first report of hyperandrogenemia secondary to an ovarian cyst, although an oestrogen-secreting ovarian cyst has been reported in a postmenopausal woman¹.

Reference

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THE IMPACT OF SMOKING AND HYPERTENSION ON THE PREVALENCE OF MACROVASCULAR COMPLICATIONS IN NIDDM

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The impact of smoking and hypertension on the prevalence of macrovascular complications (coronary artery disease, CAD; cerebrovascular disease, CVD; peripheral vascular disease, PVD) was analysed in 600 randomly chosen NIDDM patients. The population was subdivided into 4 groups based on smoking (smoker, S; non-smoker, NS) and blood pressure status (hypertension, HT; normotension, NT). Age, HbA1 and cholesterol in each group were similar. The impact of smoking, indicated by comparing NSNT to SNT, caused an increase in prevalence of CVD from 2.6 to 10.2%, $p = 0.01$, of CAD from 13.7 to 22.3%, $p = 0.05$ and of PVD from 12.8 to 23.9%, $p = 0.01$. The impact of hypertension, indicated by comparing NSNT to NSHT, caused an increase in prevalence of CVD to 9.5%, $p = 0.03$, of CAD to 30.5%, $p = 0.003$ and of PVD to 17.9%, $p = 0.3$. The impact of combined smoking and hypertension (NSNT vs SHT) caused an increase in prevalence of CVD to 16.5%, $p < 0.001$, of CAD to 30.8%, $p = 0.001$ and of PVD to 24.8%, $p = 0.016$. These data confirm smoking and hypertension as important risk factors for macrovascular disease; while smoking played the dominant role in PVD and hypertension in CAD, the combination caused an incremental increase in CVD.

INSULIN ACTION FOLLOWING LOW AND CONVENTIONAL DOSE BENDROFLUAZIDE IN NON- DIABETIC AND DIABETIC HYPERTENSIVE PATIENTS

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Thiazide diuretics appear to cause insulin resistance. To determine if this can be avoided using lower doses we performed two separate double-blind randomised crossover studies in 15 hypertensive non-diabetic (HN) and 13 hypertensive non-insulin dependent diabetic patients (DH) after 6 weeks placebo run-in and following two 12 week treatment periods with either low (1.25mg) or conventional (5mg) dose bendrofluzide. Low and conventional doses produce similar decreases in systolic and diastolic blood pressure (HN 17/10 and 23/13, $p < 0.05$; DH 21/8 and 23/11 mmHg, $p < 0.005$ respectively for low and conventional dose). In HN glucose infused during hyperinsulinaemic ($1 \text{ mU} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) clamps (measure of peripheral insulin sensitivity) was similar between doses (low 23.1 \pm 1.9

v conventional $21/5 \pm 1.9$ $\mu\text{mol.kg}^{-1}.\text{min}^{-1}$, $p=\text{NS}$) and unchanged from baseline (22.9 ± 1.9 $\mu\text{mol.kg}^{-1}.\text{min}^{-1}$). In DH glucose infused during hyperinsulinaemia ($2\text{mU.kg}^{-1}.\text{min}^{-1}$) remained greater during low compared to conventional dose (27.6 ± 3.6 v 23.2 ± 2.9 $\mu\text{mol.kg}^{-1}.\text{min}^{-1}$, $p<0.05$) and unchanged from baseline (27.3 ± 3.5). Postabsorptive hepatic glucose production (NH and DH) was greater following conventional dose HN 10.9 ± 0.3 v 9.9 ± 0.2 $\mu\text{mol.kg}^{-1}.\text{min}^{-1}$, $p<0.05$; DN 11.7 ± 0.5 v 10.2 ± 0.3 $\mu\text{mol.kg}^{-1}.\text{min}^{-1}$, $p<0.05$) and was increased from baseline (HN 10.0 ± 0.2 ; DN 10.6 ± 0.4). Bendrofluzide 1.25mg is as effective as 5.0mg in lowering blood pressure in both non-diabetic and diabetic hypertensive patients. Conventional dose bendrofluzide impairs peripheral insulin sensitivity in DH and increases hepatic glucose production in HN and DH. Low dose bendrofluzide does not affect insulin action in either group.

IN THE ERA OF PETROSAL SINUS SAMPLING, IS LUNG CT SCANNING NECESSARY IN ALL CASES OF ACTH DEPENDENT CUSHING'S SYNDROME?

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The differentiation between ectopic and pituitary dependent Cushing's syndrome is difficult. CT scanning of the lung is advised in all cases of ACTH dependent hypercortisolism before pituitary surgery is considered. Is this still necessary when bilateral inferior petrosal sinus sampling is available?

We have reviewed 31 cases where both procedures had been performed. 25 had normal lung scans. Of the 25, 23 had a higher inferior petrosal sinus to peripheral ACTH ratio > 1.5 . None of the 25 patients have subsequently been shown to have ectopic ACTH syndrome after careful follow up. Six patients had abnormal findings on lung CT scans. In 2 of these patients the ratio was ≥ 1.5 . Subsequent investigations suggested pituitary disease and hypercortisolism resolved following pituitary surgery. Incidental lung findings were shown in 2 of the remaining 4 patients and pituitary abnormalities were demonstrated after surgery. No evidence of ectopic ACTH syndrome has emerged in a third patient following bilateral adrenalectomy. The fourth patient had an abnormal CT scan and a small cell carcinoma was confirmed histologically.

CT scanning of the chest is only necessary when bilateral inferior petrosal sinus sampling does not demonstrate a significant step-up in ACTH levels.

EXPRESSION OF PROGESTERONE RECEPTORS IN OSTEOBLASTS

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Our objective is to understand how steroid hormones and their receptors are involved in the control of the bone forming function of osteoblast cells. This may aid in the development of strategies for prevention and treatment of osteoporosis, a disease which is characterised by a net reduction in bone mass in postmenopausal woman. It is well established that estrogen and progesterone deficiencies are risk factors for osteoporosis. This suggests that steroid hormones have a direct effect on bone forming cells. Recently it was shown that

estrogen receptors are expressed in osteoblast cells. Our research has concentrated on the expression of progesterone receptors in osteoblast cell-lines. Using the sensitive Polymerase Chain Reaction and primers which flank the progesterone binding domain we detected progesterone receptor mRNA in a number of osteoblast cell-lines. In addition we examined immunostaining as an approach to visualise progesterone receptor (PR) protein in cells. Two osteoblast cell-lines showed specific staining for PR. The signal obtained when compared to that detected in PR positive MCF-7 cells was significantly lower though well above levels detected in the PR negative breast cancer cell-line MDA.MB.231. The finding that PR is expressed in several osteoblast like cell-lines suggests that progesterone acts directly on osteoblasts. Progesterone exposure may thereby modulate the physiological role of osteoblasts in bone mass maintenance.

GASTROENTEROLOGY

SERUM TUMOUR MARKERS IN OESOPHAGEAL CARCINOMA

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The value of serum tumour markers in diagnosis and prognosis of oesophageal carcinoma was assessed in an ongoing study. Serum levels of 6 different tumour markers - CEA, CA199, SCC, CA125, BHCG and ferritin - were assayed using an automated enzyme immunoassay system in 12 patients with oesophageal carcinoma confirmed by endoscopy. Patients had no evidence of metastatic disease. All patients subsequently underwent oesophagectomy.

CA125, BHCG and ferritin were unhelpful. One or more markers from a combination of CEA, CA199 and SCC were positive in 7 of 8 patients with lymph node involvement on histological examination (Stage IIb or above). All 3 of these markers were negative in 4 of 4 patients without lymph node involvement (Stage IIa or earlier), $p=0.01$, Fisher exact test. Mean survival to date following oesophagectomy is 7.2 months for patients with negative markers, and 3.7 months for patients with one or more positive markers ($p=0.048$). This combination of markers - CEA, CA199 and SCC - may be of value in pre-operative staging of oesophageal carcinoma, as serum levels appear to correlate with tumour burden.

MYOCARDIAL BRADYKININ IMPAIRS LOWER OESOPHAGEAL SPHINCTER FUNCTION

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Stimulation of myocardial vagal receptors has been demonstrated to impair lower oesophageal sphincter (LOS) function offering an explanation for the high incidence of gastro-oesophageal reflux in patients with coronary artery disease. The precise cause of receptor activation in this situation remains unclear. This study assesses if ischaemia directly evokes this reflex and if bradykinin, a substance produced in increased quantities by ischaemic myocardium, may stimulate these receptors. Thirteen adult mongrel dogs were studied under general anaesthesia. Group 1 ($n=5$) underwent 90 secs of myocardial ischaemia by occlusion of the LAD coronary artery. Group 2 ($n=8$) had a bradykinin patch ($100\mu\text{g/ml}$) applied to the epicardium. LOS tone, ECG and blood pressure were continuously

monitored. Results: Myocardial ischaemia in group 1 animals produced no significant alteration in any parameter. The application of a bradykinin patch in group 2 animals, however, produced a rapid fall in LOS tone [12.7(1.5) to 6.0(0.7), ($p < 0.005$)] associated with a fall in blood pressure [95(5) to 86(5), ($p < 0.01$)]. Endogenous bradykinin produced by the ischaemic myocardium may be the cause of vagal receptor stimulation leading to impaired LOS function.

HELICOBACTER PYLORI: DENSITY OF ANTRAL ORGANISM AND SERUM IgG ANTIBODY LEVELS

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The relationship between the density of antral Hp and the systemic immunological sensitisation and production (s-IgG antibodies) to Hp was studied in 94 patients presenting for endoscopy to University College Hospital, Galway, for investigation of upper gastrointestinal symptoms. There were 46 males and 48 females with age range 19 - 86 years, mean age 56 years. Hp colonisation of the antrum was identified by histology and/or culture. 56/94 (59.6%) were found to have antral Hp. Serum IgG antibody levels were assayed using ELISA test (Biometra Germany). The density of antral Hp colonisation was coded on 5 um H & E sections and graded into (0 - 2), 0 = no bacteria seen, 1 = few bacteria seen, and 2 = abundant bacteria seen on antral sections. There were 35 patients with grade 0, 31 with grade 1, and 28 with grade 2 density. The results were analysed using One-Way Analysis of Variance. There were increasing levels of IgG antibody to Hp with increasing grades of bacterial density.

Conclusion : The density of antral Hp colonisation is positively correlated with the serum IgG antibody levels to Hp infection.

HELICOBACTER PYLORI SERUM IgG ANTIBODY LEVEL MIRRORS SEVERITY OF ANTRAL INFLAMMATION.

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The relationship between the degree of antral inflammation and the systemic immunological sensitisation and production (s-IgG antibodies) to Hp was studied in 94 patients presenting for endoscopy to University College Hospital, Galway, for investigation of upper gastrointestinal symptoms. There were 46 males and 48 females with age range 19 - 86 years, mean age 56 years. Hp colonisation of the antrum was identified by histology and/or culture. 56/94 (59.6%) were found to have antral Hp. Serum IgG antibody levels were assayed using ELISA test (Biometra Germany). The severity of antral inflammation was coded on 5 um H & E sections and graded into (0 - 3), 0 = no inflammation, 1 = mild inflammation, 2 = moderate inflammation, and 3 = severe inflammation. There were 25 patients with grade 0, 28 with grade 1, 31 with grade 2 and 10 with grade 3 inflammation. The results were analysed using One-Way Analysis of Variance. There were increasing levels of IgG antibody to Hp with increasing grades of inflammation.

Conclusion : The degree of Hp antral inflammation is positively correlated with the serum IgG antibody levels to Hp colonisation.

THE DEVELOPMENT OF SIMPLE CLINICAL TESTS FOR MONITORING MENTAL STATUS IN METABOLIC DISORDERS

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Methods of monitoring changes in mental status in metabolic disorders such as drawing five pointed stars are difficult to calibrate and subject to differences in observer interpretation. In order to fill this gap three simple forms have been designed which can be applied repeatedly at the bedside to assess alterations in cognitive function and graphic dexterity. The three tests take 4 minutes to complete and in index score related to speed and accuracy is derived for each test (deleting P, joining numbers and trail marking). Alterations in index scores on serial application of the tests demonstrate improvement or deterioration. Preliminary experience of the tests has been obtained in endoscopy subjects (pre and post sedation), controls and in the metabolic disorders hepatic disease and respiratory failure. Deterioration in all three tests occurred after sedation and with progression of liver failure, whereas improvement in scores were noted in patients with respiratory failure as the arterial blood gases normalised. Further studies are being undertaken to assess their efficacy in wider clinical practice.

LEWIS ANTIGEN AND HLA STATUS IN COELIAC DISEASE IN THE WEST OF IRELAND

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Recently, blood group non secretion, has been linked with susceptibility to Coeliac Disease. Our aim was to investigate further, this possibility, and to correlate HLA Antigens with secretor status. By determining red cell Lewis (Le) antigen phenotype, which correlates with secretor status, non secretor prevalence was determined in coeliac patients and disease free controls from the West of Ireland. Class I HLA antigens were determined in both groups. Determination of Class II HLA antigens was performed on the coeliac population only. Six (9%) of 64 patients with coeliac disease and 1 (2%) of 43 controls had the recessive Lewis phenotype (Le a, b-). These patients were assigned to a separate group as their secretor status cannot be determined. Non secretor prevalence was 38% (22/58) among the remaining coeliacs, 28% (12/42) among controls. No difference was found amongst non secretors with regard to HLA status, being consistent with the Classical Extended Coeliac Phenotype. Our study confirms an increased prevalence of non secretors and recessive phenotypes in the coeliac population which is not related to the HLA antigens.

IMAGE QUALITY DIFFERENCES BETWEEN FIBRE-OPTIC AND VIDEO FLEXIBLE ENDOSCOPES

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(i) Purpose of Study: To determine the differences for resolving power and colour rendition between fibre-optic and video endoscopes quantitatively.

(ii) Methods: Resolving power for both types of endoscopes was

measured while the video endoscopes were measured for modulation transfer functions (MTF). Transmission characteristics of a fibre-optic endoscope were measured as was the colour rendition of an equivalent video endoscope.

(iii) Summary of Results: Video endoscope resolution limit values were higher than for fibre-optic endoscopes. The MTF plots indicated a boost to the systems resolving power during electronic processing. The transmission characteristics of the fibre-optic endoscope show that its colour rendition is consistent but not ideal. The rendition of video endoscopes was found to be dependent on a number of factors which vary with time and usage of the equipment.

(iv) Conclusions: The video endoscopes are better at resolving fine detail in an image and the boost to the resolving power identified by the MTF is indicative of edge enhancement which the eye finds more subjectively pleasing. The enhancement identified is compatible with the size of small lesions. The colour rendition of video and fibre-optic endoscopes are different with video endoscopes. To maintain consistency, a routine quality assurance programme needs to be implemented.

ENDOSCOPIC PALLIATION OF OESOPHAGEAL CANCER: EXPERIENCE WITH A NOVEL EXPANDABLE (MICROINVASIVE) METAL PROSTHESIS

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The optimal palliation of malignant dysphagia has not been established. Furthermore, the role of expandable metal stents remains unclear. We report our preliminary results using a novel metal mesh prosthesis.

Patients and methods: Fourteen patients (30-85yrs, male:female 6:6) with inoperable oesophageal cancer had a mean dysphagia score of 2.5 (Mellor & Pinkas). The lesions ranged from 4-10 cms in length and tumour margins ranged from 19 cms (proximal) to below the GOJ. Seven patients had prior unsuccessful attempts at laser palliation. An expandable mesh stent (Microvasive Ultraflex, 7-17cms in length) was inserted across the lesion endoscopically under fluoroscopic control without complication.

Results: Within 48 hours the stent was fully expanded and all patients were swallowing normally. Chest pain requiring NSAD or opiate occurred in 4 patients while 4 patients had severe reflux symptoms responsive to omeprazole. After short term follow-up (median 10 weeks, range 2-22), 9 patients (75%) had normal swallowing score (0) while 3 patients had recurrent dysphagia from tumour ingrowth which responded to laser therapy.

Conclusion: Our preliminary results suggest that the microinvasive expandable metal prosthesis provides rapid and effective palliation for malignant dysphagia although tumour ingrowth may necessitate adjuvant therapy.

HLA-G POLYMORPHISM IN HEREDITARY HAEMOCHROMATOSIS

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It is well established that the hereditary haemochromatosis (HH) gene is closely linked to the HLA-A but studies to date using probes for HLA-A, B, C and E have failed to show any characteristic restriction fragment length polymorphism (RFLP) in HH. There are at least 18 genes in the MHC Class I region including the HLA-G, one or more of which could be adjacent to the HH gene. The aim of this

study was to analyse RFLP pattern in HH using the HLA-G specific probe 23.2d.

Patients and Methods: HH was diagnosed using the standard diagnostic criteria. Ten HLA typed HH patients and 10 HLA typed controls (normal iron studies) were studied. DNA was extracted, digested with restriction enzymes, electrophoresed, Southern blotted and hybridised with 23.2d. Restriction fragments were detected by autoradiography at -80°C.

Results: The 23.2d probe detected 6 ECORI fragments in the controls. The smallest of the 6 fragments was absent in 9 of the 10 HH patients.

Conclusions: HLA-G probe 23.2d detects an ECORI fragment which is absent in majority of the HH patients. Since HLA-G is expressed only on extraembryonic trophoblasts it is unlikely to be implicated in the pathogenesis of HH. Our results, however suggest that the HH gene is located either between HLA-A and G or is telomeric to the HLA-G locus.

ENDOSCOPIC BALLOON SPHINCTEROPLASTY (EBS) FOR BILE DUCT STONES: EFFICACY AND FOLLOW-UP IN THE FIRST 90 PATIENTS

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Since papillotomy accounts for the major morbidity/mortality associated with ERCP, we have previously proposed sphincteroplasty (EBS) as a safe and effective alternative for small to medium sized bile duct (BD) stones (<20mm). We now report the efficacy and complications of EBS in a series of 90 patients.

Patients and Methods: EBS was considered for BD stones up to 20mm in 90 patients, 24 post cholecystectomy, (mean age 64, range 19-89, 66 female, 24 male), of whom 17 were under 40 yrs. Stone size ranged from 3-20mm (mean 10mm, max 8). EBS was performed using a balloon tipped catheter (Microvasive) over a 0.21 guidewire inflated across the papilla (60secs x 2) to a diameter of 10mm allowing access for stone retrieval. Median follow-up was 10 months (range 0.5-20).

Results: Using EBS alone, the bile duct was cleared in 70 patients (76%). Mechanical lithotripsy was used to remove large stones (15-20mm) in 13 (15%). Of the 20 EBS "failures" (24%) papillotomy was required to clear the duct in 7 (9%). A pigtail stent was inserted in 13 (15%) to maintain biliary drainage a) as a temporary measure because of doubt about residual stones (n=7, 9%), or b) as a definitive measure in elderly high risk patients with multiple stones >15mm (n=6, 6.5%). ERCP was repeated in 14 (16%) for stent removal ± replacement or repeat EBS-duct clearance (n=4). There was no papillary haemorrhage, while uncomplicated pancreatitis was observed in 4 patients (5%).

Conclusion: EBS is a safe and effective sphincter preservation technique for the management of BD stones up to 20mm in size, which significantly reduces the need for papillotomy.

HELICOBACTER PYLORI AND GASTRIC CANCER: REAL OR APPARENT ASSOCIATION?

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Accumulating epidemiological evidence based on serological studies suggests that *Helicobacter pylori* (HP) colonisation predisposes

to the development of gastric cancer. Given the high prevalence of HP in the normal middle-aged to elderly population, we assessed HP colonisation in patients with gastric cancer.

Patients and Methods: Three groups of patients were included in this study, a) gastric carcinoma $n = 128$, mean age 67, male/female 74/54, b) benign gastric ulceration (GU), $n = 131$, mean age 64 male/female 63/68 and c) normal/gastritis on upper GI endoscopy $n = 113$, mean age 59 male/female 54/59. HP status was determined from histopathology by 2 "blind" observers (intraobserver and inter-observer error <5%), * $p < 0.05$.

Results

	Carcinoma	GU	Normal/Gastritis
Total no.	128	131	113
HP+	46%*	68%	60%
HP+ male	43%*	72%	57%
HP+ female	50%	63%	60%

Conclusion: HP colonisation is less common in gastric cancer, particularly in males, than suggested from serological studies.

DOES CLOSTRIDIUM DIFFICILE PRECIPITATE OR EXACERBATE INFLAMMATORY BOWEL DISEASE?

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It has been hypothesised that an infectious agent may either precipitate or exacerbate inflammatory bowel disease (IBD). The aim of this study was to assess the potential role of Clostridium Difficile (C. Diff) infection/exotoxin production in IBD.

Patients and Methods. Over an 8 month period specimens from 748 patients with liquid diarrhoea were assessed for C. Diff. In addition to C. Diff culture, stool specimens were assessed for Toxin A by immunoassay and Toxin 9 by cytotoxicity assay.

Results: Of the 48 patients who were C. Diff culture \pm toxin positive, 10 (21%) had known IBD. Prior antibiotic ingestion was noted in 5/10 (50%) of IBD compared to 29/38 (76%) of non-IBD patients. Colonoscopy in the IBD group revealed moderate to severe colitis with pseudomembranous colitis (PMC) in only 1 patient. Histopathology showed features consistent with the endoscopic findings. Colonoscopy in 6 of the non-IBD group was normal or showed mild colitis but there was biopsy evidence of PMC in 3 patients.

Conclusion: 1) C. Diff may contribute to the morbidity of IBD even in the absence of prior antibiotic exposure, 2) The diagnosis of C. Diff should be based primarily on microbiological rather than colonoscopic / histopathological criteria.

PROGNOSTIC SIGNIFICANCE OF RETINOBLASTOMA GENE PRODUCT EXPRESSION IN COLORECTAL CANCER

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Loss or inactivation of the retinoblastoma (Rb) gene has been demonstrated in several non-GI human malignancies. Recently, altered Rb gene expression has been reported in colorectal cancer

(CRC) but the prognostic significance of this finding has not been determined. The aim of this study therefore was to correlate Rb gene product expression with longterm survival in CRC

Patients and Methods: CRC samples from 76 patients collected over 3 years (1984-86) were analysed for Rb gene product nuclear protein expression by immunohistochemistry using the monoclonal antibody PMG3.245. Unlabelled CRC tissue and bladder cancer tissue were used as negative and positive controls, respectively. Prognostic significance was established from Kaplan-Meier curves which were generated from actuarial disease free survival, with difference in survival being compared by means of logrank analysis.

Results: Positive Rb expression of >80% in tumour cells was observed in 33/76 (44%) patients. Heterogenous Rb expression (20-80%) was seen in 39/76 (51%) patients while no Rb expression occurred in the remaining 4/76 (5%) Rb expression of >80% correlated closely with poor survival ($p = 0.03$)

Conclusion: These findings suggest that the Rb gene is of prognostic significance in CRC and has an oncogenic-like function, in contrast to its reported tumour suppression activity in other human malignancies.

MICROALBUMINURIA CORRELATES WITH TNF IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: We have previously demonstrated microalbuminuria in patients with active inflammatory bowel disease (IBD). It is shown in animal studies that proteinuria may result from cytokines induced microvascular damage, as cytokines may disrupt sulphated glycosaminoglycan (GAGs) function.

Objective: The aim of this study was to determine whether TNF and IL-6 are important in the pathogenesis of microalbuminuria in patients with IBD.

Methods: We measured serum TNF, IL-6, ESR, and C-reactive protein (CRP), and microalbuminuria in 48 IBD patients. **Results:** Microalbuminuria levels were higher in IBD patients compared to healthy controls (222 ± 24 vs 28 ± 4 ; $p < 0.001$). Significantly higher levels of microalbuminuria were detected in patients with active IBD compared to those in remission (299 ± 36 vs 118 ± 12 , $p < 0.005$). Serum TNF was higher in IBD patients versus controls (16.04 ± 2.35 vs 6.62 ± 1.3 ; $p < 0.01$) and in those with active vs inactive IBD (20.1 ± 1.9 vs 13.0 ± 2.04 ; $p = 0.056$). Microalbuminuria strongly correlated with TNF ($r = 0.60$, $p < 0.01$), ESR (0.61 , $p < 0.02$), CRP ($r = 0.93$, $p < 0.01$) and HBI ($r = 0.82$, $p < 0.001$). TNF also significantly correlated with CRP ($r = 0.54$, $p < 0.01$). However microalbuminuria did not correlate with serum IL-6.

Conclusion: The significant correlation of microalbuminuria with TNF suggests that TNF may be important in the pathogenesis of microalbuminuria in IBD patients possibly through TNF induced disruption of GAGs in the glomerular basement membrane.

MICROALBUMINURIA CORRELATES WITH INTESTINAL HISTOPATHOLOGICAL GRADING IN IBD PATIENTS

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Introduction: We have previously demonstrated microalbuminuria

in IBD patients and correlated strongly with markers of clinical and laboratory disease activity.

Objective: The aim of this study was to determine whether microalbuminuria accurately reflects intestinal inflammation by correlating it with intestinal inflammation using a standard histopathological grading system in patients with IBD.

Methods: We recruited 42 patients with IBD who had undergone endoscopic examination of the colon for the assessment of severity and extent of the disease. Each patient's colonic biopsy specimens were scored blindly by a histopathologist and a composite score was compiled. We also measured microalbuminuria, ESR, and CRP in the same patients.

Results: Patients with active IBD had higher levels of microalbuminuria compared to those patients in remission (230 ± 187 vs 117 ± 90 , mean \pm SD, $p < 0.02$). Microalbuminuria levels were higher in patients with extensive IBD compared to those patients with rectosigmoid disease; (321 ± 176 vs 121 ± 95 , $p < 0.001$). Microalbuminuria correlated with intestinal histopathological scoring in IBD patients with rectosigmoid disease ($r = 0.77$, $p < 0.001$), and extensive disease ($r = 0.71$, $p < 0.01$). The standard histopathological grading system also correlated with the clinical disease activity ($r = 0.64$, $p < 0.005$), and CRP ($r = 0.62$, $p < 0.02$), however it did not correlate with ESR.

Conclusion: The strong correlation of microalbuminuria with a standard intestinal histopathological grading system suggests that microalbuminuria accurately reflects the severity of intestinal inflammation in IBD patients.

CELLULAR AND PHARMACOLOGICAL CONTROL OF SEROSAL MEMBRANE POTASSIUM CONDUCTANCE OF THE HUMAN COLONIC EPITHELIUM

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We had previously documented Na^+ K^+ and Cl^- channels in the mucosal membrane of the human colonic epithelial cells and on the serosal membrane a $\text{Na}^+:\text{K}^+:\text{Cl}^-$ cotransporter and a $\text{Cl}^-:\text{HCO}_3^-$ exchanger. In these studies we examined the serosal membrane K^+ conductance and its cellular and pharmacological control.

Isolated human colonic epithelium was mounted in an Ussing chamber and the spontaneous trans-membrane voltage clamped to 0mV by a short circuit current (SCC). By permeabilising the mucosal membrane with the ionophore nystatin and by creating a mucosa to serosa K^+ gradient, the serosal K^+ conductance was studied.

The dominant K^+ channel serosally was inhibited by tolbutamide, by increasing intracellular Ca^{2+} or by decreasing intracellular pH. It was up-regulated by the K^+ channel opener diazoxide, by decreasing intracellular ATP levels and by aldosterone. Aldosterone produced a biphasic increase in SCC, the immediate portion of which was inhibited by inhibiting $\text{Na}^+:\text{H}^+$ exchange with amiloride.

This K^+ channel plays a vital role in Na^+ transfer across the cell, as has been seen in other Na^+ absorptive epithelia. Therefore an understanding of its regulation is important if fluid and electrolyte transfer across the human colon is to be manipulated pharmacologically.

ELEVATED URINARY NITRITE, A MARKER OF NITRIC OXIDE METABOLISM, IN ACTIVE INFLAMMATORY BOWEL DISEASE

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In the gut, nitric oxide (NO) is a neurotransmitter, it regulates splanchnic blood flow and modulates intestinal permeability. NO production is enhanced by proinflammatory cytokines (eg. IFN- γ , TNF, IL-1) and endotoxin. In inflammatory bowel disease (IBD), NO may contribute to disease pathogenesis as a proinflammatory free radical, by its neurotransmitter effects and by direct relaxation of colonic smooth muscle. This study investigated the value of measuring urinary nitrite in IBD patients as a marker of disease activity.

Methods: Urinary Nitrite (uNO_2^-), a stable end product of NO, was measured using a microplate assay method. 24 hour urine collections were performed in 46 patients with IBD. The Griess reagent was added (1% sulphanimide, 0.1% naphthylethylene diamine dihydrochloride, 2.5% phosphoric acid) to urine samples and standards. Absorbance was determined at 540nm by spectrophotometry. Disease activity was measured using the Simple Index of Harvey Bradshaw, ESR and C-reactive protein (CRP).

Results: 27/32 patients with active IBD vs. 1/14 with inactive IBD, $p < 0.01$; (Chi Square), had detectable uNO_2^- ; sensitivity 84%, specificity 93%. Levels of NO_2^- were significantly higher in those with active vs. inactive IBD; median (range); 35 (0-250) vs. 0 (0-2) $\mu\text{mol/l}$, $p < 0.05$. Patients with detectable uNO_2^- had higher CRP than those without: mean/sd CRP, 32/49 vs 5.7/9.2 mg/l , $p < 0.05$.

Conclusion: Urinary nitrite is a sensitive and specific marker of active IBD.

ELEVATED VCAM-1 IN PATIENTS WITH ACTIVE INFLAMMATORY BOWEL DISEASE

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VCAM-1 (vascular cell adhesion molecule-1) is a member of the immunoglobulin superfamily of adhesion molecules and is expressed on cytokine activated endothelium (IL-1, TNF, IL4) and on follicular dendritic cells. VCAM-1 is responsible for adhesion of memory T lymphocytes and CD8 lymphocytes to endothelium through their VLA4 (very late antigen-4) ligand. The aim of this study was to determine whether soluble VCAM-1 is elevated in patients with active IBD.

Methods: Serum VCAM-1 levels were determined by ELISA in 15 patients with active IBD. In addition, follow up VCAM-1 levels were repeated after at least one month at which time patients had either significantly improved or gone into remission. Serum VCAM-1 levels were also measured in 14 healthy volunteers. Disease activity was measured in IBD patients by the Simple Index of Harvey Bradshaw (HBI), ESR and C-reactive protein.

Results: VCAM-1 levels were significantly higher in patients with active IBD compared to controls; mean/sd VCAM-1; 1080/1129 vs. 320/102 ng/ml , $p < 0.05$. VCAM-1 levels fell in IBD patients when their disease became less active; VCAM-1; 1326/1213 vs 468/287 ng/ml , $p < 0.001$.

Conclusion: Serum VCAM-1 is elevated in patients with active IBD and levels fall as patients improve. VCAM-1 may be important in lymphocyte recruitment into areas of the bowel affected by IBD.

MANIFESTATIONS OF ASYMPTOMATIC GASTRO- OESOPHAGEAL REFLUX DISEASE

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Increased distal oesophageal acid exposure is associated with the development of symptoms and complications of reflux disease, such as heartburn, oesophagitis and stricture formation. The incidence of asymptomatic gastro-oesophageal reflux disease is unknown. The prevalence of extra-oesophageal, atypical manifestations of gastro-oesophageal reflux disease is increasingly appreciated. Often reflux symptoms are absent.

Three groups of patients were studied. Ten normal controls, 10 patients with symptoms of gastro-oesophageal reflux and 10 patients with atypical symptoms of reflux.

Results

	Control	Refluxers	Atypical
Distal acid Exposure	2*	9	5.9*
Symptom Score	4	22*	7**

*p < 0.05 compared with controls Wilcoxon Rank Sum Test

**p < 0.01 compared with refluxers

Eight of ten patients with atypical presentation denied any symptoms of reflux. This reflux migrated high in the oesophagus leading to abnormal proximal oesophageal acid exposure. This increases the potential for the development of respiratory and otolaryngological manifestations of reflux.

ASYMPTOMATIC GASTRODUODENAL PATHOLOGY

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Helicobacter pylori is associated with a wide range of symptomatic upper gastrointestinal disease. However, the prevalence of pathology in an asymptomatic *H. pylori* positive population is unknown. The aim of this study was to assess the incidence of asymptomatic gastroduodenal pathology in *H. pylori* positive subjects. Serum from 650 Irish blood donors was obtained and *H. pylori* seropositivity was determined. Seropositive patients were interviewed, a formal symptom score was carried out, and endoscopy was offered. 267 of 650 subjects (41%) were seropositive. Seropositivity increased with increasing age and decreasing social status. Twenty three seropositive subjects have been interviewed to date. Sixteen (69%) had first degree relatives with peptic ulcer disease. Three subjects were excluded; two were symptomatic and one had previous surgery for peptic ulceration. Endoscopy was performed in 20 asymptomatic individuals and in all antral biopsies confirmed the presence of *H. pylori*. At endoscopy, antral erosions (N=6), duodenal erosions (N=3), antral and duodenal erosions (N=3), macroscopic antral gastritis (N=4) were found and only 4 subjects had a normal endoscopy. This study demonstrates that the presence of *H. pylori* in asymptomatic individuals is associated with a wide range of gastroduodenal pathology.

DECISION ORIENTATION - A REPRODUCIBLE APPROACH TO THE PATIENT RECORD

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Many of the observations for the advances of medicine are contained in the routine patient record. Much of the observations are difficult of access and of interrelation. Use of a proforma for data considerably reduces observer error in diagnosis. A similar approach might be used for patient management. The structuring feature chosen was the clinical decision to define the pathological process, to order a test or to change treatment. It was applied in the first instance to the decision to treat acute cholecystitis conservatively or surgically. It was tested originally on 8 patients. The accumulating clinical evidence, the decisions and their causes and outcomes were logged, totalling 400 hours observation, 820 clinical data, 33 test, and 48 treatment decisions. The record was neat, compact and rapidly readable. It is reproducible between observers. It was extended to include patients presenting with jaundice (24 patients, 9 diseases, 450 decisions), and to other disease presentations. It enabled correlation of the clinical and the test data with the decisions and outcomes, definition of the decisional significance of data, tests and treatments, and rapid access to diagnostic and clinical management data. The detailed results will be presented.

GENERAL PRACTICE

EVALUATION OF MEDICAL CONTENT IN BEST-SELLING WOMEN'S MAGAZINES

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This study evaluates the medical content in bestselling women's magazines. Over a 12-week period, 90 best-selling women's magazines (6 weeklies and 6 monthlies) were prospectively analysed for medical content. 638 articles and 286 readers' letters on medical issues were identified and categorised. They occupied 625.5 of 6,528 pages (9.6%). Articles most commonly addressed obstetrical and gynaecological issues (24.5%). Other common categories included: diet/nutrition (12.4%), mental health (8.3%), skin disease (8.2%), cardiovascular (6.6%), neurological problems (6.1%) and eating disorders (4.5%). 67 articles were case reports (10.5%) and 20 were promotional (3.1%). A doctor, institution or medical journal was cited in 181 articles (28.4%). Helplines/addresses were provided in 128 (20.1%). 78.7% of readers' letters on medical issues were answered by doctors. Cigarette-related problems were highlighted in 24 articles and letters (3.8%) and cigarette advertisements occupied 38 pages (0.6%). No article or letter reply was considered to offer misleading medical information or advice. Promotional articles were clearly identified. In conclusion, women's magazines provide an important forum for medical education and health promotion. Considering the strong editorial interest in medical issues, cigarette advertisements remain an incongruous and unacceptable feature of women's magazines.

PREHOSPITAL MANAGEMENT OF AMI IN IRISH GENERAL PRACTICE

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Acute myocardial infarction (AMI) is a common and serious

event within the community; its management is evolving rapidly with an increasing emphasis on the pre-hospital phase both in terms of resuscitation and thrombolysis. Little Irish data is available regarding the primary care management of AMI. The objective of this study, which was funded by Irish Heart Foundation and the Irish College of General Practitioners (ICGP), was to provide survey information on the current prehospital management of suspected AMI in both rural and urban Ireland. Specific outcome measures included incidence of suspected and proven AMI per GP, delay times, management (eg aspirin/analgesia), eligibility for thrombolysis and complications.

This prospective case finding study was conducted from 1.2.93 to 31.1.94. GP's were recruited through their ICGP faculties in Donegal (73) and south Dublin (53). Each participating GP was provided with an explanatory booklet and report form. These were completed for all cases of suspected AMI seen during the year. A six week follow-up form was also completed. To date more than 200 patients have been entered into the study. Analysis of data will be completed by March and available for presentation.

This data will help to clarify the prehospital management of AMI and contribute to the current debate regarding integration of acute cardiac services in Ireland.

GENETICS

CONGENITAL HAND DEFORMITIES IN THE WEST OF IRELAND

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31 Cases with congenital hand deformities presented to the Department of Plastic Surgery in University College Hospital, Galway between September 1989 and September 1993.

They were classified into the following groups:

- 8 Cases of Syndactyly
- 6 Cases of Polydactyly
- 4 Cases of Clinodactyly
- 4 Cases of Trigger Digits
- 3 Cases of Hypoplastic Digits (one of them with absent phalanges)
- 3 Cases of Camptodactyly
- 1 Case of Radial Deficiency
- 1 Case of Hypoplastic Thumb
- 1 Case of Bilateral Clasped Thumb

Some of these Cases and their x-rays will be discussed.

GENOMIC TYPING OF *ACINETOBACTER SPP.* USING DNA AMPLIFICATION FINGERPRINTING

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Acinetobacter are important emerging nosocomial pathogens. Thirteen random *Acinetobacter spp.* from intensive care patients were isolated. These were initially characterised using the API-20 NE biotyping system and antibiogram analysis. A DNA based method to characterise these *Acinetobacter spp.* isolates is described, which utilises a modified polymerase chain reaction (PCR), capable of generating genomic fingerprints, known as DNA Amplification Fingerprinting (DAF). Purified total genomic DNA of cultured clinical isolates of *Acinetobacter spp.* were subjected to DAF using

the M13 universal sequencing primer. The polymorphic DNA bands produced were visualised after agarose gel electrophoresis and ethidium bromide staining. Results demonstrated that six of the thirteen clinical isolates represented one group which displayed identical fingerprint patterns, as did a second group of two isolates, the remaining four isolates were all unique. Compared with other methods of identification using DNA, the DAF technique offers the advantages of simplicity, rapidity, reproducibility and could prove to be a method which can specifically type *Acinetobacter spp.* for epidemiological purposes.

Reference

Graser, Y. et al. *J. Clin. Micro.* 1993; 31: 2417-2420.

DNA AMPLIFICATION FINGERPRINTING OF A GROUP OF ENTEROTOXIGENIC *ESCHERICHIA COLI*

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The importance of Enterotoxigenic *Escherichia coli* (ETEC) as a microbial cause of diarrhea has been noted. To fully understand ETEC epidemiology, studies need to be carried out. However current epidemiological methods depend on the use of bioassays which are prone to variable phenotypic expression and in addition can only be offered in specialised centres. A rapid, sensitive and specific DNA typing method based on a modified Polymerase Chain Reaction (PCR) assay has been described (and references therein). Using a randomly selected primer, DNA Amplification Fingerprinting (DAF) can distinguish different organisms by producing simple fingerprint patterns. These fingerprints were generated for control ETEC and a number of clinical isolates obtained. Results demonstrated that ETEC could be divided into two groups on the basis of their fingerprints: genetically similar or distinctly polymorphic. The genotype method described may have potential as a simple, rapid and reproducible means of typing ETEC for epidemiological evaluation.

Reference

Grayer et al. Epidemiological study of an *Acinetobacter baumannii* outbreak by using Polymerase Chain Reaction Fingerprinting. *J. Clin. Micro.* 1993; 31: 2417-2420.

GERONTOLOGY

VITAMIN D SUPPLEMENTATION: REVIEW OF SAFETY AND EFFECTIVENESS OF DIFFERENT REGIMES

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Vitamin D deficiency and associated bone disease is common in elderly people especially in countries where effective sunlight or exposure to sunlight is limited. Two regimes for Vitamin D supplementation i.e. low dose daily oral supplementation and intermittent high dose administration, were examined with regard to their relative safety and effectiveness. 12 papers reporting studies in 489 elderly subjects were reviewed. The majority of studies were performed in subjects on oral low dose Vitamin D supplementation (n=406). The average maximum concentration of 25(OH)D in serum varied from 45 to 91 nmol/L on low dose continuous supplementation compared to 30 to 87 nmol/l following high dose vitamin D administration. These mean values fall within the physiological range for young

adults. Hypercalcaemia occurred in only 3 subjects and was associated with a predisposing cause in 2 of 3 subjects. We suggest that low dose continuous supplementation is the regime of choice, but high dose intermittent supplementation (2.5 mg Vitamin D six-monthly) may be a suitable regime for institutionalised elderly subjects.

DECISION-MAKING AND RESUSCITATION STATUS OF MEDICAL PATIENTS

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Cardiopulmonary resuscitation (CPR) has become a standard medical intervention for all hospital in-patients unless specified by a written 'Do not resuscitate' order. There is a sub-group of patients for whom CPR is inappropriate so medical and nursing staff are increasingly reflecting on the "resuscitation status" of individual patients. Few guidelines exist however to assist in this decision making process, with the result that no decision may be reached, or it may be improperly communicated, or left to the most junior staff.

We studied 50 acute admissions to acute medical and geriatric medical departments (mean age 78) in two Teaching Hospitals and compared the assessment for fitness for CPR by i) the admitting senior house officer, ii) the consultant physician and iii) the team nurse on the ward, and whether these views are consistent with regard to individual patients. Decision for resuscitation revealed incomplete agreement in 11 out of 50 cases (22%). Consultant physicians were more likely to opt for CPR (74%) than SHO's (64%) or nurses (66%). Within this decision, there were differences with regard to ventilation [Consultants 48%, SHO's 32% and nurses 34%], but similarity with regard to antibiotic usage [Consultants 88%, SHO's 92% and nurses 90%].

The BMA/Royal College of Nursing guidelines for resuscitation are useful but this study highlights the difficulty of decision-making, particularly with older patients with multiple pathology. We are currently correlating these findings with the patients' own preferences at the time of discharge.

DETECTION OF FUNCTIONAL DISABILITY IN OLDER PATIENTS IN THE ACUTE HOSPITAL

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Functional deficit (i.e. immobility, incontinence), which often represents underlying disease processes, are present in 50% of 75 year olds and 75% of 85 year olds (UK National Survey of Disability, 1990).

Despite a rapidly growing ageing population in Ireland, there is evidence that disability may not be detected in older people in the community⁽¹⁾. Do medical and nursing staff detect functional disability in older patients in the hospital setting?

We assessed detection of disability by doctors and nurses in 52 referrals to an acute geriatric medical service from departments of medicine, surgery, orthopaedics and urology. This was compared with a recognized index of function, the Barthel Activities of Daily Living Index⁽²⁾. We found that the medical staff detected 41 out of 384 functional deficits (11%) and nurses detected 211 out of 384 functional deficits (55%). The finding suggests that a large reservoir of undetected functional deficits is present in older patients in the

acute hospital setting, and in some cases corresponding undetected disease processes. The higher awareness of nursing staff of functional status may be as a result of more structured assessment or different training. Training in detection of functional disability should be incorporated into undergraduate and post-graduate medical education.

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HAEMATOLOGY

THE PHENOMENON OF DONOR LEUKAEMIA FOLLOWING BONE MARROW TRANSPLANTATION

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While Bone Marrow Transplantation is a successful therapy for a variety of haematological malignancies, the problem of leukaemia relapse remains. Leukaemic relapse normally occurs due to reemergence of leukaemic recipient cells. However there have been rare reports of leukaemia relapse occurring in donor cells. We wish to report on 4 cases of leukaemic transformation of donor cells which we have documented through the use of the polymerase chain reaction (PCR). Two cases involved leukaemic transformation in patients transplanted for Severe Aplastic Anaemia. In both cases leukaemic transformation occurred in the first year post transplant. PCR of short tandem repeat sequences (STRs) indicated that the leukaemic clone had arisen in donor haemopoietic cells. One patient had a 9;11 translocation which is diagnostic of Acute Myeloid Leukaemia (AML) FAB type M4 in his donor cells while the second patient developed an undifferentiated leukaemia. We also confirmed a previously reported case of leukaemic transformation in a patient transplanted for Chronic Myeloid Leukaemia using PCR of archival material. Recently a fourth case has been documented involving a patient with Acute Lymphoblastic Leukaemia. In addition a patient who was transplanted for AML 5 years ago recently developed a non random chromosomal abnormality (del 11q23) which was found to be in donor cells. A fuller understanding of this phenomenon may aid in the understanding of the etiology of leukaemia.

MOLECULAR MONITORING OF TRANSPLANTATION OF UV B IRRADIATED PRECURSORS IN RODENTS

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Graft versus host disease (GvHD) and graft rejection (GR) remain serious problems following allogeneic BMT. Previous work has indicated that ultraviolet B light (UV B) can inhibit lymphocyte reactivity and prevent GvHD following murine BMT. In order to assess the efficacy of UV B in abolishing GvHD while preserving stem cell viability, we have assessed the chimeric status of mice who have received UV B treated marrow in semi allogeneic or allogeneic BMTs. 12 STR markers were assessed for strain specific polymorphisms between three strains of mouse (CBA/J, Balb/c and C57/B16) in a PCR based assay. Initially mouse polymorphic markers were used to assess the degree of chimerism at a single timepoint

in Fl mice (CBA/J X Balb C) receiving marrow from CBA donors which had been treated with different doses of UV B (0240 J/m²). Mice receiving untreated marrow remained donor chimeras while mice receiving UV B treated marrow showed low levels of recipient cells. Subsequently recipients of allogeneic BMT were studied serially using tail vein samples. Engraftment occurred in two phases, an early phase in the second week post BMT and a later phase between weeks 4 and 5. In the UV B treated group, 75% of mice receiving 50J/m² were predominantly donor chimeras and showed biphasic engraftment. STR markers are useful in assessing chimerism post BMT in rodents in a serial fashion and initial results indicate that UV B treated marrow can reconstitute haemopoiesis in mismatched BMT.

SERUM IMMUNOREACTIVE INTERLEUKIN-6 (IL6) AND C REACTIVE PROTEIN (CRP) IN PLASMA CELL DYSCRASIA (PCD)

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IL6 is a growth factor for myeloma cells and an inducer of acute phase proteins in the liver. High levels of serum bioactive IL6 and CRP have been suggested as predictors of poor prognosis in PCD. However reported levels of immuno-reactive IL6 (irIL6) have varied considerably and the role of IL6 in the pathogenesis of PCD and its value as a prognostic marker is unclear. The aim of this study was to measure IL6 and CRP to further clarify their prognostic role.

Serum irIL6 was measured with a sensitive sandwich type ELISA assay (detection limit 2.5 pg). CRP was measured using a semiquantitative colorimetric assay. Patients with PCD were staged according to standard criteria.

irIL6 levels were elevated in 27% of patients with PCD. CRP was elevated in all patients with elevated irIL6 levels. There was a poor correlation between irIL6 levels and disease stage. We conclude that raised serum irIL6 levels are clearly detectable in PCD if a sensitive assay is used but there is little correlation between serum irIL6 levels and disease activity.

A COMPARISON OF A COMMERCIAL* REVERSE DOT BLOT SYSTEM TO STANDARD SEROLOGICAL, PCR SSP AND OLIGOTYPING FOR CLASS II HLA ANTIGEN DETERMINATION

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The development of molecular biological techniques such as RFLP, Oligotyping and PCR SSP has had a major role in improving the definition of antigens and their subtypes for HLA DR, DP and DQ markers in Matched Unrelated Donor (MUD) searches and subsequent transplantation procedures. These techniques to-date have been time consuming and labour intensive to perform. However their accuracy is unquestionable and to-date a comparison of standard serological techniques for HLA DR antigens with DNA techniques has shown a 10-20% discrepancy in antigen determination⁽¹⁾. In this laboratory we have noted a difficulty in defining some DRw6 subtypes, notably DRw14 with serological techniques.

With the development of new commercial kits to define DR, DP and DQ alleles it is hoped to reduce the need for serological determination and rely exclusively on DNA techniques to determine these Class II antigens. Furthermore it is now possible to perform

these assays in a 3-4 hour period which has the added advantage of making them available for emergency use, particularly in solid organ transplantation.

The presentation will compare the standard serological test with 3 molecular typing techniques and outline their efficiency and accuracy in defining HLA DR allelic markers in 200 randomly chosen samples.

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*Roche AmpliCor DRBI Generic Kit

MIXED CHIMERISM PREDICTS GRAFT REJECTION AFTER BONE MARROW TRANSPLANTATION

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Graft rejection (GR) can be a serious problem following bone marrow transplantation (BMT) for severe aplastic anaemia (SAA). Early detection of GR may allow prior clinical intervention. We have investigated the detection of re-emerging cells post BMT or mixed haemopoietic chimerism (MC) as a prognostic indicator of rejection. 70 recipients of BMT for SAA have been studied from 13 participating centres as part of the European Bone Marrow Transplant Working Party on Severe Aplastic Anaemia. Serial monitoring is performed using the polymerase chain reaction (PCR). PCR of short tandem repeat sequences (STRs) allows the detection of MC. Patients have been monitored as early as day 17 and as late as day 4987 post BMT. 35 patients showed complete donor chimerism at all times post BMT and 1/35 rejected their graft. Transient MC was seen in 15 patients with no instances of graft rejection. Recipient cells persisted in 20 patients beyond 100 days post BMT. 7 patients showed levels of recipient cells less than 10% with a follow up of 1-5 years. All these patients are alive and well. 13 patients showed evidence of recipient cells at higher levels (15-80%) and 10/13 rejected their graft. In 5 of these patients elevations in recipient cells and subsequent GR occurred while these patients were being taken off cyclosporin therapy. All information was provided to referring physicians and was used in some instances to aid clinical management. Thus elevated levels of recipient cells post BMT were predictive of GR in patients transplanted for SAA.

IMMUNOLOGY

HEREDITARY TERMINAL COMPLEMENT DEFICIENCY AND RECURRENT MENINGOCOCCAL INFECTION

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Hereditary deficiency of any of the terminal complement components predisposes to recurrent meningococcal infection. The occurrence of two episodes of meningococcal infection each in two brothers of an Irish family prompted investigation of the family for terminal complement deficiency. A novel assay was developed to screen for deficiency of C5, C6, C7 and C8 and was used to investigate this family. The two affected brothers were found to be completely deficient in C7, while the remaining sibling and both parents had detectable but reduced serum levels of C7. C7 M/N protein polymorphism allotyping was carried out to investigate the segregation of the deficiency gene in this family and showed that the

unaffected sibling is a carrier of the deficiency gene. Complement deficiency states may be more prevalent in Ireland than is presently thought. Screening for terminal complement deficiency should be carried out in any individual suffering meningococcal infection over 10 years of age, suffering recurrent infection, infection with an organism of unusual serogroup or whose family are affected by recurrent meningococcal infection. Detection of the carrier state in the unaffected sibling does not enable informed genetic counselling to be given.

MCWE - A NOVEL IMMUNE STIMULANT IN BREAST CARCINOMA

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

RAG LOCUS mRNA IN HUMAN GUT: EVIDENCE OF EXTRATHYMIC T CELL DIFFERENTIATION

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Animal studies have suggested that, contrary to immunological dogma, T cells do not mature exclusively in the thymus. For this project, the possibility that the adult human gastrointestinal tract is a site of extrathymic T cell differentiation was investigated.

To confirm that maturing T cells are present in the small intestine, reverse transcriptase polymerase chain reaction (RT-PCR) was carried out to detect RAG1 and RAG2 specific mRNA. The recombination activating genes, RAG1 and RAG2 are only expressed in immature T and B cells which are undergoing gene rearrangement and therefore would only be present in gut tissue if it were a site of T cell maturation. Total RNA was purified from small intestinal

biopsies from 4 patients. cDNA was synthesised. Using PCR, nested PCR and 4 pairs of specific primers for nucleotide sequences at the 5' end of both RAG1 and RAG2, RAG specific mRNA was detected in 3 of the 4 patients studied (ages 35-65). No RAG message was detected in the fourth patient (age 82). Separation of the epithelial layer from the underlying lamina propria led to the detection of both RAG1 and RAG2 mRNA, indicating the message is of T cell origin as B lymphocytes are effectively excluded from intestinal epithelium. Evidence of RAG1 and RAG2 expression support the hypothesis that T cells can mature extrathymically in the intestine.

IMMUNOLOGICAL ROLE OF THE SMALL INTESTINAL ENTEROCYTES

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Enterocytes are uniquely positioned, acting as an interface between lumen derived antigens and the cells of the gut immune system. They might, therefore, play an important part in influencing local immune responses. In this study, the immunological role of enterocytes in T cell activation was investigated. Single cell suspensions from human small intestinal biopsies were obtained. Significant expression of HLA-DP (MFI: 11.78±13.26 SD), DQ (MFI: 4.15±4.09 SD) and DR (MFI: 30.88±13.1 SD) molecules on the surface of the enterocytes was detected by FACS analysis. The possible role of these Class II MHC molecules in antigen presentation was studied. Enterocytes were used as antigen presenting cells (APC) to autologous peripheral blood T lymphocytes. Cells were cultured for 6 days in 96 microwell culture plates, in the presence of PPD as antigen, at a concentration of 10^5 T cells/well and 10^4 APC/well. T cell proliferation was measured as uptake of 3 H-thymidine using a b-scintillation counter. Monocytes, used under the same conditions as control antigen-presenting cells, induced significant proliferation (mean: 17,121 cpm ± 11,039 SE). However, enterocytes had no effect on T cell proliferation (mean: 633 cpm ± 41.5 SE). An explanation for this lack of induction of T cell proliferation might be that enterocytes are presenting antigen in the context of their Class II MHC molecules, but not providing the requisite secondary signals necessary for T cell activation. This possibility was explored. Using FACS analysis, the presence of B7 and CD40 on the surface of enterocytes was investigated. The results show that only a small percentage of enterocytes expressed B7 (mean: 11.9±5.9 SD) and CD40 (mean: 5.25±6.1 SD). T lymphocyte activation requires both an antigen-specific signal delivered through the antigen receptor and non-specific costimulatory signals provided by CD28 and its ligand B7 on the antigen presenting cell and gp39 and its ligand CD40 on the APC. B7 absence on enterocytes may lead to T cell clonal anergy, explaining immunological tolerance to dietary antigen.

'MEMORY' AND 'NAIVE' T-LYMPHOCYTE SUBSETS DECREASE WITH INCREASING AGE INTO VERY OLD AGE

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'Naive' or the antigenically unstimulated CD4 lymphocytes are present in large numbers at birth while 'memory' or antigenically

stimulated cells become much more numerous during early life. It was therefore of interest to assess the effect of increasing age on numbers of 'naive' and 'memory' lymphocyte subsets.

In this preliminary study the CD4 45RO+ (memory) and the CD4 45RA+ (naive) subset of lymphocytes were measured in 211 free living young, young old, old and very elderly persons (81 males, 130 females), age range 19-102 years, mean age 76 (SD24) years, using flowcytometry and dual labelling monoclonal antibodies. Absolute values (Mean (SD) x 10⁹/L) for both 'naive' and 'memory' cells decreased with increasing age into very old age with no differences between male and female subjects.

Age Group	Memory CD4 45RO+	Naive CD4 45RA+
Young	0.55 (0.24)	0.24 (0.22)
70s	0.48 (0.22)	0.15 (0.15)
80s	0.41 (0.23)	0.12 (0.09)
90+s	0.38 (0.22)	0.14 (0.15)

This study challenges the explanation that increasing antigenic exposure throughout life increases the 'memory' cell compartment of the immune system while at the same time the 'naive' cell reservoir becomes used up.

INFECTIOUS DISEASE/GU MEDICINE

REGIONWIDE SURVEILLANCE OF SEXUALLY TRANSMITTED INFECTIONS IN A THAMES REGION

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In Spring 1992 Genito-Urinary Medicine (GUM) services in South West Thames (SWT) region and information relating to sexually transmitted infections (STIs) in SWT were reviewed. The surveillance data available included laboratory reports of certain STIs to the Public Health Laboratory Service (PHLS) Communicable Disease Centre (CDSC) as well as the statutory KC60 return to the Department of Health. These provide little information about potential risk factors for infection. Recommendations were made which included the installation of a standard surveillance system regionwide in line with the 1988 Monk's Enquiry Report recommendations.

During 1992/93, in collaboration with GUM physicians in the region plans were made to implement this recommendation. Issues of concern included confidentiality and security of data as well as the training which would be required. Agreement was reached regarding a core dataset which will be analysed centrally.

The detailed process of project development and results of the collaboration will be discussed as well as the potential benefits and output envisaged from the system.

THE USE OF THE POLYMERASE CHAIN REACTION (PCR) IN DETECTING HIV INFECTION IN CHILDREN

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Human Immunodeficiency Virus (HIV), can be transmitted from infected mothers to their children in utero or at birth. Detection of HIV antibodies in the newborn does not necessarily imply HIV infection as maternal HIV antibody crosses the placenta. It may take up to 15 months for these antibodies to be lost. The presence of HIV

antigen would indicate infection but antigen is not always expressed at detectable levels.

The purpose of this study was to assess the usefulness of the PCR technique in determining HIV status in children born to infected mothers. We compared the results of the PCR technique with those of the antibody and antigen tests. In the period 1990-93, PCR results are available on sixty-nine children. HIV DNA was detected in seventeen, fifteen of whom remain antibody positive after three years of age, one has died and one other age ten months is HIV antigen positive. Fifty one of the remaining children have tested negative for HIV antigen at various stages, there was insufficient specimen in one for antigen testing.

This study indicates that PCR is a valuable technique in determining HIV status in children when used in conjunction with routine diagnostic tests.

A PROSPECTIVE STUDY OF CENTRAL LINE RELATED SEPSIS IN HIV PATIENTS

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Studies have reported that nosocomial catheter related sepsis occurs in 15-20% of patients. We conducted a prospective surveillance of central catheter related sepsis in 20 HIV seropositive patients. Nine of the patients were homosexual men and 11 were intravenous drug users, of whom 6 were actively abusing illicit drugs. 15 (75%) underwent central line insertion for therapeutic regimes. 5 patients (25%) had central lines inserted because of poor peripheral venous access as a consequence of intravenous drug misuse. All patients were HIV CDC IV with a CD4 lymphocyte range of 0-60 x 10⁶/l. 2 patients received parenteral nutrition. There was no correlation between duration of line insertion and catheter related sepsis. 9 lines (45Z) had to be removed because of suspected sepsis after a range of 3-10 days, of which microbiological review showed that 8 patients (40%) had confirmed catheter related sepsis. The most commonly isolated organism was Staphylococcal aureus occurring in 5 patients with Staphylococcal epidermidis occurring in 4 patients. 1 patient had both organisms isolated. Furthermore 2 patients had Enterococcus faecium isolated. Of the remaining cases, 4 patients (20%) had evidence of local infection only not requiring removal. Subsequently after removal of the catheters 4 patients (20%) had colonisation of the catheter tip and 5 patients (25%) had no evidence of infection. Continued use of illicit drugs via the central line in 6 patients surprisingly did not correlate with an increased risk of sepsis. Nosocomial sepsis is a major cause of patient morbidity.

INDICATIONS FOR LIVER BIOPSY IN HIV POSITIVE PATIENTS

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To document the commonest indication for liver biopsy in a HIV positive group; the range of histological abnormalities reported; and to assess the diagnostic value of liver biopsy and complication rate in these patients. Retrospective analysis of forty HIV positive patients from whom forty one liver biopsies were taken in the period 1987-1993. We noted the indication for biopsy, hepatitis serology, risk factors for HIV, pathological findings and any complications. 23

patients were intravenous drug abusers. There were sixteen hetero/homosexual contacts and one Haemophilic. The commonest indication for biopsy was to establish the extent of liver damage in patients with abnormal L.F.T.'s and positive hepatitis B \pm C serology. (24 cases). All these biopsies were abnormal, most commonly showing Chronic Active Hepatitis (13 cases). In 9 cases biopsy was performed to rule out opportunistic infection in patients with P.U.O. and abnormal L.F.T.'s. Only one biopsy confirmed infection with cryptosporidium. Although three others showed granulomatous hepatitis, no organism was identified. M.T.B. was diagnosed in two cases by alternative means. On eight patients undergoing biopsy to rule out malignancy, no biopsy was positive. One patient had Hodgkin's disease diagnosed on lymph node biopsy. Complications arose in 3/41 (7.3%) patients with no deaths. Liver biopsy contributed significantly to understanding underlying liver pathology in patients with a history of hepatitis B \pm C. In our patient group it was not useful in investigating P.U.O. or suspected malignancy.

SEXUAL ACTIVITY AND SEXUALLY TRANSMITTED DISEASES AMONGST THE GERIATRIC POPULATION

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Previous studies have conflicted over the decline in sexual interest among male and female geriatric patients. As the general public and the medical profession do not readily associate sexual activity with the elderly population, we retrospectively reviewed all patients over the age of 65 attending the GUM clinic in S.J.H. All medical records were analysed for age, sex, marital status, place of residence, referral pattern, presenting complaints, diagnosis, treatment, sexual inclination, time of last sexual intercourse and number of sexual partners. Total patient attendances per year average at 16000. 80 new patients over 65 presented for assessment (age range 65-92). Return patients are not included in this analysis. Sex distribution and marital status are illustrated (figs 1&2). The most common reason for presentation was referral because of positive syphilis serology. Of 10 patients requesting HIV testing, 9 were male, 2 of the men were homosexual and the rest were heterosexual. 2 admitted to hiring prostitutes and 1 had a casual encounter. All were HIV sero negative. The rest of diagnoses are tabulated (table 1). The elderly population share the same spectrum of STD. All 3 bisexual men were diagnosed with an STD while only 1 of the homosexual men had a positive diagnosis. 5 men admitted to hiring prostitutes and 3 of them had STD's. We advise all health care workers looking after the elderly to be more aware of the existence of sexual activity and the possibility of STD's in this cohort.

MICROBIOLOGY

CHARACTERISATION OF A HAEMAGGLUTININ ASSOCIATED WITH INFECTIOUS STRAINS OF *MORAXELLA CATARRHALIS*

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Moraxella (Branhamella) catarrhalis once considered a

commensal in the nasopharyngeal tract has been increasingly recognised as a pathogen⁽¹⁾. The adherence of *M. catarrhalis* to oropharyngeal cells has been correlated with the occurrence of infection⁽²⁾. A study of the haemagglutinating activity of *M. catarrhalis* revealed a significantly higher percentage of infectious strains were haemagglutinating positive when compared with the carrier strains. This indicates that the haemagglutinin may play a role in the infectious process.

To study the nature of the interactions occurring between the haemagglutinin of *M. catarrhalis* and the human red blood cell Transmission Electron Microscopy studies were used: fimbrial attachment was not apparent, a very close association between the red cell and bacterial surface was noted, suggesting the haemagglutinin may be an outer membrane protein. To determine the character of the haemagglutinin bacteria were treated with enzymes, chemicals and heat, prior to haemagglutination studies. Cell surface protein analysis was performed using SDS PAGE. The results indicate that the haemagglutinin was a heat sensitive outer membrane protein with a molecular weight of c200 kDa.

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ESCHERICHIA COLI 0157 INFECTION IN SOUTH WEST LONDON

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An outbreak of *Escherichia coli* 0157 infection occurred in July 1993 in South West London affecting six children living in an area of 1.5 mile radius. Three developed Haemolytic Uraemic Syndrome (HUS) and one child died. A full epidemiological and microbiological investigation was carried out. Isolates of *E. coli* from stools were forwarded to the PHLS Laboratory of Enteric Pathogens (LEP) for confirmation of identity, phage typing and additional tests including plasmid analysis, and VT gene analysis with DNA probes. An environmental investigation included sampling and culture of a variety of food items potentially capable of transmission of infection, as well as a thorough investigation of paddling pools thought to have been associated with infection. The results of the investigation will be presented.

POLYMERASE CHAIN REACTION BASED TYPING OF ENTEROBACTER CLOACAE

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During July, 1993 a small self-terminating outbreak of resistant *Enterobacter cloacae* occurred in the Intensive Care Unit at U.C.H.G. Three of the seven patients simultaneously nursed in the unit were involved in the outbreak. Extensive environmental sampling of the I.C.U. was carried out during the episode.

A Polymerase Chain Reaction-based DNA fingerprinting method (RAPD) was applied to the clinical and environmental isolates of

Enterobacter cloacae recovered, in addition to biochemical profile and extended antibiogram.

Six strains from the I.C.U. (3 clinical and 3 environmental) gave the same antibiogram and biochemical profile. RAPD typing indicated that 5 of the isolates were identical and one environmental isolate differed.

URINARY TRACT PATHOGENS IN THE GREATER MUNSTER AREA: ANTIBIOTIC SUSCEPTIBILITY PATTERNS DURING 1992 AND 1993

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Dept. of Medical Microbiology, Cork Regional Hospital.
On behalf of the Infoscans Editorial Board.

Antibiotics are among the commonest drugs prescribed in hospital and community medicine. Knowledge of the prevalent local pathogens and their antibiotic susceptibility patterns enables clinicians to treat patients empirically while awaiting culture and sensitivity data from the laboratory. This is particularly pertinent in the treatment of urinary tract infections. In this presentation we show the prevalent urinary pathogens and their sensitivity to commonly used antibiotics in the Munster area. During a four week period in 1992 and again in 1993, microbiological data pertaining to 1,400 consecutive urinary infections was collated. Reporting laboratories included Limerick, Waterford, and Cork Regional Hospitals, the Bon Secours and Mercy Hospitals, Cork and Tralee General Hospital. 56% of samples originated from general practice and 44% from hospital. The most prevalent pathogen, both in the hospital and GP setting was Coliform (lactose fermenting Gram-negative rods). Organisms such as *Proteus spp.*, *Streptococcus spp.* and *Pseudomonas spp.* were more common in hospital patients. In 1993 a similar distribution of urinary pathogens was detected.

As regards antibiotic sensitivity data, co-amoxiclav and cephadrine were the most effective agents in 1992 and surprisingly resistance to these agents was slightly lower in 1993.

On the basis of this data co-amoxiclav and cephadrine were recommended as the most effective agents for empiric treatment of urinary tract infections.

ENTERIC PATHOGENS IN THE GREATER MUNSTER AREA DURING 1992 AND 1993

D. Whyte, B. Cryan.

Dept. of Medical Microbiology, Cork Regional Hospital.
On behalf of the Infoscans Editorial Board.

World-wide enteric pathogens are responsible for 600 million cases of diarrhoeal illness and 800,000 deaths each year. The major impact of these organisms is in the developing world. Although the mortality rate is lower in the developed world they are a significant cause of morbidity and may be fatal in vulnerable patients such as the very young and very old. In this presentation the laboratory data pertaining to gastrointestinal pathogens detected during 1992 and 1993 are presented. Laboratories reporting data: the Limerick Regional, Waterford Regional, Cork Regional, Tralee General, Mercy Hospital Cork and Bon Secours Hospital Cork. During 1992 a total of 1,212 pathogens were detected. In 1993 1,662 pathogens were reported.

Rotavirus was the most common organism detected, 876 reports in 1992 and 650 reports in 1993. *Campylobacter* species were the most frequently isolated bacterial pathogens. They were prevalent throughout the year but particularly during the summer months.

Shigella sonnei isolation was also relatively common, 191 in 1992 and 252 in 1993. Many of these organisms were associated with shigella sonnei outbreaks, two of which occurred in 1992 and one in 1993. Enteropathogenic *E. coli* and *Salmonella* species organisms were most common during the summer months. *Salmonella* species organisms were less common than in 1991 and 1990. Cryptosporidium detection was also down from previous years.

INFOSCAN: SOUTHERN COMMUNICABLE DISEASE REPORT; ORIGINS AND DEVELOPMENT

D. Whyte, B. Cryan.

Dept. of Medical Microbiology, Cork Regional Hospital.
On behalf of the Infoscans Editorial Board.

In early 1991, microbiologists and public health doctors came together to coordinate the first infectious disease surveillance bulletin for the southern province of Ireland. Envisaged in this report was the goal, "to increase awareness of infectious diseases in community and hospital practice, thereby optimising the investigation, diagnosis, therapy, control and prevention of such illness".

Weekly reports are submitted from Cork, Limerick and Waterford Regional Hospitals, the Bon Secours and Mercy Hospitals, Cork, Tralee General Hospital and St. John's Hospital Limerick. These reports are collated in a database and presented graphically by the use of several computer software programmes, central to which is a Desk Top Publishing facility. The report consists of current news from periodicals or the locality, two or three "focus" articles and a breakdown of pathogens isolated every quarter.

INFOSCAN is distributed to over 1500 General Practitioners in Munster and to laboratories and community care doctors all over Ireland. The report is prepared by the editorial body and given "camera ready" to the printer. This leaves the Editorial Board in full control of content and minimises cost.

THE MECHANISM OF THE BACTERICIDAL EFFECT OF SERUM ON *MORAXELLA CATARRHALIS*

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Moraxella catarrhalis is a lower respiratory tract pathogen which can also exist as an asymptomatic coloniser of the oropharynx. These colonising strains are significantly more likely to be sensitive to the bactericidal effect of normal serum than infective strains⁽¹⁾. This bactericidal activity of serum is complement mediated. Our study aimed to determine which complement pathway mediates the bactericidal effect of serum on susceptible strains of *Moraxella catarrhalis*.

The differential ion requirements of the classical and alternate pathways were utilised. The classical pathway requires both calcium (Ca²⁺) and magnesium (Mg²⁺); the alternate pathway, Mg²⁺ only. EDTA chelates both Ca²⁺ and Mg²⁺ thus blocking both the classical and alternate pathways. EGTA chelates Ca²⁺ alone thus inhibiting the classical pathway only. 12 serum sensitive strains of *Moraxella catarrhalis* were studied. A standard serum bactericidal assay was performed using non-chelated and chelated serum. All assays were performed in duplicate.

Serum chelated with EDTA lost its bactericidal effect on the strains studied. Serum chelated with EGTA however retained its bactericidal effect. It can be concluded therefore that the bactericidal

effect of serum on colonising strains of *Moraxella catarrhalis* is mediated by the alternate complement pathway.

Reference

1. Murphy, S. et al. The bactericidal effect of normal human serum on *Moraxella catarrhalis*. *Age Ageing* 1994; 23: S342.

THE RIBOSOMAL INTERGENIC SPACER REGION: A TARGET FOR THE PCR BASED DIAGNOSIS OF TUBERCULOSIS

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The polymerase chain reaction (PCR) permits rapid detection of the *Mycobacterium tuberculosis* complex (*M. tuberculosis*, *M. bovis* and *M. microti*) in clinical specimens. We have determined the DNA sequence of the 16S/23S ribosomal intergenic spacer region of the *M. tuberculosis* complex in an attempt to develop a primer/probe format with a view to differentiation between the members of the *M. tuberculosis* complex and the mycobacteria other than tuberculosis (MOTT). A specific PCR and DNA probe assay was developed for the detection of the *M. tuberculosis* complex, along with an internal PCR standard for use with this primer/probe set. The efficiency of the internal standard in detecting inhibitors of PCR in clinical specimens and its value in determining the maximum quantity of crude sputum extract permissible without inhibition of PCR was assessed. The conservation of the sequence in the 16S/23S spacer regions, between members of the *M. tuberculosis* complex supports the close relationship of these organisms documented by the sequence homology reported elsewhere in their genomes.

NEUROLOGY/NEUROSCIENCES

RECURRENT MENINGITIS: WHICH IMAGING MODALITY (CT OR MRI)?

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Coronal CT and heavily T2 weighted MRI were carried out on six consecutive patients who presented with recurrent meningitis. They were four males and two females with a mean age of 33.7 years. Five had previous trauma 1-7 years prior to presentation. Pneumococcal meningitis occurred twice in each of four patients, thrice in one and four times in another. MRI localized dural fistula in five and was negative in one patient. CT showed a bony defect suggestive of dural fistula in four and was negative in two patients. Five patients underwent surgical exploration and repair of the dural fistula. The sixth patient underwent surgery on the basis of positive CT only and no dural fistula could be found. Therefore CT was falsely positive in one and falsely negative in two patients. Thus, it was concluded that MRI should be the initial investigation in patients with recurrent meningitis.

SK&F 83959, A DOPAMINE 'D-1-LIKE ANTAGONIST' AND ITS PARADOXICAL BEHAVIOURAL EFFECTS

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Dopamine [DA] receptors appear more diverse than envisaged

initially within the D-1/D-2 schema, in terms of both linkage to second messenger systems other than adenylyl cyclase [AC] and of molecular diversity. The benzazepine SK&F 83959 has been identified as inhibiting the stimulation of AC induced by DA, i.e. to act as a D-1 antagonist, yet paradoxically exerting certain D-1 agonist effects on behaviour. Using previously described procedures, rats [n=8 per group] were challenged s.c. with vehicle or 0.011.25 mg/kg SK&F 83959, or with 0.05 mg/kg SK&F 83959 following pretreatment with vehicle or the selective D-1 antagonists SCH 23390 and BW 737C, or the selective D-2 antagonist YM 09151-2. SK&F 83959 at 0.01-0.05 mg/kg induced intense grooming and vacuous chewing; these responses tended to decline at higher doses with the emergence of sniffing, rearing and chewing. Intense grooming was readily blocked by 0.01-1.0 mg/kg SCH 23390 and by 0.04-5.0 mg/kg BW 737C, and also by 0.005-0.5 mg/kg YM 09151-2. Conversely, vacuous chewing was not blocked by SCH 23390, which induced vacuous chewing when given alone or by BW 737C, and was enhanced by YM 09151-2. Intense grooming was induced by SK&F 83959 and blocked by each of two chemically distinct selective D-1 antagonists; thus, SK&F 83959 appears to stimulate a 'D-1-like' receptor unlinked to AC but participating in cooperative D-1:D-2 interactions that regulate such typical DAergic behaviours; conversely, the failure of these antagonists to block vacuous chewing suggests either an action at a distinct 'D-1-like' site, at which SCH 23390 also shows agonist activity and which participates in oppositional D-1:D-2 interactions that regulate such atypical behaviours, or the involvement of non-DAergic mechanisms.

This work was supported by the Royal College of Surgeons in Ireland. We thank Schering, SmithKline Beecham, Wellcome and Yamanouchi for gifts of drugs.

THE IRISH HEAD INJURY ENDEMIC: PROBLEMS AND SOLUTIONS

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We reviewed all acute head injury admissions to our unit over a twelve month period in order to assess the types of injury sustained, the treatment administered and the final outcome. A total of 225 patients admitted to our Neurosurgical Unit (NSU) were reviewed (169 males and 56 females; age range = 7 months to 83 years; mean = 28.3 years; median = 22 years; 57.3% < 25 years). Road traffic accidents (RTA) accounted for 45% of all injuries, falls accounted for a further 37%, assaults = 8% and sports injuries = 2%. There was definite evidence of alcohol intake in 31% of adult cases (50/161). Patients were admitted directly to the NSU as well as being transferred from all parts of the country; distance travelled (Km); range = 0-255; mean = 69.5; median = 32. Duration (hours) from time of injury to arrival at the NSU; range = 1-288; mean = 24.8; median = 17. Fifty-four percent of injuries occurred at weekends and Bank Holidays. Patients were categorised according to the Glasgow Coma Scale (GCS) into mild (26%), moderate (23%) and severe (51%) head injuries. Extracranial fractures were present in 23%. Computerised Tomography (CT) revealed cerebral contusions, acute subdural haematomata, extradural haematomata and cerebral edema in 25%, 20%, 16% and 9% respectively. The Glasgow Outcome Score was; Full Recovery = 53%; Disabled (independent) = 17%; Disabled (dependent) = 8%; Vegetative = 5%; Death = 17%. In conclusion, we confirm that head injuries are most commonly associated with young adult males and with RTAs. These have major rehabilitation, medical, social and fiscal implications.

INTRACRANIAL ABSCESSSES: A CLINICO-MICROBIOLOGICAL STUDY

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The successful treatment of any intracranial abscess depends largely upon early diagnosis. In addition, the incidence appears to be increasing. We report our experience with this type of intracranial infection outlining the mode of presentation, diagnosis, bacteriology, management and outcome. Fifty-nine patients with intracranial abscesses were reviewed. The male-to-female ratio was 42:17 (71%:29%) and the age range was 1-82 years (mean = 36.9 years; median = 37.0 years). Headaches was the commonest presentation (61%) followed by focal neurological signs (48%), pyrexia (46%), altered level of consciousness (36%), confusion (32%) and seizures (24%). Local factors (e.g. sinus and middle ear infections) were the principle cause of intracranial abscess whilst in nine cases (15%), no aetiological factor was ascertainable. All patients had Computerised Tomography (CT) of the brain. All patients had either Burr Hole or formal craniotomy to decompress/aspirate the infective focus. Bacteriological analysis of specimens from these foci revealed single organisms in 55.5% of cases which consisted of Gram positive organisms (41%), Gram negatives (14%) and anaerobes (0.5%). Multiple cultures were found in 14% and in the remaining eighteen cases (30.5%), there were sterile cultures. There were eight deaths (14%). In conclusion, despite advances in antimicrobial therapy and neuroradiology, intracranial abscesses remain a serious source of morbidity and mortality. The diagnosis should be suspected in patients with neurological signs and pyrexia and referred to a neurosurgical unit for further evaluation.

SURGERY FOR PITUITARY TUMOURS: A REVIEW OF 226 CASES

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Pituitary tumours are frequently occurring neoplasms accounting for 10-15% of all intracranial tumours. We reviewed our experience of pituitary tumours managed neurosurgically with emphasis on diagnosis, pathology, management and outcome. Two hundred and twenty-six cases were reviewed (age range = 14-87 years; median = 44 years) with a male-to-female ratio = 4 : 5 approximately. All patients had full endocrinological profiles and neuroradiological imaging prior to surgery. Non-functioning adenomas were the commonest tumours encountered (31.4%), followed by acromegaly (24.8%), prolactinomas (24.4%), Cushing's disease (9.8%), apoplexy (5.3%). Collectively, the endocrine active tumours were the most common category of tumour (60.6%). Visual deterioration and headaches were the commonest symptoms (27% and 25% respectively). The mean duration of these symptoms was 12.7 months and 5.2 weeks. Bitemporal hemianopia was detected 38 cases (17%) of whom 29 (76%) had non-functioning adenomas. Trans-sphenoidal surgery was performed in 194 cases (86%). Computerised Tomography revealed pituitary tumours in 90% of cases of whom 62% were intrasellar lesions and the remaining extended beyond the sella turcica. Most of the latter had non-functioning tumours (55%). Fiftythree patients (24%) developed post-op diabetes insipidus and there were five cases (2%) of post-op meningitis. There were four deaths (2%) in this series, two were unrelated to the surgery. Follow-up records were available in 86 cases (38%) and this revealed visual improvements in 14% of cases, no change in 78% and deterioration

in 8%. Normalisation of hormones in endocrine active disease was best attained in acromegalics (7/12; 58%).

We illustrate the beneficial and prompt effects of surgery for pituitary tumours in terms of resolution of both the hyper-endocrine states and of the compromised visual fields.

CEREBRAL ARTERIOVENOUS MALFORMATIONS: A NEUROSURGICAL PERSPECTIVE

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Arteriovenous Malformations (AVM) of the brain are congenital lesions consisting of one or more direct channels between arterial inflow and venous outflow without an intervening capillary bed. The usual presentation is seizure activity or haemorrhage. We reviewed our experience with twenty-three cases of cerebral AVMs admitted to our department. The male-to-female ratio was 13:10 and the age range between 11-70 years (mean = 36.8; median = 31.0). Six cases presented electively with epilepsy (3), persistent headaches (2) and recurrence of AVM (1). The remaining seventeen cases presented as emergency with acute headaches (13), collapse (5), hemiparesis (4), meningism (2), seizures (1) and visual field defect (1). These urgent cases presented in mild (13), moderate (3) and deep (1) levels of unconsciousness according to the Glasgow Coma Scale (G.C.S.). Sixteen (16/17; 94%) cases had evidence of intracranial haemorrhage on Computerised Tomography (CT). Cerebral angiography confirmed the diagnosis in all cases. These AVMs were categorised according to the Spetzler grading system into Grades I (22%), Grade II (22%), Grade III (26%), Grade IV (13%) and Grade V (17%) according to the site, size and venous drainage pattern. Twenty-two patients (96%) had the AVMs excised. There were three deaths (13%). The final functional outcome on discharge was full recovery (52%), mild disability (26%), moderate disability (9%) and death (13%). In conclusion, we confirm that cerebral AVMs presenting to a NSU are usually adults and despite the associated with morbidity and mortality, neurosurgical excision offers excellent results in selected cases.

SYRINGOMYELIA, REVIEW OF 51 PATIENTS

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A review of 51 patients treated for syringomyelia is presented. Twenty-four were males and 27 were females with a mean age of 4.5 years. Fifty-four per cent presented with neck pain and suspended sensory disturbance. The syrinx involved the cervical spinal cord in all cases. It extended caudally into the thoracic cord in 14% and upwards into the brain stem in 4%. It was associated with spina bifida in 14%, scoliosis in 25%, and hydrocephalus in 18%. All but one were associated with Chiara malformation. Treatment options included CSF diversion for hydrocephalus, and foramen magnum decompression for Chiari malformation. Two-thirds of patients improved following surgery, 15% remained unchanged and the rest required syringopleural shunts to halt their progress. We advocated CSF diversion for hydrocephalus, foramen magnum decompression for tonsillar hernia or ectopia then syringopleural shunts in that order. Patients with syringomyelia should have their head as well as spine scanned to detect hydrocephalus and/or Chiari malformation as these associated conditions are amenable to surgical treatment.

SPATIAL ORIENTATION AND MEMORY FOLLOWING TEMPORAL LOBE SURGERY FOR EPILEPSY

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The right hemisphere of the human brain is traditionally viewed as playing a dominant role in processing visuo-spatial stimuli. This study looked specifically at the role of the temporal neocortex and mesial temporal lobe structures in the formation and storage of internal representations of a real-life environment.

Twenty patients, who had undergone unilateral temporal lobectomy or neocorticectomy for the relief of intractable epilepsy (11 left, 9 right), and 10 matched control subjects viewed video presentations of routes through a novel urban area. Learning and memory were then assessed across several parameters.

Analyses revealed deficits after both left and right temporal lobe surgery. Both patient groups required significantly more exposures to the video before a criterion level of learning was reached ($p < 0.01$). Analysis of error types in recognition memory during learning showed that the left temporal group made significantly more omission errors ($p < 0.01$), while the right temporal group made significantly more inclusion errors ($p < 0.05$). Furthermore, patients after right temporal surgery were significantly impaired, relative to controls and the left temporal group, on proximity ($p < 0.05$) and distance judgements ($p < 0.01$) and on landmark selection ($p < 0.01$).

Findings argue for a role of both left and right temporal lobe structures in different aspects of spatial representation of everyday environments.

THE SPECTRUM OF NONMALIGNANT SENSORY POLYGANGLIONOPATHY

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Nine patients presenting with features of nonmalignant inflammatory sensory polyganglionopathy were seen. The clinical features included facial sensory loss and Adies pupils in seven, generalised areflexia and asymmetrical limb ataxia in six. Four patients had evidence of a collagen vascular disease, one had a monoclonal gammopathy and another had diffusely raised gamma globulin. Sjogrens syndrome was present in four. Six patients had abnormal electrophysiological tests with diminished or absent sensory nerve action potentials but normal motor studies. The course was subacute or chronic over many years. Dorsal root ganglionitis has been shown to be the underlying pathology and an autoimmune pathogenesis seems probable. A single patient responded to plasma exchange but response to corticosteroids and immunosuppression has been poor.

VOGT-KOYANAGI-HARADA SYNDROME, A CASE REPORT AND LITERATURE REVIEW

M. Norton, B. McGeeney, M. O'Connor, J. M. T. Redmond.
St. James's Hospital, James's Street, Dublin 8.

A twenty nine year old woman presented with headache, blurred vision and unsteady gait.

Examination revealed a spastic paraparesis, reduced visual acuity, pigmentary retinal changes and bilateral uveitis.

M.R.I. examination of the brain was normal. CSF examination revealed an aseptic meningitis. Fluorescein angiography confirmed retinal pigmentary abnormalities.

A diagnosis of Vogt-Koyanagi-Harada (V.K.H) syndrome was made and the patient was commenced on immunosuppressive therapy with good clinical response.

V.K.H. is a rare disorder in the western world with-neurological, ophthalmological, dermatological and otological features. The literature on the subject is reviewed.

MITOCHONDRIAL CYTOPATHIES, A CASE REPORT AND LITERATURE REVIEW

B. McGeeney, M. Norton, S. Feely, J. M. T. Redmond.
St. James's Hospital, James's Street, Dublin 8.

A 43 year old man presented with lower limb numbness, poor balance and weakness. His sister had similar symptoms with epilepsy and cerebral degeneration.

On examination there was bilateral ptosis, external ophthalmoplegia, dysarthria, sensory neuropathy, muscle weakness, lower limb areflexia and ataxia.

An EEG was abnormal and a muscle biopsy confirmed the diagnosis of Mitochondrial Cytopathy.

This case illustrates the hereditary nature and heterogeneous clinical features of this increasingly recognised group of disorders.

A MODEL OF THE INTERACTION OF OCULAR MICROTREMOR AND RETINAL SAMPLING

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Fixational movements of the eye include a minute high frequency tremor called Ocular Microtremor (OMT). The amplitude of this tremor is of the order of the width of a single photoreceptor. An image of a stationary object formed on the retina is not stable but moves relative to the photoreceptor mosaic in response to fixational eye movements. A theoretical model was developed to investigate the potential impact of OMT on photoreceptor sampling of the retinal image.

The photoreceptor mosaic was considered to be a sampling array of circular receptors with a given temporal response, moving in a fashion approximating OMT. An expression was developed relating theoretical image degradation in the image of a sinusoidal grating of given spatial frequency and the motion of the photoreceptor mosaic. The results are compared with existing studies of the potential effects of eye movements on acuity.

The developed expression represents a useful base to which theoretical considerations of the effects of OMT may be referred.

OBSTETRICS/GYNAECOLOGY

IS SPATIAL SEPARATION THE ONLY DIFFERENCE BETWEEN STAGE I AND STAGE III OVARIAN CANCERS?

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In ovarian cancer between 50% to 90% of patients present with Stage III disease. This late presentation is attributed both to the relative inaccessibility of the ovary to the clinician and to the non specific nature of the presenting symptoms. Screening is limited by the paucity of knowledge of the natural history of ovarian cancer. The

purpose of this study is to ascertain by studying the pathological features of ovarian cancer, whether Stage I cancers are tumours at an earlier stage than Stage III cancers.

We reviewed retrospectively the pathology of all ovarian cancers over a ten year period looking at histological grade, ovarian size, uni or bilaterality of the cancer and involvement of peritoneal washings.

We found that Stage III cancers were more likely to be poorly differentiated, bilateral with smaller sized ovaries and positive peritoneal washings. This contrasted with Stage I cancers which tended to be well to moderately differentiated, unilateral with larger sized ovaries and negative peritoneal washings.

These findings suggest that Stage I and Stage II cancers may be biologically different. This raises the possibility of an aggressive, rapidly growing form of ovarian cancer which metastasizes early from the ovary, thus presenting clinically as Stage III. If this is so ultrasonic screening is unlikely to pick up these cancers at an earlier stage.

CLASSICAL CAESAREAN SECTION: A 10 YEAR REVIEW

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Coombe Women's Hospital, Dublin.

To Review Classical and Inverted T. Caesarean Sections over a 10 year period.

Retrospective Study by Chart Review of 42 patients who underwent Classical/Inverted T Caesarean Section between 1983 and 1992.

Classical/Inverted T Caesarean Section accounted for 0.8% of all Caesarean Sections and 0.07% of all deliveries during the 10 year period. Fifty percent of patients had previous abdominopelvic surgery including Caesarean Section, 50% were under 37 completed weeks and 50% were in labour. The main indicators for classical/inverted T Caesarean Section were poorly formed lower segment (33.3%), and transverse lie or shoulder presentation (70.8%). Peri-operative complications included infection (47.9%), haemorrhage (18.7%) and hysterectomy 6.2%; scar separation occurred in 11.8% of those with a subsequent pregnancy.

Nineteen of the 51 infants (38%) delivered, weighed less than 1500g. There were 8 perinatal deaths (15.7%), all weighing less than 1500g, 4 being due to congenital malformation.

In this study Classical/Inverted T Caesarean Section was associated with a significant maternal morbidity; there was also a significant perinatal mortality due to prematurity and congenital malformation.

DAY CARE AND THE CLASSIFICATION OF GESTATIONAL HYPERTENSION

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Elevation of blood pressure in the clinical situation due to anxiety and stress (White Coat effect) is well recognised. Gestational hypertension (GH) has been defined as two consecutive measurements of a diastolic blood pressure of 90 mmHg four or more hours apart in the absence of proteinuria¹. This clinically based definition corresponds with the practice of admitting hypertensive patients and taking blood pressure at intervals of 4-6 hours.

The aim of this study is to assess the effect of day care on the classification of GH in pregnancy. The Rotunda Hospital DCU records from February 1993 - December 1993 were analysed. Of 343

patients who were seen in the unit 152 patients fulfilled the selection criteria in that their referral diastolic BP was > 90 mmHg, their first diastolic BP recorded in the DCU was > 90 mmHg. In the DCU five BP readings were taken between 0830 hours and 1230 hours. Only 26 (17%) of this group had a mean diastolic BP > 90 mmHg. The first BP reading was significantly higher ($P < 0.001$) than other individual readings.

We conclude that the first BP measured in a DCU reflects patient anxiety; it should not be used in the classification of hypertension. We suggest instead that a mean diastolic value of > 90 mmHg be used to define hypertension. This study is ongoing.

Reference

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DOWN-REGULATION VERSUS NON-DOWN REGULATION REGIMES FOR CONTROLLED OVARIAN STIMULATION IN AN IN VITRO FERTILISATION PROGRAMME. A PROSPECTIVE RANDOMISED STUDY

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R. F. Harrison.

Human Assisted Reproduction Ireland, Department of Obstetrics & Gynaecology, Rotunda Hospital, Dublin 1.

A prospective randomised study was carried out to determine whether the routine use of gonadotrophin releasing hormone analogues (GnRH-a) produces any significant advantage with regard to the clinical outcome of an in vitro fertilisation (IVF) cycle.

One-hundred and fifty couples having their first ever IVF attempt were randomly divided into three groups. The non down-regulation regime consisted of clomiphene citrate / human menopausal gonadotrophin (HMG) (Group A). The down-regulation regimes consisted of pre-treatment with long protocol GnRH-a administration in the form of a depot preparation (Group B) or as a daily nasal spray (Group C), prior to the HMG.

Follicular recruitment, number of oocytes obtained, fertilisation rates, number of embryos transferred and pregnancy rates were studied, in addition to the cancellation and complication rates.

No significant differences were noted with regard to any of the parameters studied. The pregnancy rates per cycle were 32%, 28% & 31% for Group A, B & C respectively. Group A showed a 10% incidence of premature luteinising hormone surge / ovulation, which was not observed in the down-regulation regimes. A significantly higher dose of HMG ($P < 0.001$) was required in the down-regulation regimes.

Down regulation with the use of GnRH-a's for all couples undergoing their first cycle of IVF has practical but no significant medical advantage in terms of the clinical outcome.

RECURRENT OVARIAN CARCINOMA: DIAGNOSIS AND SECOND LINE THERAPY

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Purpose of the Study: To ascertain the incidence, method of diagnosis and outcome of recurrent ovarian cancer.

Methods: All cases of recurrent ovarian cancer were recorded prospectively over a 15 year period. Methods of diagnosis were compared. Second line chemotherapy and outcome was observed.

Results: From 1978 - 1992, 142 patients presented with ovarian

cancer. 12 patients presented with recurrent disease, all of whom had chemotherapy. Of these 12, 1 was unsuitable for second line chemotherapy, 4 did not respond to treatment, 4 had a partial response and 3 have had an apparent cure. The diagnosis of recurrence was made based on an elevated CA125 only, in 4 cases (mean interval time of recurrence, 12 months) and clinically in 8 cases (mean interval time of recurrence 30 months). Chemotherapy was mainly with the Platinum drugs \pm an alkylating agent. The agents used for second line therapy were similar to primary treatment.

Conclusions: CA125 is a very sensitive method of diagnosing recurrent ovarian cancer. 8% of patients will develop recurrent ovarian cancer. These patients should be followed up aggressively as second line therapy can induce long remissions.

FIVE YEAR REVIEW OF UROGYNAECOLOGY CLINIC

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The computerised records of 655 women attending a Urogynaecology Clinic over a 5 year period were reviewed. One hundred and forty two patients (21.6%) were over 65 years and 99 (15.1%) had undergone previous surgery for urinary incontinence. Based on perineal pad testing 274 (41.8%) were considered to have severe / very severe incontinence. At least one diagnosis was made in 565 patients (86.3%), genuine stress urinary incontinence (GSUI) being the most common (349; 53.3%); detrusor instability (DI) was diagnosed in 157 (24%), bladder hypersensitivity in 79 (12.1%) and voiding dysfunction (VD) in 69 (10.5%). Sixty four patients (12.8%) had either mixed GSUI / DI or urinary incontinence / VD. Genital prolapse was diagnosed in 198 patients (31.2%) and 186 (28.4%) had additional gynaecological complaints. The importance of a careful gynaecological history and physical examination must not be obscured by exclusive urodynamic considerations.

PROFILE OF TEENAGE GIRLS ATTENDING A DUBLIN ADOLESCENT ANTENATAL CLINIC

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A structured computer coded questionnaire was administered to 120 consecutive teenage girls attending an adolescent antenatal clinic in order to examine their sociodemographic characteristics, attitudes to pregnancy and sexual behaviour. The mean age of attenders was 17.7 (range: 14-19); 5 (4.1%) were under 16 years. The mean gestation at booking was 16.4 weeks (range: 6-34); 29 (24.2%) were more than 20 weeks. Fifteen (12.5%) no longer had a relationship with the father of the baby. Fifteen (12.5%) were at secondary school; 59 (49.2%) were unemployed. Although only 17 (14.2%) said that they planned the pregnancy, eighty five (70.8%) were happy about being pregnant and 106 (88.3%) intended to keep the baby. Sixty two (51.7%) had used contraception in the past but only 17 (14.2%) at the time of conception. Seventy three (60.8%) had incorrect or no knowledge of their cycle-related fertility. Pregnant teenage girls in general show little evidence of beneficial sex education.

ANATOMY OF URETHRAL NEEDLE SUSPENSION

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The purpose of this study was to describe the surgical anatomy of urethral needle suspension (UNS) operations so as to explain their

effect on urethral support. UNS was performed on two unembalmed cadavers; these were then serially sectioned and subjected to anatomic and histologic examination. The paraurethral supporting tissues incorporated into the suspensory sutures included that portion of supporting endopelvic fascia that lies between the vagina and the levator ani muscles (i.e. the fascial attachments of the urethra), the arcus tendineus fascia pelvis and the surgically perforated, partially detached portion of the superior fascia of the levator ani. UNS operations work by stabilising the proximal urethra, the suspensory sutures providing a new point of lateral fixation for its supporting endopelvic fascia.

DETECTION OF ANAL SPHINCTER DEFECTS USING A NEW MANOMETRIC TECHNIQUE

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Occult damage to the anal sphincters during vaginal delivery may cause later faecal incontinence. Most available methods of detecting such damage are specialised and thus inconvenient for clinical practice. We have devised a manometric technique which is practical and which accurately detects anal sphincter defects. Using a station pull-through microtransducer technique in eight radial planes, anal sphincter function was assessed in 20 women before and after their first vaginal delivery. Detailed resting (internal sphincter) and voluntary squeeze (external sphincter) pressures were evaluated. The manometric data was computed to construct a vectogram of anal pressure and a vector symmetry index (VSI) was calculated⁽¹⁾. The results were compared with anal ultrasonography using a 5 MHz endosonographic probe.

Of 20 patients studied six showed evidence of anal sphincter defects after delivery, three of the external and three of the internal sphincter; two of these had clinical continence difficulties. The results correlated directly with ultrasound findings.

This new technique is quick, easy to perform, accurate and acceptable to patients and will have a wide application in the evaluation of obstetric and other anal sphincter damage.

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EFFECTS OF PERITONEAL FLUIDS FROM WOMEN WITH MINIMAL STAGE ENDOMETRIOSIS AND A NORMAL PELVIS ON SPERM MOTILITY

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We have investigated if the peritoneal fluid in women with minimal stage endometriosis (EPF) produces different effects on sperm motility parameters compared with the fluid in women with a normal pelvis (NPF). A previously collected and frozen sample of peritoneal fluid (PF) from women with MSE or NP was brought to 37°C and used in parallel with control samples incubated with Earles Balanced Salt Solution. Fresh semen was obtained from fertile volunteers and sperm motility analysed using a Hamilton Thorn Research Motility Analyser. Six parameters of motility which included % Motility (MOT), Curvilinear Velocity (VLC), Straight

Line Velocity (VSL), Linearity (LIN), Amplitude Lateral Head Displacement (AHL) and Beat Cross Frequency (BCF) were studied within 1 hour of semen collection and then at five hours. The values obtained from control samples were deducted from those of PF incubations and data analysed using Student's *t* test. The results given are mean \pm SEM (n=9). Spermatozoa incubated for 1 hour with NPF gave a MOT value of $0.11 \pm 2/03$ which was significantly changed to 14.28 ± 4.16 at 5 hour incubation ($p < 0.004$). Following 1 hour incubation the spermatozoa produced VCL, VSL and LIN values of -5.39 ± 2.18 , -5.83 ± 2.31 and -6.22 ± 2.97 which were respectively changed to 6.61 ± 2.89 , 6.11 ± 2.57 and 2.61 ± 1.42 after 5 hours of incubation. There were also significant differences between the group values in each case ($p < 0.01$ for the three comparisons). The differences between 1 hour and 5 hour incubations were however not significant when spermatozoa were incubated with EPF. Values for ALH and BCF from spermatozoa incubated with NPF or EPF at 5 hour were not significantly different from their respective values after 1 hour incubation. It is suggested that NPF contains some factor(s) which can affect sperm motility parameters and these are inactive and/or missing in women with minimal stage endometriosis.

RELATIVE INTRAUTERINE GROWTH RETARDATION, AN UNDIAGNOSED ENTITY

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Objectives: To identify by means of two third trimester scans, fetuses with evidence of intrauterine growth retardation (I.U.G.R) but who are born with birth weights above the 10th centile for gestational age. To determine if these constitute a high risk group by comparing the incidence of obstetric intervention, of intrapartum complications and of neonatal morbidity between this group and the group of infants who showed no ultrasound evidence of I.U.G.R.

Prospective study estimating fetal weight by ultrasound twice in the third trimester. A fall of > 20 centiles was taken as evidence of relative I.U.G.R. and this group of babies was compared with the group not showing evidence of relative I.U.G.R regarding the incidence of intrapartum and perinatal complications.

Results: Seventy-five patients showed a drop of greater than 20% between scans. The incidence of admission to the special care baby unit was greater in those infants demonstrating relative I.U.G.R. ($X^2 = 6.80$, OR = 3.11, 95% CI. = 1.19-8.52; $p < 0.05$).

Conclusions: Infants showing evidence of relative intrauterine growth retardation have an increased incidence of admission to special care baby units. However this is due to medical disorders complicating pregnancy, in particular the development of gestational diabetes mellitus which requires monitoring of blood glucose levels in the infant following delivery.

Relative I.U.G.R. per se, is not associated with an adverse outcome.

ANTIBIOTIC PROPHYLAXIS FOR CAESAREAN SECTIONS

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Purpose: Despite proven efficacy few guidelines or protocols exist in maternity departments regarding use of antibiotic prophylaxis for Caesarean sections. This study observed current use of peri-operative antibiotics in a maternity hospital in the hope that recommendations could be made regarding future prophylaxis.

Methods: A prospective survey of 264 patients undergoing

Caesarean section. A record was made of patients' age, parity, weight, course of labour, and operative details. Following surgery daily examination and regular temperature checks were complemented by relevant microbiological investigations, e.g. wound swab, high vaginal swab, midstream specimen of urine, sputum sample. Blood cultures were performed for pyrexia over 38°C . Any infection occurring up to 6 weeks post-partum was recorded.

Results: 67 patients (25.7%) developed post-operative infection, with similar rates and types of infection for elective and emergency cases. Only in emergency surgery did antibiotics confer a lower infection rate - relative risk 0.7%. Infection rates were higher in obese women ($> 80\text{kg}$) and with junior operators (N.C.H.D.s 28% v consultants 19%). A single intra-venous dose of amoxicillin and clavulanic acid (Augmentin) was used most frequently.

Conclusion: Single agent intra-venous antibiotic prophylaxis at induction of anaesthesia provides cost-effective reduction in infection rates following emergency Caesarean delivery.

MEDICAL AUDIT - AN OBSTETRICAL MODEL

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To be carried out effectively medical audit requires good data collection, data retrieval and data analysis. The medical audit cycle¹ can then be used to determine and compare standards, assess and modify management when necessary, and most importantly to continue to audit the effect of any changes made in order to try and improve patient care.

A specially written intrapartum audit software programme² has helped us to achieve this in the management of labour in nulliparous women with epidural analgesia. We present the labour outcome of 2402 consecutive nulliparous women, all with epidural analgesia and a single oephalic pregnancy at term. 70% had a normal delivery, 15% a forceps delivery, 5% a ventous delivery and 10% were delivered by caesarean section. The average length of labour was 7 1/2 hours, the first stage 6 hours, and the first and second phases of the second stage of labour 35 and 40 minutes respectively. The oxytocin rate in the first stage was 67% and in the second stage 8%. Providing the management of labour is modified, spontaneous vaginal delivery occurs in the vast majority of nulliparous women with epidural analgesia.

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IMMUNOHISTOCHEMICAL LOCALISATION OF uPA AND PAI-2 IN CANCERS OF THE UTERUS AND OVARY

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Alterations in the coagulation-fibrinolysis balance are commonly seen in malignancy; invasion and metastasis are linked with increased tumour fibrinolytic activity. Pericellular proteolysis is mediated by plasmin, a potent proteolytic enzyme. The plasminogen activator, Urokinase (uPA) plays a central role in activating plasminogen to plasmin. Regulatory enzyme Plasminogen activator

inhibitor 2 (PAI-2) combines specifically and irreversibly with uPA. This study investigated the distribution pattern of uPA and PAI-2 in normal tissue and cancerous tumours of the uterus and ovary using immunohistochemistry (IHC). Cases of carcinoma cervix, endometrium, ovary, and normal cervix, endometrium & ovary (n=12) were stained using the StreptABC technique. Cytoplasmic uptake for cytokeratin, an epithelial cell marker, was noted in normal and malignant epithelial cells. Urokinase was localised to the cytoplasm of malignant cells, was variable in endometrial cancer and minimal in ovarian cancer with 80% of malignant nuclei staining positive. Malignant cells in cervical cancer stained strongly positive, particularly at the invading edge. Normal ovarian and cervical tissue failed to stain, while endometrial glands showed weak apical staining. PAI-2 uptake was variable, localised to malignant cell cytoplasm in carcinoma cases, with positive nuclear staining in ovarian cancer. PAI-2 was not expressed in normal ovarian and endometrial tissue, superficial squames of the normal cervical epithelium demonstrated minimal cytoplasmic uptake. These results show a definite activation of the fibrinolytic system in cancers of the uterus and ovary. The invading edge of cervical cancer has an increased uPA content thus facilitating local invasion. Tumour heterogeneity is reflected by variable expression of PAI-2.

OCCUPATIONAL MEDICINE

CANCER RISK IN AGRICULTURAL WORKERS: A POSSIBLE LINK WITH WORK PRACTICES

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This case control study was carried out to examine occupational histories of 90 cases of specified cancers identified in a census survey in the Western Health Board area, in the 16-65 year age group residing in Co. Galway and diagnosed between 1980-1990. 54 controls were selected from two general practices. A questionnaire evaluated all residences, past medical history, reproductive history, occupational history and chemical exposure in the home, garden, farm, fish farms. Data were analysed by chi square analysis, as appropriate. 33% of cases were farmers. Males of S.C. 4 for longest held occupation ($P=0.02$) and males of S.E.G. 9 for most recent occupation ($P=0.05$) were significantly more frequently represented among cases than controls. Farming cases were more likely to use back-pack or hand-held methods of application of pesticides ($P=0.008$) and were less likely to wear protective equipment ($P=0.003$) than controls. Greater potential for exposure to herbicides using the back-pack or hand-held applicator without using proper protective equipment was consistent with other studies and is a potentially important occupational hazard for agricultural workers meriting further investigation.

ONCOLOGY

PRODUCTION OF MONOCLONAL ANTIBODIES (Mabs) TO AN OVARIAN CANCER CELL LINE

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Mabs can bind to antigens on tumor cells with specificity and have potential uses in the diagnosis and treatment of cancer. Ovarian cancer is the most common gynecologic cancer with poor prognosis.

Our research was designed to produce novel Mabs for cancer treatment. Antibodies were raised by immunisation of Balb/c mice to OAW42 cell line (donated by A. Wilson), established from a patient with serous ovarian adenocarcinoma. After fusion, hybrid clones were screened against the cell line and positives were tested for specificity, initially with BSA. Following a number of fusions several antibodies reacting with OAW42 cell line and showing some specificity were obtained. These were cloned and screened against a variety of antigens and cells. Many displayed limited specificity and were mainly of the IgM isotype regardless of the immunisation protocol. However, an IgG1 type Mab of good titre and specificity was isolated from one clone and has been grown in bulk. This recognises an antigen of approx. 48 kDa on the cell membrane. We also report the successful isolation of IgC type antibodies against OAW42 whole cells employing a CEL-PRIME in vitro immunisation technique. Further characterisation of these antibodies is continuing to evaluate their potential use in ovarian cancers.

c-ERBB-2 ONCOPROTEIN EXPRESSION IN NONINVASIVE BREAST CANCER

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Background: The c-erbB-2 oncogene encodes a protein which is a putative growth factor receptor. While overexpression of c-erbB-2 oncoprotein in invasive breast cancer is usually an indicator of poor outcome, the biological significance of c-erbB-2 in noninvasive breast carcinoma has yet to be determined.

Aim: The purpose of this study was to address the relationship between c-erbB-2 oncoprotein expression and clinico-pathological parameters in noninvasive breast carcinoma.

Patients and methods: Sixty nine patients with noninvasive breast cancer were studied. Eleven patients had lobular carcinoma in situ (LCIS) while 58 patients had ductal carcinoma in situ (DCIS). Of the 58 patients with DCIS, 36 had their disease initially detected clinically while 22 had mammographically-detectable disease only. Paraffin-fixed sections were stained immunohistochemically with antiserum to c-erbB-2 oncoprotein.

Results: c-erbB-2 oncoprotein was not detected in any of the patients with LCIS. In patients with DCIS, c-erbB-2 oncoprotein was expressed in 23 cases (40%) and was significantly associated with tumour necrosis ($p<0.001$) and the comedo subtype ($p<0.02$). Elevated levels of c-erbB-2 oncoprotein were found in 22/36 (61%) of patients presenting with clinical disease but in only 1/22 (4.5%) patients presenting with mammographically-detectable disease ($p<0.01$).

Conclusion: This study supports the hypothesis that clinically detected and mammographically detected DCIS are biologically different diseases. The study also demonstrates that the molecular pathogenesis of DCIS differs from that of LCIS.

TPS - A NEW TUMOUR MARKER IN BREAST CARCINOMA

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The role of tumour markers in breast cancer diagnosis and follow-up is controversial. TPS (Tissue polypeptide specific antigen) formed

and released during the late S and G2 phase of the cell cycle is a marker of cell proliferation. This marker was assessed in 97 patients with breast carcinoma using the monoclonal antibody M3 against the specific epitope of TPS and compared to 43 patients with benign breast disease. The mean level in patients with benign breast disease [55.7(5.9)] was similar to the pre-operative levels in patients with operable breast carcinoma [71.7(11.3), P= ns]. TPS was measured during follow-up in 80 patients. Forty-nine patients have not developed recurrence and TPS levels were not significantly different from the operable group [81.2(9.1), P= ns]. In the 17 patients with loco-regional recurrence. TPS was elevated [112.9(35.8)]. In the 14 patients who progressed to systemic metastases TPS levels increased significantly to a mean of 569(149.7) (P<0.05, Mann Whitney U) demonstrating a substantially elevated level in 8 of the 14 patients. This study demonstrates that this marker is useful as an index of tumour burden and may have application in the identification and follow-up of patients who develop recurrent disease.

n.b. TPS levels given as mean (SEM) and in U/l.

RETINOIDS INHIBIT THE GROWTH OF BREAST CARCINOMA

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The retinoids, a class of natural and synthetic compounds structurally related to Vitamin A, play an important role in cellular growth and differentiation. Three naturally occurring retinoids, retinol, all-trans retinoic acid and 13-cis retinoic acid and the synthetic compound fenretinide are potential modulators of epithelial cell proliferation. The aim of the present study was to assess their effect on growth of the oestrogen receptor (ER) positive cell lines MCF-7 and ZR-75-1 in vitro.

retinoid	dose (mcg/ml)	percent inhibition of growth	
		MCF-7 day 7	ZR-75-1 day 8
retinol	0.15	43.2	69.6
"	0.75	88.5	100
all trans RA	0.15	60.0	20.6
"	0.75	85.3	75
13-cis RA	0.15	71.7	31.5
"	0.75	84.1	97
fenretinide	0.15	+39.6	+32.1
"	0.75	4.0	84.8
"	1.5	12.7	80

This study demonstrates that retinoids inhibit tumour growth in a dose dependant manner at naturally occurring levels. The synthetic fenretinide is less effective than naturally occurring compounds in particular at lower concentrations. This effect of retinoids has major implications for their use in an adjuvant setting.

LARGE LOOP EXCISION OF THE TRANSFORMATION ZONE (LLETZ). SEE and TREAT? TOO MUCH, TOO SOON

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Large loop excision of the transformation zone (LLETZ) has made diagnosis, treatment and cure of cervical intraepithelial neoplasia

(CIN) at the first visit a possibility. Concern has been expressed at the high rates of negative histology in the loop specimens and the unknown long term effects of the procedure. A retrospective analysis of 913 consecutive patients treated with large loop excision of the transformation zone (LLETZ) between May '89 and May '93 was performed with a view to identifying factors common to patients who were subsequently found to have negative histology.

One hundred and sixty five patients had negative histology (18%) had a referral smear and coloscopic assessment graded as CIN 1 or less ($X = 45.33$, $p < 0.01$; OR = 3.32, 95% CI = 2.27 - 4.84). Twenty patients (2.2%) required further treatment for recurrence of cytological or colposcopic abnormalities. Seven (1.8%) came from the group of 165 patients with negative histology. Thirteen (0.8%) recurrences occurred in the group with positive histology.

Follow-up, rather than treatment with LLETZ, of patients with a referral smear and colposcopic assessment graded as CIN 1 or less would reduce by half the incidence of negative histology without missing an invasive carcinoma. Patients with negative histology still require follow-up as recurrence of CIN is as likely to occur in this group as it is in those patients who have positive histology ($X^2 = 3.96$, OR = 2.5, 95% CI = 0.83-6.88; Fisher exact test = 0.07).

SUPEROXIDE DISMUTASE DEFICIENCY IN BREAST CANCER?

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Cytochemical measurement of Glucose-6-Phosphate Dehydrogenase (G6PD) activity is routinely performed under an atmosphere of N₂ to prevent H⁺ reacting preferentially with O₂ and thus being unavailable to reduce a neotetrazolium (NT) H⁺ acceptor. G6PD activity was minimal when benign tissues were reacted under an atmosphere of O₂. An unexplained finding was that in many malignant tissues a significant amount of G6PD activity is retained under O₂. Measurement of G6PD activity in frozen sections from benign breast tissues (N=29) gave a mean of 22.1 ± 1.4 U when reacted under O₂. This declined to 0.81 ± 0.2 U when measured under O₂. In contrast, malignant tissues (N=25) demonstrated O₂ insensitivity in that significant G6PD activity was retained under O₂ (N₂ 36.7 ± 2.8 U; O₂ 26.1 ± 2.9 U; 72% of G6PD activity retained). O₂ insensitivity in malignant tissues has been attributed to the inability of such tissue to remove superoxide radicals. Frozen sections of breast tissue were incubated with the enzyme superoxide dismutase (SOD; 42-420 IU/ml) prior to G6PD measurement. Addition of SOD abolished the O₂ insensitivity of G6PD in the malignant breast rendering its behaviour similar to benign tissues which were themselves unaffected by exogenous SOD. The findings provide a theoretical basis for the O₂ insensitivity phenomenon based on the involvement of O₂ radicals and demonstrate that this investigation is a true metabolic index differentiating between benign and malignant breast tissues.

THE DETECTION OF COLORECTAL LIVER METASTASES USING DUPLEX COLOUR DOPPLER SONOGRAPHY: THE DOPPLER PERFUSION INDEX.

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Colorectal cancer is the second most common malignancy in the

UK with 27,000 new cases per year. 25% of patients will have hepatic metastases at time of presentation. Patients with a curative resection have a 5 year mortality rate of 50%. The presence or absence of liver metastases determines the likelihood of dying from disseminated disease.

Work by Leen using Duplex/Colour Doppler sonography demonstrated clear differences in the patterns of liver blood flow in controls and patients with liver metastases using a parameter called Doppler Perfusion Index (DPI), the ratio of hepatic arterial to total liver blood flow.

This study of 44 patients (10 controls, 10 with overt colorectal liver metastases, and 24 with an apparently curative resection) demonstrated clear separation of DPI values between the metastatic and control groups ($p=0.0022$) 10 patients in the "cure" group also had abnormal DPI's, and we feel this represents the presence of occult liver metastases.

OPHTHALMOLOGY

PUPILLOMETRY IN CATARACT PATIENTS

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The aim of this study is to examine the suggestion that the presence of cataracts sufficient to reduce vision and require surgery does not affect the pupil reflexes. Patients with loss of vision to an equivalent degree from other causes have a relative afferent pupil defect.

The IRIS pupillometer uses an infrared light reflection technique. Infrared light is reflected by the iris and absorbed by the pupil. A Maxwellian view stimulator ensures that retinal illuminance is independent of pupil size. The patient fixates on a cross hair in focus within the light stimulus and is dark adapted for five minutes. A pulse light stimulus of fixed intensity and 1.5s. duration is used. This allows maximal constriction and the 5s. interval between stimuli allows complete redilatation. Thirty patients were studied. The data is computerised and stored on floppy discs.

The latency between the onset of stimulus and the start of constriction was quantified as was that between the stimulus onset and the moment of peak constriction velocity. The mean constriction latency was 120ms. The mean peak constriction velocity latency was 200ms.

These results correspond with values obtained from normal subjects in another pupillometry study carried out in this hospital over the same period of time. This implies that the reflex nerve pathways are not functionally altered by the presence of cataracts.

PUPIL DYNAMICS IN NORMAL PATIENTS

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The aim of this study was to analyse the pupillary light reflex in a group of normal subjects. Measurements were recorded of constriction latency and peak constriction velocity latency. From these measurements, the time lapse between onset of constriction and the peak constriction velocity can be measured. An infrared oculo-graphic pupillometer, based on the technique of reflection and absorption of infrared light by respectively the iris and the pupil was used to measure the light reflex. 37 normal subjects between the ages of 17

and 70 were willing to take part in the study. The light stimulus used to provoke the pupillary light reflex is produced by a stimulator containing a small LED (Light Emitting Diode). The duration of the pulse of light is long enough to obtain a maximal constriction but short enough to prevent pupillary adaptation resulting in redilatation. Results showed that overall the mean constriction latency of each person varied between 100 and 140 milliseconds. The mean peak constriction latency lay between 198 and 200 milliseconds. The constriction latencies using this technique were shorter than values previously established. 180-200 milliseconds is the normal range found by Loewenfeld 1993.

PUPILLARY DYNAMICS IN PSEUDOEXFOLIATION

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The aim of this study is to assess the pupillary light reflexes in a group of patients with the pseudoexfoliation syndrome using the technique of infrared pupillography.

The IRIS infrared pupillometer consists of a frame with infrared light emitting diodes and phototransistors that detect the position of the iris. The light stimulator is clipped to the front of the frame. The stimulator emits yellow light under Maxwellian viewing conditions so that retinal illumination is constant and independent of pupil size. The patient fixates a crosshair positioned at an optically infinite distance and the pupillary system is stimulated with a pulse light stimulus at a fixed intensity. The duration of the pulse is 1.5sec, long enough to obtain a maximal constriction and short enough to prevent pupillary adaptation resulting in redilatation. The period between two consecutive stimuli is 5sec. permitting complete redilatation before presentation of a new stimulus. Subjects are examined in darkness to which they have adapted for five minutes.

41 patients were recruited from the outpatients' clinic. From the average light response curve two parameters of the pupillary light reflex were determined by computer analysis.

1. The latency of constriction to a light stimulus and
2. The normal constriction velocity latency.

Preliminary analysis of the data obtained indicates that there is no significant difference in both these parameters of the direct pupillary reflex between pseudoexfoliation and patients without ocular disease.

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VOLTAGE-ACTIVATED CHLORIDE ION CHANNELS IN NON-PIGMENTED EPITHELIUM CULTURED FROM HUMAN OCULAR CILIARY BODY

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The role of the ciliary body in aqueous humor production is well established although little is known of the ion transport systems involved. The syncytial nature of the ciliary epithelium presents one of the major difficulties in assessing function of the pigmented and non-pigmented layers. In order to determine the nature of the ion channels we have applied Patch clamp techniques to an SV40

transformed cell line isolated from human non-pigmented ciliary epithelium.

The dominant conductance is a voltage-activating Ca^{2+} dependent Cl^- channel [VAC] recorded in both cell-attached and whole-cell configurations. Single channel recording identifies this channel as a 250pS outwardly-rectifying Cl^- channel. The activity of the VAC channel was increased by membrane depolarization and increased cytosolic $[Ca^{2+}]_i$. Whole cell Cl^- currents were also outwardly rectifying [activated by depolarization] and inhibited by the stilbene derivative DIDS [10uM extracellular]. This study identifies the dominant conductance in the nonpigmented epithelium as a Ca^{2+} dependent voltage activated Cl^- channel. The permeability of this channel to other anions such as HCO_3^- is being investigated.

IS THERE A SPECIFIC EYE MOVEMENT STRATEGY TO OVERCOME VISUAL LOSS DUE TO CATARACT?

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Eye movement recordings of reading in patients with cataract were recorded to study whether this group of patients develop a specific strategy to overcome their visual loss. Such a strategy is developed in patients with homonymous hemianopia and macular degeneration.

Infrared oculography was used to record the position of the iris. Immediate visualisation was afforded by a digital storage oscilloscope. A series of reading, writing slow-pursuit and saccadic eye movement tests were performed by the subject. The data collected is fed via an electronic control unit to an analog-to-digital converter and was stored on discs to await analysis. 35 patients were studied.

Subjects were compared to a normal hospital database. Initial analysis of the data suggests that the saccadic velocity and duration is relatively constant over a range of 5-10 degrees as seen from the main sequence. An increased number of saccades with retrograde drift was seen in reading and voluntary saccadic movements. There was also an increased number of retrosaccades, saccades and microsaccades during reading.

The results may have a clinical application in quantifying the degree of cataract, the resultant loss of vision and the requirement for surgery.

PAEDIATRICS/PERINATOLOGY

FEVER AND CONVULSIONS IN GASTROENTERITIS IN CHILDREN

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A retrospective study was carried out of peak rectal temperature and history of convulsions in 140 children hospitalised for gastroenteritis caused by Rotavirus (Rota), Cryptosporidium (Cryp), Campylobacter (Camp) and Shigella (Shig). Four children had 2 organisms. Results are displayed in the Table below:

Organism	Number	Convulsions(%)	% Peak Temp $\geq 39^\circ C$
(CRYP)	33	0	9
(ROTA)	71	3 (4)	20
(CAMP)	26	4 (15)	35
(SHIG)	14	3 (21)	40

Eight convulsions were first episodes and two were recurrent (Camp and Shig). Rota was a disease of younger children and Shig

in older children. Camp was in between the two but tended to cause a milder illness in children > 6 months (2 out of 4 were afebrile). Camp and Shig are significant causes of convulsions with fever in children and it is probably the height of the temperature rather than the rate of rise that is important.

Reference

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DELIBERATE SELF-HARM IN CHILDREN AND ADOLESCENTS - A TWO CENTRE STUDY

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Deliberate self harm is common in child psychiatric practice and no longer lies predominantly in the domain of older adolescents. There is little information on those aged 14 years and under, particularly in Ireland. This study provides demographic data on young people under the age of 14 years who have attempted suicide and their families and also reviews the utilisation of hospital resources.

The charts of children between 7 and 14 yrs. of age admitted to two Centres, Our Lady's Hospital for Sick Children, Dublin and University College Hospital, Galway between Jan. '88 and Dec. '92 with a diagnosis of deliberate self-poisoning were reviewed. 73 cases were identified, 61 in O.L.H.C. and 12 in U.C.H.G. 71% were female and 25% were under 11 yrs. of age. Analgesics were the most common drug taken. The commonest precipitant was a family argument and in 2/3 cases, family disharmony was identified. Suicidal intent was judged to be low in the majority of cases, with a psychiatric disorder being recorded in less than half the cases seen. While considerable hospital and staff resources are utilised, the admission can be viewed as an opportune time to intervene, it provides respite and allows the mobilisation of social and child psychiatric services.

DEVELOPMENTAL INCREASE IN GENE AND PROTEIN EXPRESSION OF SURFACTANT LIPID PRODUCING ENZYME IN FETAL TYPE II CELLS

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Lung development is characterised by a marked increase in the production of phosphatidylcholine, an essential component of pulmonary surfactant. CTP; phosphocholine cytidyltransferase (CT) is the principal rate limiting enzyme required for phosphatidylcholine synthesis. CT is also the prime target for the onset of hormonal regulation of surfactant production. The regulatory mechanisms for this enzyme remain unclear. To study this in detail, the cytidyltransferase cDNA was cloned from fetal type II cells. RT-PCR analysis demonstrated an increase in cytidyltransferase mRNA in maturing fetal type II cells. Western blot and enzyme activity assays confirmed the above. We conclude that the increase in surfactant phosphatidylcholine synthesis by fetal type II cells is due in part to an increase in the amount of cytidyltransferase protein.

Reference

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KAWASAKI DISEASE: A DIFFICULT DIAGNOSIS

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We present experience of four cases of Kawasaki Disease between the ages of 2 months and 2½ years. The initial presenting features were different in each case.

Case No. 1: 2 years and 4 months old. Rash one day, fever, sore throat 4 days. On examination pyrexial, he had blotchy erythematous perineal rash, small cervical glands, pharyngitis, slight redness of lips and conjunctival injection.

Case No. 2: 2 months old. Unwell, sneezing, fever, passing green watery stools one day, rash over the body on day of admission. On examination pyrexial, erythematous rash on limbs and trunk which disappeared in one day. Left otitis media.

Case No. 3: 2 years and 5 months. Fever, vomiting, swelling left side of the neck for 2 days. On examination pyrexial, left cervical adenopathy and bilateral otitis media.

Case No. 4: 8 months old. Fever, irritability for two days, swelling left side of the neck on the day of admission. On examination pyrexial, irritable, left cervical adenopathy, runny nose, congested eyes and throat.

All the patients were referred for cardiological assessment and subsequently received treatment.

A variability of presentation can make Kawasaki Disease a difficult diagnosis in units where it may be infrequently seen.

LATE ASSESSMENT OF AT RISK INFANTS: DRAWINGS AS AN INDICATOR OF CEREBRAL DYSFUNCTION

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Present techniques of developmental assessment fail to detect minor impairments of neurophysiological function in the pre-school child. Such defects, although subtle, can place the child at risk for disordered cognitive and emotional development. Early recognition is the key to successful remedial treatment, yet it is in the younger age group that diagnosis is most difficult. This study aimed to evaluate young children's drawings as an indicator of mental maturity and possible cognitive dysfunction. An age-appropriate modification of the Goodenough Draw-a-Man Test was administered as part of the developmental assessment of 3 to 4 year old children, and a new scoring system devised. The Test is performed in an interactive setting. The child is asked to draw "Mummy's face" and "Mummy's arms and legs", and encouraged to verbalise his intent. During the period of the study, 1985 to 1989, the numbers of babies attending the Assessment Clinic averaged 560 per year. 141 term infants with perinatal asphyxia and 59 infants less than 30 weeks gestation whose outcome was assessed as 'non-disabled' were identified. Their drawings were analysed and compared with age appropriate norms. Scores in the perinatal asphyxia group show a wide scatter, with many disorganised drawings suggestive of perceptual dysfunction. In the preterm group there is evidence of a maturational lag, discordant with growth and development patterns. Gesell and others have shown that certain behaviours are age specific in normally developing children. It appears there is also a sequence of development in representing the human figure and this sequence can be affected by immaturity of the mental processes, or by impaired perceptual function. Prospective assessment of sequential drawings by at risk children may be a useful adjunct in early detection of potential learning disability.

FETAL VARICELLA SYNDROME: A NOVEL PRESENTATION

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Primary varicella infection during pregnancy is rarely seen or reported, as the majority of women have acquired immunity by child-bearing age. It is estimated to occur in 1 in 7,500 gestations. The incidence of fetal varicella syndrome (FVS) reported in retrospective studies ranges from 0-9% among the offspring of women so infected. There have only been about 40 cases reported in the world literature, and criteria for a FVS have only relatively recently been documented.

Fetal varicella syndrome is characterized by a wide range of anomalies including cicatricial lesions of the skin with hypoplasia of tissues in a dermatomal distribution, reduced birth weight, mental retardation, ophthalmological and central nervous system anomalies, neuropathic bladder, and gastro-intestinal anomalies.

We report a case of FVS with multiple anomalies, including colonic atresia associated with abnormal colonic innervation and muscle development, linked to matching dermatomal skin lesions, in association with neurogenic bladder. This is the first time that gastrointestinal atresia has been described which corresponds to a specific area of spinal cord atrophy.

We believe this case demonstrates for the first time a rationale for the occurrence of simultaneous cutaneous lesions and gastrointestinal anomalies, associated with fetal zoster, based on a cord lesion at a level at which both sensory and autonomic nerves exit the spinal canal, by demonstrating spinal atrophy at D11. The existence of a neurogenic bladder is also consistent with this hypothesis.

This case demonstrates that the fetal varicella syndrome is a real entity which depends, like herpes zoster in the adult, on the precise dorsal root ganglion affected as to which clinical features predominate.

NEONATAL IODINE INTAKE: BREAST V BOTTLE FEEDING

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Physiological increases in renal clearance of iodine during pregnancy can result in a transient iodine deficiency state, particularly if dietary replacement is inadequate. This study proposed to investigate maternal and neonatal iodine status with particular reference to iodine nutrition in breast v bottle fed infants. Measurement of breast milk iodine (BMI) in 52 nursing mothers showed a mean value of $84 \pm 7.4 \mu\text{g/L}$ which suggest adequate iodine supply to the neonate. Urinary iodine excretion (UI $\mu\text{g/L}$) was measured in casual urine specimens obtained from 108 mothers and their 3 day old infants. Sixty four mothers were breast feeding and 44 bottle feeding. Breast milk specimens were obtained from 52 nursing mothers. The mean UI in mothers ($76 \pm 5.6 \mu\text{g/L}$) was significantly lower than that of $100 \pm 8.5 \mu\text{g/L}$ in neonates and this was reflected by the number of values $< 50 \mu\text{g}$: 26.5% in mothers v 6.25% in corresponding neonates. While UI and % $< 50 \mu\text{g}$ was similar in nursing and non-nursing mothers, the mean UI of $43 \pm 3.5 \mu\text{g/L}$ in bottle fed infants was significantly lower than that of $100 \pm 8.5 \mu\text{g/L}$ in the breast fed group and % $< 50 \mu\text{g}$ (62.5% v 6.25%) correspondingly greater ($p < 0.001$ in each case). These findings demonstrate the ability of the maternal mammary iodine pump to give priority to the breast feeding neonate and also suggest that breast feeding can maintain a satisfactory level

of neonatal dietary iodine intake which is frequently absent in bottle fed infants.

TREATMENT OF OSTEOSARCOMA WITH A REGIMEN DESIGNED TO MINIMISE LATE SEQUELAE

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The prognosis for osteosarcoma has improved but many survivors suffer significant late sequelae especially cardiotoxicity from doxorubicin and nephrotoxicity from cisplatin. Since 1988 a regimen incorporating less toxic analogues (epirubicin and carboplatin) has been used. 12 patients with primary OS (11 extremity, 1 chest wall) were treated with alternating cycles of IVA (Ifosfamide (+Mesna) 2.5 G/m²/day x 3 continuous infusion; Vincristine 2 mg/m² x 1; Actinomycin D 0.9 mg/m²/day x 2) and VCEE (Vincristine 2 mg/m² x 1; Carboplatin 500 mg/m² x 1; Epirubicin 50 mg/m² x 2; VP16 150 mg/m² x 2). Resection ± endoprosthetic replacement (1 amputation) was performed after 1-3 cycles and treatment continued to complete 5 cycles (30 weeks). Age range was 7-16 years (median 10), 4 boys and 8 girls, 1 with pulmonary metastases at diagnosis. At a median follow up of 28 months (range 2-69 mo) there has been only 1 relapse (combined local and pulmonary) at 6 months. All patients survive with minimal cardiac and renal dysfunction. We conclude that this treatment is effective and should prove less toxic than current regimens: a randomised trial is required to establish which regimen is superior.

PATHOLOGY/CYTOLOGY

THE SPECTRUM OF UNEXPLAINED STILLBIRTH AND SUDDEN INFANT DEATH SYNDROME

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Unexplained stillbirth (U.S.B.) is poorly documented. We have analysed all stillbirths at our unit between 1973 to 1992 (n=475) using information extracted from clinical records and necropsy reports, excluding all cases with an explained cause. From 1973-'82 there were 34 U.S.B. (rate = 1.2/1000 deliveries, 10.6% of total S.B.) and from 1983-'92 there were 60 U.S.B. (rate = 2.37/1000 deliveries, 38.9% of total S.B.), a significant increase (p 0.001). The incidence of sudden infant death syndrome (S.I.D.S.) was then compared over the same period. From 1973-'92 there were 69. Summating these figures, the total U.S.B. + S.I.D.S. from 1973-'82 (34+85) = 119 and from 1983-'92 (60+69) = 129, almost identical figures. In addition there were no discriminating pathological or epidemiological differences between U.S.B. and S.I.D.S. These findings suggest the fall in S.I.D.S. is related to the rises in U.S.B. and indicate that U.S.Bs. could be "intrauterine cot deaths". Thus, we would advocate widening the spectrum of S.I.D.S. to include U.S.B. in order that study of the latter may further enlighten us about the former.

STRATEGIES TO PROMOTE ECONOMIC USE OF ANTIMICROBIAL DRUGS IN AN ACUTE GENERAL HOSPITAL

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This study assesses the effectiveness of the following strategies

in promoting more cost effective use of antibiotics in the hospital. A Registrar was appointed to the Department of Clinical Microbiology whose principle commitment was to a) ensure implementation of the existing general hospital antibiotic policy, and policies within specialist units such as Haematology/Oncology and Intensive Care by regular ward rounds. b) Conduct antibiotic audits to assess the appropriateness of inpatient antibiotic use. c) Provide information monthly, to medical staff on ward use of intravenous (IV) antibiotics. d) Encourage early switch therapy to oral agents. It was found that IV preparations account for 2/3rds of the total cost of antibiotics. Medical patients are prescribed 42% and surgical patients 56% of these agents. The results of antibiotic audit showed a significant reduction in inappropriate use of antibiotics over a six month period and an increased switch from IV to oral therapy. Monitoring antibiotic policies within specialist areas resulted in a 21% reduction cost. It is concluded that close monitoring of antibiotic usage and dissemination of information to junior hospital doctors can influence prescribing and encourage cost effective use of antimicrobials.

PAPILLARY MUSCLE OF THE HEART: THE SPECTRUM OF HISTOLOGICAL CHANGES

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The histology of left ventricular papillary muscle (LVPM) in health and disease is poorly defined. Histological sections of papillary muscle and standard blocks of LV myocardium were compared in a series of 21 consecutive autopsies with respect to ischaemia and other disease processes. The parameters studied included changes of early ischaemia (wavy fibres, contraction banding, eosinophilic fibres), recent infarction, patchy fibrosis, and scar formation. The average number of sections of myocardium examined was 4.3, and 5.5 for LVPM. Of the 21 cases (age range 45 to 86), the LVPM showed evidence of recent or old ischaemia in 16. In all these cases the abnormalities in the LVPM mirrored those found elsewhere in the myocardium. Although in three the changes were of significantly greater degree in the LVPM. A similar concordance of histological findings was seen in two of the remaining cases, one with disseminated aspergillus, the other, with bacterial myocarditis. Three cases showed no abnormality in either myocardium or LVPM and served as baselines. These findings suggest the usefulness of routine sampling of LVPM as an adjunct to autopsy histology and also suggests that papillary muscle dysfunction is more prevalent in IHD than clinical data suggests.

PHARMACOLOGY/THERAPEUTICS

A NOVEL ELECTROPHYSIOLOGICAL SIGNATURE FROM THE PEYER'S PATCHES OF RABBIT INTESTINE

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Due to their role as a sampling port for antigens, intestinal Peyer's patches (PP) have potential as delivery sites for oral peptides and vaccines. Normally, lymphocytes sit in the invaginated basolateral pocket of patch M cells, but it is not known whether the latter have an additional defining electrophysiological signature which might be used for drug targeting. To address this question rabbit ileal segments with and without PP were mounted in Ussing chambers for short-

circuit current (I_{sc}) recording. As shown in the table, transepithelial resistance (TER) was increased while basal I_{sc} was decreased in segments containing PP (*P < 0.002, n = 15).

Basal electrophysiological parameters from rabbit PP and matched controls

	PP	Control
TER ($\Omega \cdot \text{cm}^2$)	100.1 \pm 10.2	26.9 \pm 3.0*
I _{sc} ($\mu\text{A} \cdot \text{cm}^{-2}$)	34.7 \pm 6.3	90.2 \pm 8.6*
PD (mV)	-2.4 \pm 0.2	-2.5 \pm 0.4

Basolateral addition of carbachol (10 μM) caused an increase in outward current in PP epithelia. The EC₅₀ was 2 μM and the response could be inhibited by low concentrations of pirenzepine, tetrodotoxin and by replacing Krebs with bicarbonate-free solution. In comparison, control intestine responded to carbachol with an increase in inward current, also with an EC₅₀ of 2 μM . The results support the hypothesis that M cells of rabbit PP are responsible for electrogenic bicarbonate absorption when stimulated by cholinomimetics, whereas intestinal columnar cells respond to these agents by electrogenic chloride secretion.

THE COST OF PRESCRIBED DRUGS TO MEDICAL PATIENTS DISCHARGED FROM ACUTE HOSPITAL CARE

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Cost containment is increasingly on the agenda, especially when prescribing. This is particularly difficult at the hospital-general practitioner interface⁽¹⁾. We calculated drug costs in 107 consecutive medical patients on admission and on discharge from hospital. The estimated (mean \pm SD) daily cost of drugs per patient rose from $\text{£}0.90 \pm 1.32$ on admission to $\text{£}2.06 \pm 2.57$ on discharge ($P < 0.01$), partly due to an increased number of drugs on discharge (4.6 ± 3.0 vs. 2.8 ± 2.4 on admission, $P < 0.01$), but also due to an increased mean daily cost per item per patient [from $\text{£}0.23 \pm 0.30$ on admission to $\text{£}0.38 \pm 0.39$ on discharge ($P < 0.02$)]. Neither patient age nor duration of hospital stay influenced this cost. We conclude that medical patients discharged from hospital are prescribed more drugs and that each item tends to be more expensive. We believe that there is a need for an agreed hospital/general practitioner formulary and that community physicians should be represented on hospital formulary committees concerned with choice and cost of medications.

Reference

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ANALYSIS OF ANTI-ULCER DRUG USAGE AMONG GMS PATIENTS IN THE CATCHMENT AREAS OF THE LARGE DUBLIN HOSPITALS IN AUGUST 1992

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The aim of this study is to measure prescribing of anti-ulcer drugs for GMS patients in the catchment areas of the main Dublin teaching hospitals and to see whether there is any evidence of differences between them.

The Eastern Health Board has assigned each electoral ward and District Electoral Division (DED) to the catchment area of whichever hospital is most appropriate in terms of proximity and access. Therefore although a strictly defined catchment area is not available

for the principal Dublin hospitals a catchment in terms of DEDs is definable for each major acute general hospital. The Health Information Unit routinely assigns a DED code to the GMS prescription claims records received from the GMS Payments Board each month. All records were extracted for the following anti-ulcer drugs: cimetidine, ranitidine and omeprazole, from the August 1992 GMS claims details file. The number of claims for each drug was computed and classified by hospital catchment area using the DED code as the common key.

There were 8,341 claims for anti-ulcer drugs for GMS patients resident in Dublin, and 95% of these (7,964) were DED coded. There was considerable variation between catchment areas in the pattern of drug usage (Table I) and in the individual anti-ulcer drugs used.

Table I

Hospital	No. of claims	Percentage of total
Beaumont	1338	16.8
James Connolly	696	8.7
Mater	1862	23.4
Meath	1139	14.3
St. James	1958	24.6
St. Vincents	971	12.2
TOTAL	7964	100.0

The findings suggest that hospitals may have a significant effect on the usage of what is the most expensive group of drugs prescribed in the GMS. Further investigation is needed to identify the reasons for these differences.

INTERETHNIC DIFFERENCES IN DRUG PROTEIN BINDING AND α_1 ACID GLYCOPROTEIN CONCENTRATION

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Interethnic differences in drug responsiveness may in part be accounted for by differences in drug disposition. We investigated the reversible binding interaction between representative acidic (warfarin) and basic (lignocaine) drugs and plasma constituents by equilibrium dialysis in 20 healthy age and sex matched Iranian and Irish subjects. The unbound fractions of warfarin and its major binding protein, albumin, were similar in the two groups. In contrast unbound lignocaine was higher in Iranian subjects (49.6 ± 7.0 vs $37.7 \pm 3.5\%$, mean \pm SD, $p < 0.05$). The lower binding in Iranians was associated with lower plasma concentrations (48.8 ± 10 vs 60.5 ± 8 mg/dl, $p < 0.01$) of α_1 acid glycoprotein which also binds tricyclic antidepressants and other antiarrhythmics. Such alterations may result in differences in responsiveness in addition to predictable pharmacokinetic consequences. Protein binding should be included in comparative studies of drugs in subjects of different races.

DOCTOR'S KNOWLEDGE OF COST AND GENERIC NAMES OF DRUGS

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Attention has focused lately on the desirability of generic prescribing as a means of controlling spiralling healthcare costs. The percentage of prescriptions written generically is about 15% in

general practice and approximately 30% in our hospital. To determine if prescribers knew generic names and the relative costs of different drugs we asked 50 of the medical staff the cost per patient per day of a standard dose and the generic names of each of the 13 most commonly prescribed drugs.

SHO's gave a mean of 92% correct replies for generic names followed by Consultants (90%), Registrars (88%) and Interns (85%). The respondents over-estimated the cost of all the drugs in the survey except the most expensive; Cefotaxime. Range: Digoxin (Lanoxin PG), - cost over-estimated by 1400%; Claforan (Cefotaxime) - cost under-estimated by 100%.

The survey demonstrated that doctors have a good knowledge of the generic names of drugs and this is not the reason for a low level of generic prescribing. Doctors generally greatly over-estimate the cost of inexpensive drugs and under-estimate the cost of the most expensive drug in the survey.

EDUCATIONAL VALUE OF DRUG ADVERTISEMENTS

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Recent studies described advertisements in various medical journals as misleading and breaching guidelines laid down by the pharmaceutical industry¹. As no audit had been conducted in Ireland we assessed the quality and quantity of information in 100 consecutive pharmaceutical advertisements in Irish medical journals and cross referenced them with the Federation of Irish Chemical Industries data sheet compendium; 29 occupied a full page (A3 or A4) or more, 87 were in full colour and 27 illustrated the product. Size was not related to the quantity of information contained. Only 30 advertisements stated possible side effects or contraindications of which 50% and 10% respectively did not include all the information provided by the compendium. In 78 advertisements, claims were made about the product, 25 of which were supported by references. Of 100 doctors, (30 general practitioners, 36 registrars/consultants, 34 SHO's/interns) completing a questionnaire relating to 10 randomly selected advertisements, 72 felt the advertisements were not of good educational value and 80 were not comfortable that information relating to side-effects, contra-indications or precautions had been excluded. Our study highlights inadequacies in pharmaceutical advertisements in Ireland and the need for independent (medical/pharmaceutical) monitoring to assure acceptable scientific standards and informed prescribing of drugs.

Reference

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A DERMAL ASPIRIN PREPARATION WITH UNDETECTABLE SYSTEMIC BIOAVAILABILITY RESULTS IN MARKED SUPPRESSION OF PLATELET CYCLOOXYGENASE

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Transcutaneous administration of aspirin may inhibit platelets while avoiding the gastrointestinal toxicity of oral preparations. We examined the effects of a patch containing solid phase aspirin 160mg

in an acrylic matrix in 4 male volunteers. This preparation delivered aspirin 40mg/24hr over 100cm². Plasma aspirin and salicylate and serum TXB2 were determined by gas chromatography, mass spectrometry. Aspirin applied for 14 days resulted in 78±6% suppression of TXB2, an index of platelet cyclooxygenase activity, while plasma aspirin levels were below the sensitivity of the assay (1 ng/ml). Plasma concentrations of salicylate, the inactive metabolite of aspirin, were 90±18ng/ml in 3 volunteers. As serum TXB2 must be reduced by at least 93% for maximum suppression of platelet activity, we addressed ways to enhance aspirin delivery through the skin. Limonene 12% increased the rate of transfer of aspirin across rat skin by 4-fold in vitro. Patches containing limonene were applied to 2 volunteers and resulted in 91% and 99% suppression of serum TXB2. Plasma salicylate levels were 179 and 166 ng/ml respectively with no detectable aspirin. These dermal aspirin preparations inhibit platelet cyclooxygenase locally at the site of application with low systemic bioavailability of active drug. This provides a novel parenteral approach of achieving selective inhibition of platelet cyclooxygenase in man.

LIPOSOMAL DOXORUBICIN IN THE TREATMENT OF KAPOSI'S SARCOMA ASSOCIATED WITH AIDS - AN IRISH PROSPECTIVE

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Liposomal doxorubicin has been shown to improve drug delivery to Kaposi's sarcoma (KS) lesions while reducing delivery elsewhere in the body, thereby reducing potential toxicity. We report our experience with Liposomal Doxorubicin in the Irish HIV+ cohort. 7 patients were followed prospectively with histologically proven KS who were treated with Liposomal Doxorubicin at 20 mg/m² monthly for 6 months and subsequently treated with a maintenance dosage of 10mg/m². One patient had disseminated pulmonary, gastrointestinal and cutaneous disease, 2 patients had extensive KS associated peripheral lymphoedema, 2 patients had gastrointestinal and cutaneous disease and the remaining 2 patients had extensive cutaneous disease. 1 patient had previously been treated with Vincristine and Bleomycin with poor clinical response. Patients were assessed for tumour response and drug toxicity. All concomitant therapies and Stage IV illnesses were recorded. All 7 patients have shown good tumour response. Patient tolerability & compliance have been excellent. One patient developed recurrent anaemia, but this may have been compounded by myelosuppressive polypharmacy. To date only One patient has received G-CSF support. Previous chemotherapy entailed the use of multiple drugs with associated accumulative myelosuppression. Liposomal doxorubicin may enable us to maximise tumour response, to improve patients quality of life and at the same time reduce toxicity. Our experience to date appears to confirm this.

INTERACTION OF ALCOHOL WITH SODIUM-LITHIUM COUNTERTRANSPORT

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Variations in the activity of the transportation that mediates external sodium stimulated lithium efflux (SLC) have been reported in a number of disease states, but data on its possible interaction with

environmental factors are scanty. We studied its possible interaction with alcohol. Eleven healthy volunteers (M:F, 4:7) aged 31.1 ± 5.9 years (mean \pm SD) and weighing 66.9 ± 8.3 kg participated. SLC was measured before and one hour after alcohol (0.8g/kg) with "Coke" as vehicle. In some ($n=4$), additional measurements were made at 4 and 24h post alcohol. Alcohol increased passive lithium efflux at 1.0h (0.208 ± 0.061 vs 0.223 ± 0.067 mmol/L cell h, $p < 0.007$) and at 4.0h (0.210 ± 0.052 vs 0.251 ± 0.051 mmol/L, $p < 0.038$) but not at 24h post dosing (0.210 ± 0.052 vs 0.222 ± 0.048 mmol/L). V_{max} fell (0.381 ± 0.194 vs 0.317 ± 0.180 mmol/L cell h, $p < 0.002$) and (0.540 ± 0.129 vs 0.443 ± 0.163 , $p < 0.038$) and (0.540 ± 0.129 vs 0.448 ± 0.156 , $p < 0.035$) respectively. K_m values (median, mmol/L) were unaltered - 109 vs 116, 115 vs 120 and 115 vs 114 respectively. "Coke" alone did not alter any of the parameters.

We suggest that alcohol increases passive lithium efflux as well as inhibits SLC. There was a recovery of the former within 24h, but the latter effect persisted.

GENERAL PRACTICE PRESCRIBING: INFLUENCES OF PHARMACEUTICAL REPRESENTATIVES AND CONSULTANT/HOSPITAL RECOMMENDATIONS

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To establish the main sources of information used by General Practitioners in prescribing "old" (on the market more than 5 years) and "new" (less than 5 years) drugs, we carried out a postal survey among 200 randomly selected members of the Irish College of General Practitioners (ICGP) and received 105 completed replies.

For both old and new drugs, prescribers considered the Drugs and Therapeutics Bulletin (DTB) and medical journal articles, the most important sources of information in approximately 75% of cases. Recommendations from Consultants/Hospitals and Pharmaceutical Representatives were considered relatively important for new drug information only while MIMS, BNF and non sponsored meetings were of moderate importance for both old and new drugs. Direct mail, journal advertisements and sponsored local meetings were considered unimportant. However when asked about the initial source of information on the last new drug prescribed (e.g. omeprazole, fluoxetine, ofloxacin), Pharmaceutical Representatives and recommendations from Consultants/Hospitals were the sources in 42% and 37% of cases respectively with medical journal articles (8%) and DTB (0%) unimportant.

Many prescribers underestimate the considerable influence of Pharmaceutical Representatives and recommendations from Consultants/Hospitals when prescribing new drugs.

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GENERIC PRESCRIBING: PRACTICES AND CONCERNS IN GENERAL PRACTICE

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Only 10-20% of general practice prescriptions are written generically in contrast to 40-50% in Northern Ireland. We surveyed 200 randomly selected members of the Irish College of General

Practitioners (ICGP) to establish the level of attendance at meetings on economic or generic prescribing over the past year. We then asked each participant to estimate the percentage of prescriptions written generically and to indicate his or her main concerns about generic prescribing.

We received 105 completed questionnaires and 57% of respondents had attended a meeting on generic or economic prescribing of which 38% of cases were sponsored by the ICGP and 29% by local G.P. groups. Just under half of the prescribers felt that they were 25% or less of their prescriptions generically while 38% estimated that 25-50% of prescriptions were in generic form. Only 15% wrote over 50% of prescriptions generically. Three quarters of prescribers expressed concern about the reliability and quality of generic products while 65% were concerned about the risk of prescriber liability in certain cases of adverse events. The substitution of more expensive branded products for generics by Pharmacists was of concern to 44%. The risk of reduced pharmaceutical company sponsorship in the event of increased generic prescribing was of minor concern. These are important considerations, which need to be addressed if the rate of generic prescribing in general practice is to increase.

Supported by the Health Research Board.

LIPID PEROXIDATION AND HYPERTENSION

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Plasma lipid peroxide concentrations measured as malondialdehyde (MDA) are elevated in patients with vascular diseases and in diabetes. A number of studies suggest that populations with a high intake of antioxidant vitamins C and E have reduced prevalence of ischaemic heart disease (IHD). We therefore measured MDA with high-performance liquid chromatography in 41 patients with primary hypertension. The relationship of MDA concentration to gender, age, smoking habits, hypertensive disease, IHD, obesity, positive family history of IHD and hypertension, intake of anti-hypertensive drugs (single drug or combination) was examined. Results showed that the MDA value was significantly higher in hypertensive patients than in healthy people (1.18 ± 0.32 umol/L vs 0.48 ± 0.1 umol/L, $p < 0.001$). The addition of vitamin C in concentrations of 50, 100, 200 mg/L to the plasma of these patients showed a dose related antioxidant effect with a reduction ($p < 0.001$) in the normal increase in MDA concentration that occurs over 5 days at room temperature. Whether this occurs in vivo requires to be studied.

PSYCHIATRY

IN-PATIENT LIAISON PSYCHIATRY: THE EXPERIENCE OF TWO IRISH GENERAL HOSPITALS

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The aim of this study was to examine the provision of psychiatric care to in-patients in two Irish general hospitals without psychiatric units and to comment on (a) how this service model compares with previous Irish studies, (b) whether it meets the goals of liaison psychiatry, and (c) the implications for future service planning.

Demographic and clinical details relating to all the psychiatric consultations to in-patients (i.e. there was no emergency service to

the casualty department) in two general hospitals were collected over a six month period.

Although the service was provided on a non-emergency basis the referral rate [1.6% of total admissions], patient characteristics, reasons for referral, diagnoses, and suggested management strategies were very similar to previous Irish studies. Assessment of deliberate self-harm cases was the most common reason for referral [37.9% of 145 referrals]. Notably, there was a high level of diagnostic accuracy from non-psychiatric colleagues in this liaison model.

This study, of a service model characterised by an emphasis on liaison, points to efforts on the part of the psychiatrist to improve communication with medical and surgical colleagues as being of primary importance in the development of general hospital psychiatry services.

SCHIZOPHRENIA AND PARENTAL SOCIAL CLASS

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If lower social class is related to a causal factor in the development of schizophrenia, one might expect that an excess of patients should be born into the lower social classes.

This study examined parental occupation data obtained from the birth registration records of 391 ICD-9 schizophrenic first admission patients to a community psychiatric service, who were subsequently hospitalised. The paternal occupation of the next same-sex birth in the registration district was recorded and used as a matched control. We determined parental social class in accordance with the Irish Census based Social Class Scale.

We found no evidence that the patient group originated disproportionately in the lower social classes. Fathers of patients with schizophrenia had the same social class profile as the control group except in Social Class IV where patients' fathers were underrepresented ($L_2=4.2$, $df=1$, $p=0.04$). This finding was confined to the fathers of male patients ($L_2=3.4$, $df=1$, $p=0.06$).

Significant social class of origin differences were found in relation to patient's age at first contact with psychiatric services, at first ever psychiatric hospital admission and at first admission with schizophrenia. Patients originating in Social Class I were youngest at each point of contact, while patients with fathers in Social Class VI tended to be oldest. When analysed by sex, these differences applied only to females.

DERMATOGLYPHIC MEASUREMENTS AND LATERAL PREFERENCES IN SCHIZOPHRENIA: A CONTROLLED STUDY

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Finger and palm prints were taken from 82 patients with an DSM-III-R diagnosis of schizophrenia and 72 controls without a family history of psychiatric disorder. Dermatoglyphic measures included qualitative measures; presence or absence of single palmar creases, hypothenar patterns; and quantitative measures; bilateral total finger ridge counts, bilateral absolute finger ridge counts, total finger ridge count (R+L) and absolute finger ridge count (R+L). Measures of dermatoglyphic asymmetry included difference in A-B ridge counts, total finger ridge counts, absolute finger ridge counts and total finger ridge count for homologous pairs and number of discordant pattern

pairs. Laterality was assessed by means of the Edinburgh Handedness Inventory. Subjects were classified as right, left or mixed handed according to a 90% cutoff criteria. Similarly subjects' eye and foot preferences were divided into right, left and mixed. Stepwise logistic regression analysis identified three variables in addition to sex and age to be associated strongly ($p<0.1$) with the outcome measure i.e. whether patient or control; signed difference in absolute finger ridge counts ($p=0.049$), difference in total ridge count for the 5th digit ($p=0.013$) and foot preference ($p=0.066$). These findings suggest that quantitative dermatoglyphic measures in combination with foot preference can predict schizophrenia.

This study was supported by the Health Research Board, Ireland, the Stanley Foundation and the St. John of God Order.

PRENATAL EXPOSURE TO THE 1957 INFLUENZA EPIDEMIC AND SCHIZOPHRENIA. A CASE-CONTROLLED, FOLLOW-UP STUDY

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An increased incidence of schizophrenia has been reported following prenatal exposure to the 1957 Asian influenza epidemic. We conducted a long-term follow-up Study of 1218 individuals, exposed to this influenza strain during prenatal life, who had been prospectively studied from 1957 by one of the authors (VPC) to ascertain the possible association of prenatal exposure to influenza with congenital deformity. 591 were born to mothers who had symptoms of influenza during pregnancy and 627 were children of controls who did not have such symptoms. The names and the dates of birth of the sample were matched against the case register records of all psychiatric hospitals in Dublin and an ICD-9 diagnosis obtained for each member of our cohort who had received an inpatient treatment for psychiatric illness. In addition, we traced and interviewed 525 subjects or a close family: 238 individuals from the 'exposed' group and 287 from the control group. No excess of functional psychosis was found overall in the 'exposed' group. Four cases of ICD-9 schizophrenia were identified: 2 from the 'exposed' group and 2 from the control group. We conclude that an 'influenza effect', if present, was not of sufficient magnitude to be detected in a sample of this size.

This study was supported by the Stanley Foundation, the Health Research Board, Ireland, and the St. John of God Order.

CRANIOFACIAL ANOMALIES IN SCHIZOPHRENIA: CLUES TO THE TIMING OF DEVELOPMENTAL DISTURBANCE

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Objective: Evidence suggests that schizophrenia results from disturbed prenatal development, yet, information regarding the timing of this disruption is sparse. Minor physical anomalies (MPAs) reflect developmental disturbance, such that patterns or clustering of MPAs could be clues to the timing of prenatal disruption in schizophrenia

Method: Using a new scale, based on quantitative measurements, 174 patients with DSM-III-R schizophrenia and 80 age and sex-matched non-psychiatric controls were examined for minor physical anomalies.

Results: Patients displayed significantly more anomalies than controls. These included anomalies of the eyes (epicanthic skinfolds, $P < 0.003$), ears (widened helices, $p < 0.001$, hypoplastic lobes, $p < 0.007$), and mouth (high and narrow palates, $p < 0.0001$). Using logistic regression, the anomalies that best differentiated patients from controls included: skull base width ($p = 0.003$, lower facial height ($P = 0.04$), biocular diameter ($P = 0.001$), mouth width ($P = 0.01$), ear protrusion ($P < 0.001$), supraorbital ridge ($P < 0.001$), epicanthus ($P < 0.002$), bifid tongue ($P = 0.004$), palatal ridges ($P < 0.001$) and palatal height ($P = 0.004$).

Conclusion: These anomalies of the craniofacial area are related to the developing brain and central nervous system and result from disturbance, by genetic and/or environmental factors between the 8th and 22nd weeks of gestation. These findings suggest that this period may be critical to the aetiology of schizophrenia.

CORPUS CALLOSAL MORPHOLOGY AND ITS RELATIONSHIP TO INDICES OF NEURODEVELOPMENT

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The findings of morphometric studies of the corpus callosum (CC) in schizophrenia have been inconsistent. The present study investigated measures of corpus callosum in relation to indices of abnormal neurodevelopment in schizophrenia.

Thirty-four patients with schizophrenia and 15 controls were studied with Magnetic Resonance Imaging using a Siemens Magnetom (1.5T). Linear and area measurements of the CC at the midsagittal section were obtained using the semi-automated system, 'ANALYSE'.

No significant differences were found between patients and controls for the following CC measurements; length, width of anterior, middle and posterior sections, frontal length and area. Among patients with schizophrenia, males with a family history of the disorder demonstrated an increase of the CC area ($p = 0.04$) and an increase of the width in the middle CC ($p = 0.05$). Males with a history of obstetric complications demonstrated an increased ($p = 0.01$) frontal length (distance from CC genu to the most anterior point of the frontal lobe). CC measures were not related to handedness or minor physical anomalies.

This study was supported by the Health Research Board, Ireland and the St. John of God Order.

TURNER'S SYNDROME AND SCHIZOPHRENIA, WITH STRUCTURAL BRAIN ABNORMALITY ON MRI SCAN

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Monosomy of the X chromosome, also known as Turner's syndrome (TS) was first described by Turner in 1938. While it is one of the commonest sex chromosomal anomalies, psychosis has only rarely been described in TS. We report a case of a 28 year old girl with

TS and a DSM III diagnosis of schizophrenia. Magnetic resonance imaging (MRI) demonstrated prominent dilatation of the anterior horn of the lateral ventricles which was present at the onset of the illness. This case may support the genetic pseudoautosomal locus theories of schizophrenia. The finding of left temporal lobe abnormality provides further support for the role of this brain area in the development of schizophrenia.

This study was supported by the Health Research Board and the St. John of God Order.

SUDDEN AND UNEXPECTED DEATHS IN PSYCHIATRIC IN-PATIENTS

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Odegaard 1951, Malzberg 1952 estimated that the risk or death in new admissions to psychiatric hospitals was 4 to 10 times that of the general population. The purpose of this study was to review the causes or sudden and unexpected deaths in the psychiatric in-patient population in Ireland from 1983-1991, with a view to learning if any change in management indicated. Secondary objective was to ascertain the mortality rate for psychiatric in-patients over time. This was a retrospective study of the records or all patients whose deaths were notified between 1983 and 1991. Sociodemographic details, diagnosis, past history, history of deliberate self harm or violence, medication use and cause of death, results of post mortems were studied. A total of 188 unexpected deaths. 120 (63%) were due to suicide. There were 13 sudden cardiac deaths and 13 deaths where adverse reaction to drugs may have been significant. Barbiturates and Benzodiazepines were used in combination in five or these patients. There were three deaths due to neuroleptic malignant syndrome, 11 due to choking or aspiration, 10 patients from complications or fractures, 2 due to pulmonary emboli post ECT.

Conclusions: While not all suicides can be prevented this study showed that symptomatic improvement may be misleading and it is important that in-patients at risk of suicide are not discharged prematurely until adverse life events are resolved adequately. It is essential that in-patient units provide safe, secure environment where violent patients may be safely cared for, without the need for a chemical strait jacket. A case is made for avoiding use of high dose barbiturates for sedative purposes.

PUBLIC HEALTH/EPIDEMIOLOGY

INVESTIGATION OF AN OUTBREAK OF HEPATITIS A AMONG IRISH HAEMOPHILIACS

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An outbreak of hepatitis A (HAV) occurred among Irish haemophilia A patients in 1992. Similar outbreaks were reported in Italy, Germany and Belgium. The aim of this study was to investigate the outbreak, and test the hypothesis that it was caused by exposure to solvent-detergent (SD) treated factor VIII.

The study commenced in early 1993. The study population was derived from Irish haemophilia A patients. The outbreak was analysed by person, place and time. A case control study was devised to investigate the role of blood products and other environmental factors. The response rate was approximately 90%.

Haemophilia A cases with acute HAV (29) were compared with haemophilia A controls (78) by exposure to SD-treated factor VIII and other environmental factors. Blood product data were obtained from the National Haemophilia Register and environmental data were obtained by a telephone-administered questionnaire.

The incidence of HAV infection was higher in younger patients and those with more severe bleeding disorders. Contact with hepatitis, with children, and exposure to factor VIII were associated with increased risk. The association with factor VIII was the strongest risk factor after controlling for other factors (odds ratio 27.6, 95% CI 6.5-117.3). A dose-response effect was demonstrated.

THE ORIGIN OF AN EPIDEMIC (1988-1993)?

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The purpose of the Study was to investigate the characteristics of an epidemic of an infection that occurred in a school under care of the author, also, to seek evidence of spread in the Practice Area. The method used was a study of the Health Records at the School (boarders only) (1988-91) and of records of a random selection of practice patients (1990-93). Investigations were initiated in an endeavour to find the causative organism (serology & culture). From the records graphs showing the monthly incidence were prepared and scatter graphs showing more detail. Five hundred cases occurred in the school out of a boarder population of about 350 pupils. January/February were the months of highest incidence but cases were scattered throughout the academic year. The rate of infection was highest among new pupils, the rate of recurrence was as high as 30%. In January 1992 an outbreak of acute flu like illness appeared to put an end to the epidemic in the school. Clinically cases could be divided into MRI, GIT upset or MRI/GIT recurring cases sometimes changed from one to the other. In the Practice Area there was ample evidence of similar cases from two of these (in one family) coxsackie B2 was cultured. Otherwise viral studies were negative.

IRISH PRIMARY SCHOOL CHILDREN'S ATTITUDE TO SUN

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There is increasing evidence implicating sunburn, particularly that acquired in childhood in the aetiology of malignant melanoma. Educational campaigns have failed to modify adults' and teenagers' subsequent behaviour in the sun. In 1993, a five nation European co-operative study funded by Europe Against Cancer was carried out, to ascertain children's attitudes to sun exposure and based on the material produced, to design educational material appropriate for primary children. The study in Ireland was carried out in the North East Health board. 1231 children ranging in age from 5-12 years completed the study using the Write And Draw Technique, which enables children to communicate their ideas without adult interference. Analysis of results showed that with increasing age there was a slight increase in awareness of sunburn, only 0.2% were aware of skin cancer. Most children felt the sun was good for the skin, being tanned was desirable and very few were aware of the need for sun-protection. This technique was useful in surveying young children's attitudes and highlights the need for primary school education regarding sun exposure.

HEPATITIS A - WATER IMPLICATED

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In the summer of 1993 an outbreak of hepatitis A occurred in an area of ribbon development one mile outside a small town in County Cork. 14 cases of hepatitis A occurred within a 2 month period, 2 were hospitalised. A further 8 cases occurred in the nearby town, 6 were close contacts of original cases.

Thirteen dwellings are clustered along a half mile section of road, cases were reported from 7. All the houses use septic tanks for the disposal of effluent and have private wells for the supply of water. Analysis of the 13 water supplies identified 8 with evidence of severe contamination, 7 had reported cases of hepatitis. The water supply to the other 5 houses had little or no evidence of contamination. The relationship between cases of hepatitis and water contamination is highly significant (Fisher's exact test; two-sided; $p=0.0047$).

The following actions were taken to control the outbreak: Residents were advised not to use the contaminated water; an emergency supply was provided by the local authority; information leaflets were provided; human normal immunoglobulin was offered to recent contacts. The possibility of water contamination must be considered in areas of high density of houses with septic tanks and well water supply. Stricter controls should be imposed at the planning stage.

AN OUTBREAK OF CRYPTOSPORIDIOSIS IN SOUTH LONDON

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An outbreak of cryptosporidiosis affecting 44 people was identified through local surveillance at a South London Public Health Laboratory in January and February 1991. Preliminary enquiries revealed no common factors other than geographical association. A case control study showed a statistically significant association between illness and consumption of tap water supplied by a particular water company as well as a dose response effect. There were no apparent breaches or irregularities in the water distribution system and no indication of a problem through routine monitoring indices. This incident demonstrated the problems of establishing the source of cryptosporidiosis outbreaks in the absence of environmental abnormality and suggested that water conforming to current treatment standards may occasionally contain sufficient numbers of cryptosporidium oocysts to cause sporadic cases or clusters.

HUMAN IMMUNODEFICIENCY VIRUS INFECTION IN CHILDREN IN IRELAND

K. Butler, E. Griffin, T. Conlon, E. Hayes, T. Clarke, I. Hillary.

The Paediatric AIDS Project, Coombe Women's Hospital, Rotunda Maternity Hospital, National Maternity Hospital, Our Lady's Hospital for Sick Children, Children's Hospital, Temple Street and The Virus Reference Laboratory, UCD.

This study aims to characterise the paediatric HIV epidemic in Irish children and to determine the vertical transmission rate. Infants born to HIV infected mothers are evaluated at birth, 3, 6, 9, 12, 15 and

18 months, and depending on HIV infection status, either 3 monthly or yearly thereafter. Between August 1985 and Dec. 1993, 80 infants born to 62 HIV+ mothers were identified. 95% of maternal HIV infection resulted from IVDU, either by the mother (82%) or her partner (13%). 13 (21%) of the mothers are now dead. Of 60 children ≥ 15 months when last evaluated, 7 are infected, 52 uninfected, and one is of indeterminate status, for an overall transmission rate of 11.8% (CI 4 - 20%). HIV infection has also been confirmed in 2 additional infants < 15 months of age. Of 55 seroreverters, the median age at documented seroreversion (SR) was 16 months, the median duration of follow-up post SR is 23 months (range 0-78), and their median age is now 68 months (range 18 - 111). No seroreverting child has subsequently proved infected with HIV. Re-emergence of a single band on Western Blot was noted on at least one occasion in 15/55 (27%) seroreverters. Of the 9 infected infants, 1 died of AIDS at 27 months, 8 survive (1 CDC P1, 7 CDC-P2, 3 of whom have AIDS). IVDU is the main factor underlying HIV infection in Irish children. Despite early reports that the prevalence of HIV infection was leveling within the community, the identification of 12 HIV+ infants born in 1993 gives little reason for optimism, as this is but a fraction of the true numbers affected, and mandates urgent provision of adequate services for these children and their families.

NOTIFICATION OF MENINGOCOCCAL DISEASE AND HAEMOPHILUS INFLUENZAE MENINGITIS IN CHILDHOOD

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Medical practitioners are required by law to notify confirmed or suspected cases of bacterial meningitis (including meningococcal septicaemia) to the Medical Officer of Health (MOH). Completeness of notifications for culture confirmed meningococcal disease and Haemophilus influenzae meningitis was ascertained for 1987-1991 inclusive. Laboratory record review identified positive isolates from blood culture and cerebro-spinal fluid for 4 Dublin hospitals serving the Eastern Health Board paediatric population (<14 years). Infectious disease registers held by the MOH in Dublin, Kildare and Wicklow were inspected for evidence of notification of each culture positive case. Only 131 (44%) of 298 culture positive cases had been notified. The notification rate for H. influenzae meningitis (33%) was significantly lower than that for meningococcal disease (53%) (OR=0.4, 95% CI=0.3-0.7; $p < 0.01$). Notification rates for both forms of meningococcal disease were not significantly different (OR=1.3, 95% CI=0.6-2.8). All laboratory cases identified should have been notified. Public health assessment is required with each condition as Rifampicin prophylaxis can prevent secondary cases in close contacts of both diseases. Improved notification is essential not just to comply with the law but more importantly for better management of these diseases.

RESISTANT BOVINE AND ATYPICAL MYCOBACTERIA [MOTT] (1986-1993): COMPARISON WITH 1982-1985

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We have reported our experience with bovine, MOTT and resistant TB (IMJ, 1987; Vol 80: 66-67). We reviewed our experience between 1986-1993.

	1982-1985	1986-1993
Total culture positive patients	1002	775
Resistant M.TB	16	28
M.Bovis	9	13
MOTT	11	19

χ^2 analysis shows: (1) incidence of culture positive TB reduced by 50%. (2) absolute incidence of M. Bovis, resistant TB, MOTT has not changed. (3) relative proportion of cases due to resistant M.TB increased ($p=0.0007$). (4) relative incidence of bovine TB not changed ($p=0.014$). (5) relative incidence of atypical TB (MOTT) has increased ($p=0.028$). (6) relative increase in MOTT is not explained by patients with HIV/AIDS. (7) Only 1 patient with resistant (Inah resistance) had AIDS. No multi-drug resistant TB was seen in HIV positive patients.

Conclusion: Overall incidence of TB has declined. Relative importance of resistance and atypical TB has increased. Bovine TB has not changed significantly.

NEONATAL BCG VACCINATION IS ASSOCIATED WITH FEWER CASES OF TUBERCULOSIS IN CHILDHOOD

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Analysis of the 1991 National TB Survey indicates that a policy of neonatal BCG is associated with significantly fewer cases of TB in people <15 yrs ($p=0.0000019$). Some 900-1100 children need vaccination to prevent one case of childhood TB. In 1991 neonatal BCG was associated with preventing 6070 cases of TB in childhood (< 15 yrs). The incidence of TB in the survey was 16.3 per 100,000 for the entire country. Previous studies have shown benefit associated with neonatal BCG vaccination -

1. A. Shannon, et al
Eur. Resp. J. 1991; 4: 778-782
2. L. Clancy, et al
Evaluation of Neonatal BCG in Ireland Am. Rev. Resp. Dis. 1990; 141; No.4: Part 2: A894
3. Eastern Health Board BCG Committee Report published by E.H.B., Dublin 8.
4. H. Johnson
BCG policies and TB hospital admission rates. Proceedings of Irish Thoracic Society, Nov. 1992.

Conclusion: Neonatal BCG vaccination is associated with significant protection against TB in childhood. With a declining overall incidence of TB the benefits of neonatal BCG will probably be outweighed by the disadvantages towards the end of this decade.

THE IMPACT OF REMINDER LETTERS ON ATTENDANCE FOR BREAST CANCER SCREENING

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Eastern Health Board, Dublin on behalf of Eccles Breast Screening Project.

The objectives of this study were to quantify the response to issue of second and third postal invitations from a sample of patients invited for mammography screening and to determine any demographic differences in response to each invitation. Females aged 50-64 resident in a cluster of six previously unscreened District Electoral Divisions in North Dublin were invited by personal computer-generated letter to attend for screening. Data sources used for the

project register were, the Eastern Health Board General Medical Services data base (GMS), Voluntary Health Insurance Board (VHI) data and self-registration. Non-responders were re-invited to attend six weeks later and a final invitation was issued at 12 weeks. 1,310 females in the target age group were eligible for screening. The response rate to the first, second and third invitations is shown in Table 1.

	Eligible		Attended	
	No.	%	No.	%
1st invitation	1,310		795	(60.7)
2nd invitation	515		92	(17.9)
3rd invitation	423		32	(7.6)
TOTAL	1,310		919	(70.1)

A significantly higher proportion of those with private medical cover responded to the first and third invitations ($p < 0.05$). No difference in response to second invitations was noted ($p > 0.05$).

Women aged 55-64 were more likely to respond to first, second or third invitations than those aged < 55 years ($p < 0.001$). Although married females were more likely to respond to the first screening call ($p < 0.001$), no difference was noted in response to second or third invitations ($p > 0.05$). The study demonstrated that issue of second mailed invitations was worthwhile with an increase in overall uptake of 7% (92/1,310). Response to third invitations was small (overall yield 2.4%). Women with low incomes were as likely to respond to second invitations.

INFLUENZA OUTBREAK IN AN INSTITUTION: INVESTIGATION AND CONTROL

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Over a ten-day period in October '93 an outbreak of systemic illness occurred in a geriatric institution; an epidemiological and virological investigation ensued. The objectives were to identify the pathogen and prophylactic measures to prevent the situation recurring. 90 of the 122 patients and 15 staff were affected. Symptoms included pyrexia, sore throat, myalgia and vertigo. One patient developed pneumonia and was hospitalised, there were no deaths. Dual serology identified a 16-fold rise in titre for Influenza A in 5 patients. Nasal and throat swabs confirmed the presence of Influenza A virus (A Beijing/32/92 H3N2-like) - the first isolates of this strain in Ireland. Patients in this institution had not routinely been vaccinated against influenza. Vaccine efficacy in high-risk groups and the elderly has been identified as 66% and 77% respectively, although longitudinal studies suggest that good protection may be offered in the first year but poor protection to those vaccinated regularly⁽¹⁾. Notwithstanding this, vaccination of residents of long-term institutions is recommended as rapid spread is likely to follow introduction of infection.

Reference

1 Arnold E. Modern vaccines: a Lancet review 1990.

THE HAPPY HEART COMMUNITIES NATIONAL SURVEY 1992: HEALTH BEHAVIOURS AND SOCIAL CLASS

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The Happy Heart Research Committee, Irish Heart Foundation and Faculty of Public Health Medicine, RCPL. Dept. of Epidemiology, Royal College of Surgeons in Ireland.

This survey aimed to measure health behaviours relevant to coronary heart disease (CHD) prevention in Happy Heart Commu-

nities (HHCs) (6 counties and 1 town) and nationally. Sampling was by random selection from Electoral Registers, with clusters by prespecified directions and quota controls by age and sex. 907 men and 891 women aged 30 to 69 years participated. Findings are compared for social classes 1-3 (non-manual) and for 4-6 (manual).

	Men		Women	
	Social Class: 1-3	4-6	1-3	4-6
Number	436	468	431	459
Told high BP %	12.2	17.5	17.9	22.9
Cholesterol check %	52.1	32.9	38.5	28.5
Current smoker %	31.4	44.2	20.9	36.2
Vigorous activity %	29.8	26.5	26.6	12.8
Obese % (BMI ≥ 30)	8.9	11.3	6.0	12.8
Meat ≥ 7 /week %	9.0	10.0	3.5	7.0
Chicken ≥ 2 /week %	45.6	40.4	49.9	36.4
Fish ≥ 2 /week %	27.9	20.1	23.2	15.9
Fruit & veg. ≥ 21 /week %	29.0	17.8	45.9	31.8

The manual group should receive special attention in health promotion initiatives to prevent CHD.

AN OUTBREAK OF GASTROENTERITIS CAUSED BY NORWALK VIRUS IN A DUBLIN HOSPITAL

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In February 1993 95 persons (47 patients and 48 staff members) were affected by an outbreak of viral gastroenteritis. The causative agent was identified as Norwalk virus, using solid phase immune electron microscopy (SPIEM).

Of 67 stool samples examined, 31 (46%) were positive for Norwalk/small round structured virus, by this method. The illness was characterised by a preceding flu-like illness in 28% of cases followed by vomiting (31%), diarrhoea (23%) and abdominal pain (23%).

Screening of hospital catering services and a case control study, carried out among affected staff members, failed to identify a foodborne source. Consumption of tap water in the hospital was commoner among affected staff members than among controls, but this did not reach significance ($P = 0.1$).

This is the first report of an outbreak caused by Norwalk virus in Ireland.

EXPERIENCE WITH *ENTEROBACTER SP.* CAUSING SEPTICAEMIA IN A DUBLIN TEACHING HOSPITAL

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We reviewed *Enterobacter spp.* septicaemia over 2 years in our 600 bed hospital. There were 22 episodes of which 18 were derepressed mutants and 6 gentamicin resistant. There was an association between the use of H² antagonists, recent surgery, central venous catheters and the development of *Enterobacter* septicaemia. Gentamicin resistance was encountered significantly more often in patients who had received gentamicin within the preceding 2 weeks ($P < 0.01$) and in those who had spent more than 3 days in the ITU ($P < 0.01$). Mortality in those with gentamicin resistant isolates was 33% compared with 6% in those with gentamicin susceptible strains. Risk factor assessment can influence empiric treatment in suspected Gram negative septicaemia.

AGE SPECIFIC MEASLES, MUMPS AND RUBELLA SUSCEPTIBILITY IN IRISH CHILDREN

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Measles vaccine was introduced in 1985 and the measles, mumps and rubella (MMR) vaccine in 1988. Measles notifications reached the lowest recorded level in 1991/1992, but increased markedly in 1993. The purpose of the study was to identify cohorts of children susceptible to infection, by age group, so as to guide vaccination strategy.

The age-specific measles, mumps and rubella antibody prevalence in children aged 3 to 14 years was examined. Sera from 837 children who presented for blood sampling in the three Dublin paediatric hospitals in 1991/1992 were collected.

The prevalence of antibodies in children (boys and girls), aged 3 - 4 years, 7 - 8 years and 13 - 14 years was 84%, 81% and 93% for measles; 36%, 59% and 61% for mumps; and 86%, 64% and 86% for rubella respectively. Ninety six percent of girls aged 13 to 14 years had rubella antibodies.

Unless the measles 'susceptibility gap' of approximately 15% is narrowed by boosting immunity levels before entry to or during primary school, further outbreaks of infection in these age groups are inevitable. A high uptake of MMR vaccine prior to secondary school entry is essential to prevent a shift of disease into the teenage years.

RENAL MEDICINE

VON HIPPEL LINDAU SYNDROME - A FAMILY STUDY

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This is the family study of a patient with coincident chronic renal failure, multiple renal cysts and renal cell carcinoma (RCC). Clinically and histologically this was indistinguishable from polycystic kidney disease (PKD). Further assessment including genetic analysis of the patient's family over two generations yielded a diagnosis of Von Hippel Lindau Syndrome (VHLS). VHLS is an autosomal dominant multisystem disorder with variable expression but full penetrance. The responsible gene is at the Chromosome 3p 25-26 locus. In this case clinical screening found 6 relatives to have multiple renal and pancreatic cysts. RCC was present in 3 individuals, the youngest was 19 years, and tumour tissue was found to be heterozygous for the gene. Two cases of haemangioblastoma were found but as yet no cases of phaeochromocytoma or retinal angiomas are present. DNA was extracted from peripheral blood leukocytes and linkage analysis was performed using microsatellites in the vicinity of the gene. This succeeded in finding four previously undiagnosed individuals. We conclude that VHLS presents similarly to PKD. RCC may present at a young age. Genetic analysis can diagnose young asymptomatic heterozygotes and allow earlier recognition of complications.

WATER ANALYSIS IN A HAEMODIALYSIS UNIT

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A dialysis patient is exposed to twenty-four times the amount of water a normal person drinks per week. It is vitally important that the water used in dialysis fluid is of an adequate quality to minimise the risk of infection and the level of contaminants to the blood. Two types

of water analysis are necessary: chemical and bacterial.

Chemical analysis involved taking samples daily and testing for free and combined chlorine; aluminium, fluoride and hardness.

Samples were taken weekly for bacterial analysis. Samples were sent to the Central Pathology Laboratory for analysis and the levels of Bacteria Colony Forming Units (BCFU) were measured.

Results from the above tests were compared with maximum permissible medical limits as recommended by the AAMI.

The analysis was carried out in order to establish a base-line for results and a protocol for the analysis of haemodialysis water.

THE EFFECT OF HAEMODIALYSIS ON SODIUM-LITHIUM COUNTERTRANSPORT

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To characterise possible alteration in sodium handling in renal failure patients, we assessed transport of the cation across cell membrane using erythrocyte sodium-lithium countertransport (SLC) as an *in vitro* model. Thirteen patients (M:F, 7:6) aged 46.2 ± 10.9 years (mean \pm SD) and who have been on dialysis for 1-14 years participated. The activity of the transporter was measured after loading of erythrocytes with lithium in LiCl - LiCO₃ solution. SLC by standard method (intra-assay variation 1.6%, inter-assay variation 6.8%) significantly fell after dialysis (0.273 ± 0.103 vs 0.239 ± 0.113 mmol/L cell.h, mean \pm SD; $p < 0.003$). Detailed kinetic study revealed a corresponding reduction in V_{max} of the transporter (0.490 ± 0.154 vs 0.110 ± 0.158 ; $p < 0.004$), but its affinity for external sodium, K_m, was not altered (median: 118 vs 105 mmol/L). Plasma cholesterol fell by 0.5 mmol/L ($p < 0.001$) and so did triglyceride (1.3 mmol/L; $p < 0.05$ and HDL (0.106 mmol/L; $p < 0.04$), but none of these changes correlated with SLC changes. We suggest that a filterable factor that increases SLC possibly by increasing the turnover rate of the transporter is present in renal failure patients.

RESPIRATORY

MECHANISM OF ACTION OF INHALED CORTICOSTEROIDS IN BRONCHIAL ASTHMA

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A placebo controlled trial was carried out to investigate the effects and mechanism of action of inhaled corticosteroids in asthma. 16 patients (2F) were entered into a double blind placebo controlled parallel group study inhaling either Budesonide 800 ug daily or matching placebo for six weeks. Spirometry, bronchial reactivity to histamine, bronchodilator response to terbutaline and endobronchial biopsies were performed before and after treatment. Biopsies were analysed immunocytochemically. Therapy with budesonide lead to significant improvement in FEF₂₅₋₇₅ ($p=0.05$), morning peak flow rate ($p=0.039$) and evening peak flow ($p=0.023$). There was significant improvement in numbers of mast cells ($p=0.003$), activated eosinophils ($p=0.017$) and expression of HLA-DR ($p=0.034$) in response to treatment with budesonide. This is the first controlled study of endobronchial biopsies in asthma. These results provide new insights into the efficacy of corticosteroids and identify new

targets for asthma therapy, in particular TH2 lymphocyte clones which are known to up regulate eosinophil and mast cell activity.

THORACIC ACTINOMYCOSIS: CASE REPORT

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We report a case of thoracic Actinomyces infection, to illustrate diagnostic difficulties in such an uncommon infection. A 24 year old female student presented with a six week history of dry cough, night sweats, right sided chest pain, and a five day history of progressively enlarging chest wall swelling. Chest x-ray showed a right middle lobe consolidation and a lytic lesion of right 7th rib costochondral junction. Bronchoscopy was negative, with negative bacteriological cultures of bronchial washings. Chest wall abscess was drained, and direct staining was negative. AFB stain negative, culture negative. Biopsy of abscess wall showed typical appearances of Actinomyces infection. She is presently responding well to parental Benzylpenicillin, but chest x-ray appearances have not changed significantly.

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COLLAGEN EXPRESSION IN FIBROBLASTS FROM NORMAL AND FIBROTIC LUNG SOURCES

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In fibrotic disorders there is evidence that fibroblasts derived from diseased tissue may represent a phenotypically distinct subset with enhanced proliferative and collagen-producing capacities. In this study, we examined the differential effects of four inflammatory cytokines - interleukin-1 (IL-1), platelet derived growth factor (PDGF), interferon γ (Inf γ) and transforming growth factor β_1 (TGF β_1) - on the expression of Type I and Type III collagens in fibroblasts from normal and fibrotic lung tissue. In normal fibroblasts IL-1 stimulation increased expression of both collagen types approximately two-fold. By comparison, a seven-fold increase in Type III expression was observed in 'fibrotic' fibroblasts while Type I expression remained virtually unaltered. Stimulation with TGF β_1 increased Type I collagen expression two-fold in normal fibroblasts but did not effect Type III expression. The response of 'fibrotic' fibroblasts to TGF β_1 exhibited a similar pattern to that observed in normal cells except, in this instance, Type I expression was increased six-fold. PDGF or Inf γ had no effect on Type I or Type III expression in either cell type. These results indicate that lung fibroblasts derived from normal and fibrotic tissues exhibit significantly different responses to the regulatory cytokines IL-1 and TGF β_1 .

This work was supported by the Health Research Board of Ireland.

THE EFFECT OF MEDIATORS FROM NORMAL AND FIBROTIC LUNG FIBROBLASTS ON NEUTROPHILS

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In interstitial lung disease chronic inflammation leading to fibro-

sis is characterised by neutrophil accumulation in the lung⁽¹⁾. Fibroblasts may contribute to this by releasing cytokines such as GMCSF⁽²⁾ and IL-8. Study objectives were to determine if (a) fibroblast-derived cytokines enhance neutrophil survival and activation (b) mediators released by normal and fibrotic fibroblasts differ in their effects on neutrophils. Conditioned medium from normal fibroblast lines (NFL) and fibrotic fibroblast lines (FFL) were examined for their effects on neutrophil survival, superoxide production and granule release. The effects of addition of IL-8 and GMCSF antibodies were also examined. Results indicated that NFL and FFL enhanced neutrophil survival to 40% after 48 hours compared to 13% in control medium. NFL and FFL stimulated production of superoxide but not granule release. Control + IL-8 enhanced granule release but not survival or superoxide release. Addition of anti-IL-8 did not block the effects of NFL and FFL on neutrophils but anti-GMCSF reduced neutrophil survival and superoxide release to control levels. Thus the fibroblast-derived mediator GMCSF, enhances neutrophil survival and superoxide production but not granule release. No difference was observed between the effects of NFL and FFL on neutrophil function, indicating similar basal release of mediators from the two fibroblast types.

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EXAMINATION OF THE ORIGIN OF 'TRUNCATED' α_1 -PI IN SPUTA FROM CYSTIC FIBROSIS PATIENTS

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Neutrophil elastase (NE) plays a significant part in the lung destruction observed in cystic fibrosis (CF). Proposals for the therapeutic administration of NE inhibitor, α_1 -protease inhibitor (α_1 -PI), remain controversial as several studies indicate that endogenously produced α_1 -PI is inactivated in the CF lung and thus unable to bind NE. However, in these studies, precautions to prevent proteolysis subsequent to sample collection were not taken⁽¹⁾.

The aim of the present study was to examine the origin of 'truncated' α_1 -PI seen in CF. α_1 -PI was added to purified NE in various proportions and incubated for 0, 1, 5 and 24hr intervals at 37°C. The reaction was stopped by the addition of serine protease inhibitors. Samples were analysed by SDS-PAGE followed by immunoblotting against antibodies specific for α_1 -PI.

Results show the presence of α_1 -PI-NE complex and virtual absence of 'truncated' α_1 -PI at 0 hours. Over time, the gradual breakdown of this complex and the appearance of 'truncated' a1-PI was observed in samples with excess NE. Thus, these results suggest that truncated α_1 -PI present in CF samples may well represent a product of complex dissociation when excess NE is present as opposed to an inactive form of α_1 -PI that can not inhibit NE.

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LOCALISATION OF A NA⁺ CHANNEL IN PRIMARY CULTURES OF HUMAN AIRWAY AND SWEAT DUCT EPITHELIA

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Cystic Fibrosis is characterised by mutations in the CFTR, the protein coding for a c-AMP regulated chloride channel. The disease

is also known to affect Na⁺ transport. Na⁺ transport in the CF lung is abnormally high whereas it appears normal in epithelial sweat duct cells of CF patients⁽¹⁾.

Sweat ducts were microdissected from skin which had been pre-digested with collagen (0.02% w/v) and were separated from the dermis by shearing forces. The lung samples were obtained from biopsy samples and the epithelial alveolar tissue was again microdissected and grown on collagen-treated filters (Coster Trans-Well™).

We have detected single sodium channel activity using the patch-clamp technique. The channel has been shown to be selective for Na⁺ over K⁺ (P_{Na/K}=4). We have shown the channel was activated upon excision from the cell membrane. In the inside-out patch clamp configuration, the sodium channel was no longer exposed to the normal cell cytosol and it was possible to show that the channel was closed (or deactivated) by the addition of ATP (0-500µM). Since ATP and the cytosol have also been shown to regulate CFTR, we are investigating these effects in CF target epithelia.

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IDENTIFICATION OF K⁺ AND Cl⁻ CHANNELS IN ISOLATED PORCINE CHONDROCYTES

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Little is known about the function and regulation of normal cartilage at the cellular level. It has been previously shown that alterations in the ionic environment of chondrocytes, the cells which synthesize and secrete cartilage, affect matrix synthesis⁽¹⁾. We have investigated the cellular transport mechanisms of chondrocytes using patchclamp methods.

Chondrocytes were obtained from porcine metapharyngeal joints and isolated using collagenase dissociation. Cells were bathed in Krebs-Henseleit solution while the patch pipette was filled with KCl (120 mM). Two different voltage-activated channels were observed. The first type was a large conductance (150 pS) K⁺ channel (maxi-K) and the second was a Cl⁻ channel (SCL) of smaller conductance (10 pS). The SCL was spontaneously active at resting membrane potential and is a pathway for Cl⁻ efflux from the cell. The maxi-K channel was activated by membrane depolarization and an increased cytosolic Ca²⁺. Changes to extracellular [K⁺] and [Ca²⁺] known to occur in the compressed chondron are shown to affect ion channel activity in single chondrocytes.

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RHEUMATOLOGY AND REHABILITATION

RADIOLOGIC PROGRESSION IN RHEUMATOID ARTHRITIS OVER 6 YRS CORRELATES WITH MACROPHAGE NUMBERS IN THE SYNOVIUM

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Previous reports have demonstrated that radiologic course over one year in early rheumatoid arthritis (RA) correlated with numbers of monocyte/macrophages in the synovium. Fifty-eight patients with active RA were enrolled in a prospective study between 1984-1987. Detailed clinical, radiologic and synovial histological data were recorded at entry to the study and at follow-up 6 years later. This study sought correlations between immunohistological features in the synovium at follow-up and radiologic outcome.

Forty nine patients were alive at the time of review: 32 (65%) consented to a further synovial biopsy and detailed histological data is available in 18 of these to date: 13 were female; mean (Range) age 48 years (26-75) and duration of follow-up 5.8 years (4.3-7.3). Mean index of disease activity improved from 2.6 (1.5-3.5) at entry to 1.9 (1.0-2.7) at follow-up (p<0.001). However, mean Larsen radiologic index deteriorated from 45 (4-140) to 96 (12-158) (p<0.001). Quantitative synovial analysis revealed the following mean (SEM) cell numbers/mm²: CD3 - 354 (±127); CD4 - 319 (±139); CD8 112 (±46); CD14 - 618 (±184); CD19 - 48 (±26); blood vessels - 115 (±22). Monocyte/macrophage numbers in the synovium correlated with Larsen index at follow-up (r=0.52; p<0.05) and with change in Larsen index since entry (r=0.57; p<0.02). Number of T-lymphocytes, their subsets, B-lymphocytes or blood vessels did not correlate with radiologic outcome.

These results indicate a continuing correlation between radiologic progression over 6 years in RA and monocyte/macrophage numbers in the synovium and is further evidence of a central role for macrophages in the development of articular erosions.

ADHESION MOLECULE LEVELS IN SERUM AND SYNOVIAL FLUID FROM PATIENTS WITH INFLAMMATORY ARTHROPATHIES

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E-Selectin (ELAM) expression is up-regulated in RA synovium but not in psoriatic arthritis (PsA). Intercellular adhesion molecule (ICAM) and vascular cell adhesion molecule (VCAM) are up-regulated in both. We measured soluble adhesion molecule levels by ELISA in matched serum (Srm) and synovial fluid (SF) from patients with RA, PsA and other arthropathies (OtherA). Groups did not differ with respect to age or sex.

Mean (ng/ml) ELAM, ICAM and VCAM levels in Srm and SF were:

		RA (n=10)	PsA (n=6)	OtherA (n=5)	Normal Serum
ELAM	Srm	54.2	55.2¶	26.8¶	47.6
	SF	22.8	22.3	18.9	
ICAM	Srm	309.6*	211.9¶	230.3	208.9
	SF	207.4	155.1	222.5	
VCAM	Srm	808.1*	787.8*§	704.2§	553.0
	SF	1187.0	1291.1	1559.6*	

p<0.005 RA/PsA v Normal; ¶p<0.05 Srm>SF; §p<0.02 SF>Srm.

Although PsA synovium does not express ELAM, levels are not reduced in PsA SF compared to RA SF perhaps because SF ELAM levels reflect Srm levels rather than levels in synovium. Srm ICAM is elevated in patients with psoriasis. It is interesting, therefore, that it is not elevated in PsA patients selected on the basis of active arthritis rather than active skin disease. VCAM is expressed by the synovial lining layer and is probably shed directly into SF. Thus, it is not surprising that SF levels are higher than Srm.

A NEW CLINICAL RELATIONAL DATABASE FOR SLE USING BILAG SCORING SYSTEM

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The multi-system involvement and prolonged clinical course of systemic lupus erythematosus (SLE) produces a wealth of available clinical and laboratory data which makes effective patient management steadily more difficult. For this reason a scoring system was devised by British Isles Lupus assessment group (BILAG) which takes into account 64 of the most important clinical and laboratory factors and scores them relative to their prognostic value. Total score becomes an indicator of severity of the disease. Previous SLE databases based on Bilag have required considerable computing skills in addition to limitations imposed by the software available which did not have any facility for data collection and could not show a trend in patients indices. We have developed a new relational data base system enabling rapid retrieval of individual and collective data. The customised SLE data base uses a software package, 4th Dimension. Clinical, laboratory, therapeutic, radiological and other details are held on individual files related by a unique hospital number. The files can be reviewed at a glance and compared with data from previous visits. The new database allows for the possibility of an interface with other hospital information systems and data can be readily accessed, analysed or graphed electronically. The St Vincent's Hospital SLE relational database provides rapid access to essential clinical information which enhances management and research. This database also provides a useful model for information systems at outpatient clinics.

CORRELATION OF SCLERODERMA SKIN SCORE TO CIRCULATING SOLUBLE ICAM-1 LEVELS IN RESPONSE TO VENOUS OCCLUSION

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Intercellular adhesion molecule-1 (ICAM-1) is expressed by endothelium and shed in a circulating soluble form (sICAM-1). Systemic sclerosis (SSc) is characterised by skin and vascular changes. Venous occlusion (VO) provides a stress test on vascular endothelium.

15 patients with SSc were assessed clinically, using a validated skin score. Serum was obtained from patients and 15 healthy volunteers pre- and post-VO of the forearm. sICAM was measured using an ELISA kit. Statistical analysis by the Mann-Whitney 'U' test and Spearman correlation was used.

Pre-venous occlusion levels of sICAM-1 were significantly raised in the SSc vs normals $p=0.003$. SSc showed a significantly greater increase of sICAM-1 following VO compared to normals $p=0.002$. Skin score correlates with pre-VO sICAM-1 levels $r=0.46$ and the percentage increase in sICAM-1 levels in response to stimulation $r=0.67$.

	Median (range) sICAM-1 levels (ng/ml)	
	Pre-VO	Post-VO
SSc-p	212.4 (93.5-386.4)*	278.4 (165.0-470.6)**
Normals	106.0 (47.7-154.6)	148.7 (112.7-241.9)

*vs N, $p=0.003$; ** vs Pre-VO, $p=0.002$.

In conclusion, sICAM-1 is upregulated in SSc, rises with endothelial stimulation, and correlates with the clinical skin score. Pre- and post-VO sICAM-1 levels may be important markers for SSc severity and prognosis.

FC γ RECEPTOR-MEDIATED NEUTROPHIL ARREST AND ACTIVATION IS ENHANCED BY SUBSTANCE P

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The arrest and extravasation of neutrophil polymorphonuclear leucocytes (PMN) is an essential step in the development of inflammation in the synovium. Substance P (SP) is an important neuropeptide released in the inflamed synovial membrane. The mechanism of action of SP on PMN diapedesis is not known however it is believed to act indirectly via the vascular endothelium.

The aim of this study was to characterise Fc γ R-mediated PMN arrest and activation in response to SP using a novel *in vitro* model of a venule consisting of a cellulose acetate hollow fibre. The artificial vessel was coated with immune complexes (IC) and perfused with purified human PMN (10^6 cells/ml) at physiological flow velocity (0.1 cm/s) and temperature. PMN arrest was monitored with a low light level video camera mounted onto a phase contrast microscope and the images were recorded onto videotape.

Untreated PMN adhere avidly to IC ($11,000$ cells/cm 2 \pm 2,000) but not to laminin, fibronectin, collagen IV and fibrinogen ($\leq 1,000$ cells/cm 2). The addition of soluble immunoglobulins (3 mg/ml) resulted in $\approx 90\%$ inhibition of this adhesion, suggesting that Fc γ R is directly involved in PMN arrest. To confirm this finding we used cultured connective tissue cells transfected with hFc γ R II and demonstrated that adhesion under flow on IC is acquired by the expression of the Fc γ R. Pretreatment of PMN with SP (700 nM and 7 nM) resulted in significant increase in PMN arrest on IC (15,000 and 23,000 cells/cm 2 respectively) but not on laminin. Finally, SP-stimulated PMN produced greater lucigenin-enhanced chemiluminescence (1000 cpm vs. 400 cpm), indicative of superoxide production.

In conclusion, SP is an important neuropeptide which acts directly on PMN to increase Fc γ R-mediated arrest and respiratory burst. This may be an important mechanism in the pathogenesis of inflammatory arthritis.

OTHER

RADIO-OPACITY OF FISH BONES: A CADAVERIC STUDY

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Lateral neck radiography is routinely performed to localise impacted fish bones. This investigation has a low sensitivity. The differing radio-opacities of the bones of various fish species has been suggested as a reason for this. A cadaver head and neck and the rib bones of ten species of fish were used in this study. A laryngoscope was used to introduce a fish bone into the vallecula and then along the posterior pharyngeal wall. A lateral X-ray was taken, giving a total of 20 X-rays. Ten control X-rays were taken. The X-rays were independently reviewed by a consultant radiologist and a consultant ENT surgeon. The presence and position of any bone seen was noted. There was no inter observer variation. All species of fish bone were visible. In one X-ray the bone was not seen by either observer, giving a sensitivity of 95% and a specificity of 100%. Visualisation of fish bones is more dependent on position than the degree of radio-opacity. Routine radiography is therefore recommended.