INAUGURAL NATIONAL SCIENTIFIC MEDICAL MEETING

Friday, 13th and Saturday, 14th March, 1992

ORAL PRESENATIONS

CARDIOLOGY

APOLIPOPROTEINS AND CORONARY ARTERY DISEASE

T. Cooke, R. Sheahan, D. Foley, G. D'Arcy, M. Gibney, W. Jauch, G. Gearty, P. Crean, M. Walsh.
Deptartment of Biological Sciences, Kevin Street, and Department of Cardiology, St. James's Hospital, Dubin 8.

The association of serum lipoprotein (a) (Lp(a)), appolipoproteins A1 and B, total, HDL LDL cholesterol and triglycerides with coronary artery disease (CAD) was studied in 106 randomly selected patients undergoing an elective coronary angioplasty (PTCA) and 46 controls with normal coronary angiography. Patients with a recent history of myocardial infarction (less than 3 months) were excluded (n=22). The influence of CAD, age, sex, family history, smoking, alcohol and socioeconomic group on each lipid parameter was examined using stepwise regression analysis. Where regression analysis indicated a factor influencing the serum concentration of a given parameter, an unpaired t test was used to determine levels of significance.

Lp(a) emerged as the most significant discriminator between the 2 groups (404 v 183 mg/L, $p<0.001$). Total cholesterol (6.08 v 5.54 mmol/L), LDL cholesterol (4.21 v 3.64 mmol/L), APO A1 (109 v 125 mg/dl) and APO B (96.1 v 85.9 mg/dl) all showed significant differences at $p<0.05$. HDL cholesterol and triglyceride levels did not attain significance. When total/HDL cholesterol, HDL/LDL cholesterol and APO A1/APO B ratios were examined, APO A1/APO B emerged as the best discriminator between the disease and control groups ($p<0.001$). Therefore, Lp(a) and APO A1/APO B ratio should be considered as important additional screening tests.

ROLE OF OXYGEN RADICALS IN ENDOTHELIAL LOSS AND INTIMAL HYPERPLASIA IN VEIN GRAFTS

P. M. Murchan, M. K. O'Donoghue, P. Marks, E. J. Leen, G. D. Shanik, T. M. Feely.
Departments of Surgery and Pathology, Meath and St. James's Hospital and Trinity College Dublin.

Endothelial injury and subsequent intimal hyperplasia are considered to be important factors in the pathophysiology of vein graft failure. Endothelial cells are highly susceptible to injury by oxygen radicals, generated during ischaemic-reperfusion injury. The reversed vein graft is a perfect model of ischaemia-reperfusion, and thus the prevention of oxygen radical generation in these vessels could preserve the endothelium to a greater degree. Superior endothelial preservation has been reported for *in situ* vein grafts. Eight dogs received allopurinol and vitamin E to prevent oxygen radical generation. The degree of endothelial loss and intimal hyperplasia in reversed (RV) and *in situ* (ISV) vein grafts in these dogs was compared to untreated controls. There was no significant difference between the reversed and *in situ* grafts in control or treated groups in terms of the extent of endothelial loss or the degree of intimal hyperplasia for up to 16 weeks after grafting (table, intimal hyerplasia, m.m.).

		1 week	4 weeks	8 weeks	16 weeks
Treated	ISV	0.03	0.06	0.16	0.06
	RV	0.06	0.11	0.02	0.10
Control	ISV	0.06	0.10	0.02	0.10
	RV	0.03	0.08	0.10	0.13

Intimal hyperplasia was a universal finding, while significant re-endothelialization was evident as early as 4 weeks after grafting. It is suggested that endothelial loss and re-endothelialization and intimal hyperplasia occur to similar degrees in reversed and *in situ* vein grafts and these changes are not mediated by oxygen radicals.

RETROSPECTIVE DECISION ANALYSIS OF THROMBOLYTIC THERAPY

J. O'Riordan, J. G. Kellett.
Nenagh General Hospital, Nenagh, County Tipperary.

Half of the 50 consecutive patients admitted to Nenagh Hospital coronary care unit with a suspected myocardial infarction did not have one. Only 10 patients (20%) had definite evidence of infarction at the time of admission. Of the 40 remaining patients, only 15 (30%) subsequently developed cardiographic and enzymatic confirmation of infarction. Streptokinase was administered to 5 patients (20%) who did not infarct, and was not given to 10 (40%) patients who did. These decisions to use or withhold thrombolytic therapy were retrospectively reviewed using a decision - support computer program. This program, based on a decision analysis model for thrombolytic therapy, examined 8 scenarios that assumed different probabilities of myocardial infarction (pMI), probabilities of death from infarction (pdiMI), and different safety and efficacy profiles of thrombolytics. The most effective scenario assumed the worst published safety and efficacy profile for thrombolytics, and determined pMI from the Goldman algorithm pdiMI from patient age. Had this scenario been used 60% of patients with an infarct would still have received thrombolytic treatment. However only 8% of those patients without an infarct would have received streptokinase. The risk of inappropriate treatment would, therefore, have been more than halved.

PHYSIOLOGY OF THE INDIRECT BLOOD PRESSURE MEASUREMENT TECHNIQUE

N. F. Sheahan, M. MacMahon, M. Colgan, J. B. Walsh, G. Shanik, R. Moore, J. F. Malone, D. Coakley.
Mercer's Institute for Research on Ageing and Dept. of Vascular Surgery, St. James's Hospital, Dublin 8.

This paper describes a new technique for investigating the physiology of the indirect blood pressure (BP) measurement process. The technique involves ultrasonic imaging of the section of brachial artery underlying the pressure cuff. In order to illustrate one

application of the technique, a study of diastolic pseudo-hypertension is reported. The latter occurs (mainly in the elderly population) when the indirect BP measurement process overestimates diastolic pressure by comparison to the value obtained by direct measurement. Using the new imaging technique, we measured the external cuff pressure required to close the deperssurised brachial artery in 17 elderly patients. The pressure was found to be positively related ($p<0.001$) to the extent of diastolic pseudohypertension. The results of this study (i) provide objective support for the hypothesis that diastolic pseudohypertension stems from brachial artery resistance to closure by an external cuff, and (ii) suggest that the measurement of arterial closing pressure may provide a non-invasive means of differentiating true hypertension from pseudohypertension in the elderly population.

HEART SIZE: IS IT GOVERNED BY BODY SURFACE AREA?

K. Subareddy, J. Hurley, E. McGovern.
National Cardiac Surgery Unit, Mater Hospital, Dublin 7.

Cardiomegaly is a frequent clinical radiological diagnosis, open heart surgery allows us measure heart size directly. The aim of this study was to determine if actual heart size or size of the ascending aorta was significantly smaller in females than in males and whether it is related to body surface area. Two hundred patients undergoing isolated coronary artery byass grafting were studied. Following stabilisation of the patient post sternotomy, left heart border (LHB), inferior heart border (IHB), and maximum diameter of the ascending aorta were measured. Both groups, males (n=143), females (n=57), were similar with respect to age, number of grafts and ventricular function measured angiographically pre-operatively. Body surface area (BSA) was calculated. Mean LHB and mean IHB were significantly larger in males than females ($P<0.01$), however this difference disappeared when LHB and IHB were corrected for BSA. Mean max transfer diameter of the ascending aorta was significantly smaller in females and this difference persisted when corrected for BSA ($P<0.01$). This study shows that heart size relative to BSA is similar in males and females and is related to BSA but ascending aortic diameter is significantly smaller in females, a factor that may explain the early excess mortality in females post aorto coronary bypass surgery.

CARDIOVASACULAR HAEMODYNAMICS AT REST AND DURING EXERCISE IN HEALTHY SUBJECTS - RELATIONSHIP TO AGE

P. A. Sullivan, S. O'Mahony, K. Carroll.
Department of Medicine, Mallow General Hospital, Mallow, Co. Cork.

Thoracic electrical bioimpedance (TEB) is a rapid convenient, non-invasive method for the estimation of left ventricular/volume (SV). The aims of this study were (a) to examine the feasibility of measuring cardiovascular haemodynamics in healthy subjects during exercise (bicycle ergometry) using TEB technololgy and (b) to determine the influence of age on these variables. We investigated 62 males, age range 23-76, mean 43 yrs, at rest and between the 2nd and 3rd mins. of 3 minute bicycle exercise stages, starting at 70 watts and increasing by 40 watts per stage. Resting to maximum exercise variables were as follows: BP (mmHg) 122/64 to 194/71, cardiac index (CI, $l/min/m^2$) 4.1 to 13.6, stroke index (SI, ml/m^2) 61 to 85, and systemic vascular resistance index (SVRI, dyn $sec/cm^5/m^2$) 1849 to 692, all $P<0.0001$. Resting and exercise SVRI correlated positively with age ($P<0.05$ - $P<0.01$) as did systolic BP during exercise ($P<0.01$). C.I. was uninfluenced by age at any study point. TEB technology provides a simple means of measuring haemodynamic variables during exercise and values found correspond closely to those reported using invasive technologies. Though SI decreases, the blood pressure increase with advancing age appears to be a consequence of increased SVRI in the presence of the maintenance of C.I.

GASTROENTEROLOGY

ABNORMAL CENTRAL CHOLINERGIC TONE IN THE IRRITABLE BOWEL SYNDROME

A. Chua, R. W. N. Keeling, A. O'Kane*, T. Dinan*.
Departments of Gastroenterology and Psychiatry*, Trinity College Dublin, St. James's Hospital, Dublin.

Recent studies have provided evidence of disturbed bowel motility and an underlying autonomic dysfunction in patients with irritable bowel syndrome (IBS). Furthermore it is known that colonic excitatory innervation is via cholinergic pathways. The central cholinergic system modulates secretion of growth hormone (GH) via somatostatin secretion[1]. In this study we investigated the effect of manipulating cholinergic tone in patients with IBS by measuring the serum GH response to oral administration of pyridostigmine. Pyridostigmine, an acetycholinesterase inhibitor stimulates GH release by reducing somatostatin release from the hypothalamus by increasing central cholinergic neurotransmission. We therefore have studied GH response to pyridostigmine in 11 IBS patients (4F, 7M) and 11 gender and age matched controls. Patients with evidence of organic pathology and patients receiving medications were excluded. After 2 baseline GH levels 120mg pyridostigmine was given orally and serial samples obtained for GH estimation using radioimmunoassay. The GH responses (GH) were calculated by subtracting the basal GH level from maximum GH level post pyridostigmine.

Results: The mean + SEM GH response of IBS patients was 30.3 + 3.3mU/l, significantly higher than controls, 15.2 + 3.3mU/l ($p=0.05$). Seven of the 11 IBS patients had an exaggerated GH response.

Conclusion: These results suggest that IBS patients may have an exaggerated central cholinergic tone or an abnormally low somatostatinergic tone.

Reference

1. Massara, F. *et al.* J. Clin. Endocrinol. 1986: 111, 271-278.

IDENTIFICATION OF NOVEL TUMOUR RESTRICTED ANTIGENS IN TUMORS OF THE GASTROINTESTINAL TRACT

J. K. Collins, G. O'Sullivan, C. Hahnvajanawong, M. McCarthy, F. O'Brien.
Department of Microbiology, University College, Cork and Department of Surgery, Mercy Hospital, Cork.

The presence of a tumour clearly evokes an immune response in patients as determined by tumour infiltrating lymphocytes. However little progress has been made in identifying what antigens the patient recognises in his own tumour and if in fact there are unique tumour associated antigens. We have used autologous

immunoblotting using sera, tumours and corresponding normal tissue from patients (n=100) with oesophageal, gastric and colorectal cancer in an attempt to define antigens recognised by patients in their own tumours. Antigens recognised in both normal and tumour extracts were classified as autoantigens. Using these techniques we have defined three tumour restricted antigens in oesophageal and gastric carcinomas (TRA 158 K, TRA 73.8 K and TRA 45.5 K). More than 90% of patients with oesophageal and gastric tumours have antibodies which recognise TRA 158 K and TRA 73.8 K. We therefore provide evidence for a humoral anti-tumour immune response during tumour development and furthermore define in terms of molecular size three common tumour restricted antigens. We are currently evaluating the presence in patients of antibodies to these antigens as a screening test for precancerous or early detection.

FAMILIAL TRANSMISSION OF *HELICOBACTER PYLORI*

R. A. Collins, S. Beattie, H. Hamilton, C. A. O'Morain.
Department of Gastroenterology, Meath/Adelaide Hospitals, Trinity College Dublin.

The mode of transmission of *Helicobacter pylori (H. pylori)* is unknown. The aim of this study was to investigate the hypothesis of person to person transmission.

The families of 47 consecutive patients with endoscopically proven duodenal ulcer disease associated with *H. pylori* were studied. All family members (household contacts only) were screened for evidence of *H. pylori* infection. As a screening method the ^{13}Carbon urea breath test is quick, simple and non-invasive. ^{13}Carbon is a stable (non-radioactive) isotope. Patients drink a solution of ^{13}C-urea and breath samples collected at 0, 20, 40 and 60 minutes are analysed using mass spectrometry. An increase of greater than 5% in the ^{13}C content of each sample over the baseline measurement indicates *H. pylori* infection.

One hundred and thirty-two members were screened in total. 59/132 (44.7%) were positive for *H. pylori*. 37/132 were spouses of the index patients: 24/37 (64%) were infected. By contrast, only 35/95 (37%) of the remaining family members were *H. pylori* positive. The prevalence of infection in this group according to age was: 47% (8/17) aged 0-9 yrs., 27% (13/48) aged 10-19 yrs., 57% (12/21) aged 20-29 yrs., 1/1 aged 30-39 yrs., 1/2 aged 40-49 yrs., 0/5 aged 50-59 yrs. and 1/1 aged 70-79 yrs. The higher than expected prevalence of *H. pylori* infection among the younger age groups and spouses in each family strongly supports the theory of person to person spread of this organism.

ADHESION MOLECULES UTILISED IN BINDING OF INTRA-EPITHELIAL LYMPHOCYTES TO HUMAN ENTEROCYTES

S. Lynch, A. Murphy, D. G. Weir, C. Feighery, C. O'Farrelly, D. Kelleher.
Departments of Gastroenterology, Immunology and Clinical Medicine, St. James's Hospital and T.C.D.

The mechanisms by which the intra-epithelial lymphocyte (IEL) sub-population migrates to and adheres in the epithelial layer are poorly understood. We have developed a system for the study of adherence of IEL to human intestinal epithelial cells. This system utilises an IEL cell line derived by mitogen stimulation and maintained in the presence of irradiated accessory cells and interleukin 2. To examine adherence to this cell line we cultured the fetal intestinal epithelial cell line 1407 in confluent monolayers and examined the ability of the IEL line to bind to these cells. Results were quantitated by blinded direct counting of adherent lymphocytes in 3-6 confluent high power fields of 1407 cells following washing of plates and staining with haematoxylin and expressed as IEL binding per 100 1407 cells (%). IEL cells adhered tightly to the 1407 monolayer (26±4 cells %, n=4) while very few peripheral blood T cells adhered (1.6±3, n=4). T cells activated with mitogens PHA and PMA adhered to 1407 cells at a lower extent than IEL cells (12.3±2, n=4). A monoclonal antibody to RGD peptide sequences blocked binding of IEL to 1407 significantly (71±14% inhibition, n=3) and monoclonal antibody to VLA-4 which is known to bind using RGD sequences blocked binding to a similar extent (74±15%). Finally, a novel monoclonal antibody D.2.1 which recognises a 45 kD homodimer on T lymphocytes similarly blocked IEL binding significantly (81±1.2%). Monoclonal antibodies to the following antigens failed to inhibit IEL binding; ELAM 1, CD44, LFA-1, CD1, CD2, HML-1, CD56. These data indicate that both the VLA-4 molecule and a 45 kD homodimer are involved in adherence of IEL to a human enterocyte cell line. Increased binding of these lymphocytes to epithelial cells may be involved in the increased IEL count seen in coeliac disease.

THE ESSENTIAL ROLE OF LAPAROSCOPY IN GENERALISED PERITONITIS

D. Murphy, M. O'Brien, P. Harte, G. O'Sullivan.
Department of Surgery, Mercy Hospital, Cork.

A clinical diagnosis of generalised peritonitis is an indication for laparotomy to facilitate accurate diagnosis and definitive therapy. Because an accurate pre-operative diagnosis is not possible, selection of incision may be problematic and many conditions which can be managed non-operatively are explored.

We report our experience with laparoscopy in 77 patients, who had a clinical diagnosis of generalised peritonitis. Forty patients (52%) had perforated appendicitis, 14 (18%) had a perforated viscus, 11 (14%) had haemoperitoneum (mainly gynaecological), 5 (6%) had gangrene of a viscus, 2 (2.5%) had acute pancreatitis, 3 (4%) had primary peritonitis and 2 (2.5%) had Yersinia enterocolitis.

Laparoscopic diagnosis facilitated accurate placement of a surgical incision in 57 patients (74%). The remainder were managed by laparoscopy alone. Laparoscopic diagnosis and lavage of the peritoneal cavity was the sole therapy for perforated diverticular disease (5), haemoperitoneum (gynaecological - 7) and primary peritonitis (3).

Conclusion: Laparoscopy does not contribute to the morbidity associated with peritonitis. It facilitates accurate diagnosis and correct placement of incisions for appropriate surgical exploration. Laparoscopic lavage of the peritoneal cavity may be appropriate in the management of many causes of peritonitis and laparoscopic surgery for many problems is now feasible.

DEFECTIVE ANTIGEN-SPECIFIC RESPONSES IN PATIENTS WITH GASTRIC *H. PYLORI* COLONIZATION

C. N. Shahi, X. J. Fan, J. Huang, C. J. Smyth, A. Chua, J. McDevitt, D. G. Weir, P. W. N. Keeling, D. Kelleher.
Depts. of Gastroenterology, Immunology and Clinical Medicine and Microbiology, St. James's Hospital and Trinity College Dublin.

In this study we have examined the cellular response to *Helicobacter pylori* (HP) by measuring *in vitro* proliferative re-

sponses of peripheral blood mononuclear cells (PBMC) to inactivated whole cell HP antigens, purified protein derivative (PPDS), whole cell inactivated E. coli antigens and phythaemagglutinin (PHA) in 37 dyspeptic patients undergoing upper gastrointestinal endoscopy. HP status was determined by culture, histology and the rapid urease test on antral biopsies.

Patients with HP colonisation (HP+) had significantly lower proliferative responses to HP antigen relative to HP negative (HP–) individuals [1610±555 (n=21) vs 3946±778 (n=16) cpm 3H-Tdr incorporation, x±SEM, $p<0.01$]. There was no significant difference in proliferative response to PPD [4771±1613 vs 8109±2466, x±SEM, p. ns] or to PHA [10417±2156 vs 9510±1552]. We could not detect proliferative responses to E coli antigen at significant levels in patients or controls. γ-interferon (IFN) secretion by PBMC in response to HP antigen was also lower in HP+ individuals relative to HP– controls [5.1±0.98 (n=14) vs 12.3±3.2 (n=14) U/ml, $p<0.021$. However, neither spontaneous production nor responses to PHA were significantly different in the two groups (3.5±1.1 vs 4.8±0.96, 79.8±36 vs 71.9±24). These findings suggest a defective peripheral blood T cell response to HP antigens in HP+ individuals, possibly due to antigen-specific suppression or to failure of epitope recognition.

DERMATOLOGY/IMMUNOLOGY/ RHEUMATOLOGY

SCREENING FAMILIES WITH VARIEGATE PORPHYRIA

M. Cleary, G. Morrow, S. O'Loughlin, G. M. Murphy, *G. Elder.

Regional Dermatology Centre, Mater Hospital, Dublin and *Heath Park Hospital, Cardiff.

Variegate porphyria is a dominantly inherited disorder presented with a cutaneous, abdominal and neuropsychiatric symptoms. Gene carriers may be clinically latent but are at risk of potentially fatal acute attacks. Accurate identification of those affected is mandatory to enable appropriate advice to prevent acute attacks and allow genetic counselling. One hundred and ten members of a large kindred were examined clinically and using a new fluorimetric screening technique, thought to be more accurate than conventional urine, blood and faecal analysis, those over 15 years old were screened. Eight of 50 sera were positive. Four clinically affected members were identified. Four latent cases were identified and two previously uncertain cases were found to be unaffected. Only one asymptomatic member of this family with affected progeny (an obligate carrier) proved negative with this test and with conventional screening. Fluorimetric screening of variegate porphyria provides an accurate and easy method of screening families with variegate porphyria.

SIMULTANEOUS EXPRESSION OF CD4 AND CD8 BY GUT INTRAEPITHELIAL LYMPHOCYTES REVEALED BY FLOW CYTOMETRY

C. O'Farrelly, S. Lynch, D. Kelleher, C. Feighery, D. G. Weir.
Departments of Immunology & Clinical Medicine, Trinity College Medical School, St. James's Hospital, Dublin 8.

Phentoypic analysis of intraepithelial lymphocytes (IELs) from the gastrointestinal tract has been hampered by difficulty in obtaining tissue. We have developed a method for preparing single cell suspensions of the epithelial layer from endoscopically obtained small intestinal biopsies, suitable for flow cytometric analysis. Biopsies are taken into ion buffer containing 5% foetal calf serum and treated with 1mM dithiothreitol and 1mM EDTA for 30 minutes. Yields of $2\text{-}4\times10^6$ cells with 98-100% viability are obtained from 4 pieces of tissue. Histological examination of the remaining tissue reveals that the epithelial layer is removed without significant deterioration of the lamina propria (LP). These cell preparations are suitable for two colour flow cytometric analysis.

Flow cytometric analyses were carried out on epithelial cell preparations from 12 patients in whom gastrointestinal disease was excluded. Monoclonal antibodies against the following antigens were used: CD3, CD4, CD8, CD22, αß and γδ T cell receptors. CD3+IELs accounted for 6-17% of the epithelial cell preparations. Less than 1% of the gated IEL population were CD22 positive indicating that none were B cells and thus indicating minimal LP contamination. Using two colour analysis, 61-72% of CD3 positive lymphocytes were CD8 positive, while 5-14% were CD4 positive. In addition, a significant population (5-11%) of CD3 positive lymphocytes co-expressed CD4 and CD8 (DP+). Furthermore, 2-14% of IELs expressed the γδ TCR while 76-87% expressed the αß TCR.

Significantly, γδ+ cells were entirely CD4– suggesting that DP+ population is exclusively αß+.

Flow cytometric analysis is a powerful tool for identifying IEL subpopulations. Previously, DP+ lymphocytes were thought to be an immature population found only in the thymus. Their presence in the gastrointestinal epithelium lends support to the hypothesis that the gut is a site of extrathymic T cell differentiation.

SPECIFIC SENSITISATION TO DIETARY PROTEIN ANTIBODIES IN RHEUMATOID ARTHRITIS

M. Abouzakouk, C. Feighery, E. Casey, C. O'Farrelly.
Departments of Immunology and Rheumatology, St. James's Hospital, Dublin 8.

The possible role of diet in rheumatoid arthritis (RA) remains controversial. We are investigating the possibility that a subgroup of RA patients are specifically sensitised to dietary proteins. Ninety-nine patients with classical RA, attending the Rheumatology clinic were randomly selected for preliminary screening (69 were female, mean age 56; mean duration of disease: 10 years). All were on second-linc treatment and 65 were taking non-steroidal anti-inflammatory drugs (NSAIDS). An age-matched disease control group included 13 patients with psoriatic arthritis; 9 were taking NSAIDS.

Serum samples were taken and tested for IgG antibodies to egg, wheat and milk proteins using an ELISA system. IgAs and IgM rheumatoid factor levels were also measured using ELISA. Thirty-five RA patients (35%) had raised levels of IgG antibodies to one or more dietary proteins (DP). Only two of 24 healthy controls (8%) and one of the 13 psoriatic patients (8%) had raised levels of any one of these antibodies. Significantly, NSAID therapy was not limited to the DP antibody + group: 60% of the DP antibody +ve group, 69% of DP antibody –ve group and 69% of psoriatic patients were taking NSAIDs. Twenty-seven of DP antibody +ve patients (77%) and 67% of DP antibody –ve group had raised levels of IgA RF. IgM RF was positive in 63% of DP antibody + RA patients, 70% of DP antibody negative patients and 15% of the psoriatic patients. Four patients with raised

antibodies to all proteins had raised IgARF, disease was not controlled in 3 (75%). In contrast, disease was well controlled in 17/18 RA patients negative for DP antibodies and IgARF ($P<0.01$).

Sensitization to dietary proteins in RA patients does not correlate with NSAID treatment. Moreover, a significant proportion of DP antibody +ve patients were sensitised to one antigen alone. These results suggest that sensitisation is specific in a subgroup of RA patients. We are investigating the possibility that dietary manipulation in these patients might influence disease activity.

ADHESION MOLECULES IN PSORIATIC ARTHRITIS

D. Veale, O. Fitzgerald.
Department of Rheumatology, St. Vincent's Hospital, Dublin.

Migration of inflammatory cells into tissues first requires adhesion to endothelial cells (ECs). It has been suggested that this process is tissue specific by way of differential adhesion molecules (AM) expression by specialised ECs.

We examined the expression of intercellular adhesion molecule-1 (ICAM-1), endothelial leucocyte adhesion molecule-1 (ELAM-1) and vascular cell adhesion molecule-1 (VCAM-1) in the synovial membrane (SM), involved skin (IS) and uninvolved skin (US) from patients with psoriatic arthritis (PA) (n=15) and in IS from patients with psoriasis but no arthritis (PS) (n=5) and in normal skin (n=4). Synovium and skin was snap-frozen and monoclonal antibodies to ICAM-1, ELAM-1 and VCAM-1 were used in a standard three-stage immunoperoxidase staining technique to examine AM expression.

ICAM-1 was intensely expressed on dermal ECs and on keratinocytes (KCs) in the IS from PA and PS patients. In the SM, ECs also expressed ICAM-1 with staining in addition being observed in the lining layer and on monocyte/macrophage-type cells. There was constitutive expression of ICAM-1 on ECs only in US from PA patients and in normal skin. In contrast, ELAM-1 expression was restricted to ECs; it was widespread and intense in IS from PA and PS patients, however it was minimal on ECs in SM, in US from PA patients and in normal skin. Finally, VCAM-1 was expressed on ECs and on some dendritic cells in IS from PA and PS patients. In the SM VCAM-1 expression was confined to cells within the lining layer and to occasional dendritic-type cells within focal infiltrates. There was minimal VCAM-1 staining on ECs in US from PA patients and in normal skin.

In conclusion: (1) ECs in PA SM express ICAM-1 but minimal ELAM-1 and no VCAM-1; (2) SM lining layer expresses both ICAM-1 and VCAM-1; (3) in IS from both PS and PA patients, AM expression is up-regulated on ECs and KCs express ICAM-1. These differences observed suggest a mechanism for controlling cellular traffic in PS and in PA.

RESPIRATORY MEDICINE/MICROBIOLGY

LARYNGEAL RECEPTOR AND REFLEX RESPONSES TO CO_2

A. Bradford*, R. G. O'Regan, P. Nolan, D. McKeogh.
*Department of Physiology, Royal College of Surgeons in Ireland, St. Stephen's Green, Dublin 2, and Department of Physiology and Histology, University College, Earlsfort Terrace, Dublin 2.

In 19 anaesthetized (pentobarbitone sodium, 30-48 mg/kg i.p.), adult cats, artificially ventilated or breathing spontaneously through a tracheostomy, we have used an artificially ventilated laryngeal preparation which reproduces physiological conditions[1,2] in order to study the effects of laryngeal CO_2 on superior laryngeal nerve (SLN) afferent activity and on SLN-mediated reflex effects on diaphragm and genioglossus (GG) EMG activity.

Changing laryngeal CO_2 concentration from 0 to 5% or 9% caused marked, concentration-dependent excitation of negative-pressure receptors and cold receptors and inhibition of positive-pressure receptors.

In reflex studies, laryngeal CO_2 caused a concentration-dependent increase in GG EMG and a reduction in respiratory rate, effects which were abolished by SLN section. During laryngeal ventilation, phasic GG EMG was abolished and respiratory rate was increased by cutting the SLNs.

We conclude that laryngeal receptors are highly responsive to physiological levels of CO_2. Such CO_2-sensitivity may be important in ventilatory control and in the maintenance of upper airway patency.

References
1. Bradford, A., Bannon, C., Nolan, P., O'Regan, R. G. Chemoreceptors and Chemoreceptor Reflexes, New York, Plenum Press, 1990.
2. Nolan, P., Bradford, A., O'Regan, R. G and McKeogh, D. Experimental Physiol. 1990, 75, 271-274.

THE EPIDEMIOLOGY OF TUBERCULOSIS IN A GEOGRAPHICALLY DEFINED AREA

F. Howell.
Eastern Health Board, Tuberculosis Advisory Committee, Community Care Area 7, Aras Daimhin, Dublin 3.

Tuberculosis (TB) is a significant cause of morbidity yet epidemiological data for TB is scanty. To establish a population profile of TB for the first time in nearly 40 years, public health doctors set up a surveillance system to capture such data in the E.H.B. region. In 1990, 191 new cases of TB were notified, 15.5/100,000. Of these, 185 were indigenous to Ireland. Males accounted for 54%. Nearly 50% of cases occurring in females do so in those <35 years and for males, 45% occur in those <45 years. 103 (54%) had pulmonary TB alone and only 50 (26%) had a presumptive diagnosis. Cases occurred throughout all social classes. Nearly 50% were employed or in full time education. Of the 171 with pulmonary TB, 61% had unilateral disease, 29 cases had cavities and 24 had pleural effusions. Thirteen cases were HIV + which is a major increase from that recorded in previous studies. Contact tracing located 33 (17%) cases. The continuing occurrence of TB in our young, economically active population is in marked contrast to other EC countries and suggests a more vigorous approach is needed if eradication is a realistic goal.

SERUM AGALACTOSYL IgG LEVELS IN SARCOIDOSIS

C. M. O'Connor*, G. Rook#, M. X. FitzGerald*.
Department of Medicine, U.C.D. & St. Vincent's Hospital, Dublin. #Department of Medical Microbiology, University College & Middlesex School of Medicine, London, U.K.

Circulating levels of agalactosyl IgG (G0) have been shown to be elevated in tuberculosis, Crohn's disease and rheumatoid arthritis, all of which are characterised by a T-cell mediated response. In these diseases raised G0 levels appear to reflect

episodes of disease activity[1]. We examined serum G0 levels in sarcoidosis - a disease also associated with a T-cell response. G0 levels were assessed in serum samples from 36 biopsy proven sarcoid patients (17 female, 19 male; mean age = 32.9±8.9 yrs). Samples were taken (i) at a time when the patient exhibited clinically active disease (initial sample) and (ii) ≥3 yr later (final sample). Patients were allocated to one of four groups on the basis of disease outcome on follow-up. Allocation to groups was done without knowledge of G0 levels. Highest initial G0 levels were observed in patients who subsequently responded to corticosteroid therapy. On follow-up, serum G0 levels decreased significantly ($p<0.05$) in patients whose disease resolved. By comparison, no significant change in serum G0 levels was observed in patients whose disease remained active during the follow-up period. These results suggest that elevated serum G0 levels may reflect episodes of T-cell-dependent tissue damage in sarcoidosis and that serial G0 measurements may be useful in evaluating the need for and response to corticosteroid treatment.

Reference

1. Rook, G. A. W., Scand. J. Immunol. 1988: 28, 487-493.

BRONCHIAL ASTHMA: AN INTEGRATED PHYSIOLOGICAL/IMMUNOPATHOLOGICAL APPROACH

C. Power, S. Sreenan, L. W. Poulter*, C. M. Burke.
Department of Respiratory Medicine, SCMH, Dublin.
*Department of Clinical Immunology, The Royal Free Hospital, London.

The purpose of this study was to relate the distribution of immunocompetent cells in the normal and asthmatic bronchial wall with physiologic lung parameters and to investigate the response to inhaled corticosteroid therapy. Spirometry, broncho dilator and bronchoconstrictor responses were recorded in 25 asthmatic and 27 normal subjects. Bronchial biopsies were obtained from all subjects. These were repeated in the case of the asthmatic group after 3 months treatment with inhaled corticosteroids. Frozen sections of all biopsies were analysed using immunohistological methods to reveal cell types and HLA DR expression. Results were quantified using computerised image analysis. The results were as follows: normal/asthmatic cells per unit area: T cells 0.9/8.9; CD45RO+T cells 1.1/6.1; macrophages 0.05/2.7, dendritic cells, 0.3/2.2. HLA-DR (optical density) 0.03/1.6. In asthmatics, DR levels correlated with BHR response, ($p<0.001$). Therapy with inhaled corticosteroids caused a simultaneous reduction in both BHR, (1-2.2 mg histamine), and HLA-DR expression in the tissue, (1.6-0.9 relative optical density; $p<0.05$). Asthmatic subjects demonstrate peribronchial inflammation which is related to BHR. Efficacious therapy causes a significant reduction in immunologic inflammatory parameters.

CHARACTERISATION OF TWO FIBROBLAST CELL LINES DERIVED FROM NORMAL HUMAN LUNG

P. Shanahan, N. O'Donnell, C. M. O'Connor, M. X. FitzGerald.
Department of Medicine, University College, Dublin and St. Vincent's Hospital, Dublin.

Fibroblasts play a major role in wound healing following tissue damage. However, in situations of prolonged damage, an exaggerated fibroblast response can lead to fibrosis. The factors involved in the transition from wound-healing to fibrosis are under intensive investigation. One hypothesis suggests that a subpopulation of fibroblasts with greater proliferative and matrix-producing capacities may be differentially expanded in fibrotic situations. We have developed two morphologically distinct *in vitro* fibroblast lines from human lung tissue. One line (Line 1) displays a spindle-like morphology characteristic of fibroblasts. When confluent, the second line (Line 2) displays a 'cobblestone' morphology, reminiscent of endothelial cells. Line 2 also exhibits a significantly higher proliferative rate than Line 1. Ultrastructural examination indicates that both cell types are true fibroblasts. In addition, both cell lines react with a monoclonal antibody to a fibroblast surface antigen. Detailed morphologic studies have demonstrated the presence of large vacuole type structures in Line 2 cells at confluence. These are absent from Line 1 cells. The vacuole structures stain strongly for fibronectin and preliminary evidence suggests that they may also contain collagen. These studies indicate the existence of two distinct types of fibroblast derived from normal lung which differ in proliferative and matrix-producing capabilities.

PREVALENCE OF ANTI-HCV IN VARIOUS RISK GROUPS IN AN IRISH POPULATION

K. Birthistle, M. O'Mahony, A. G. Shattock, I. B. Hillery.
Virus Reference Laboratory, U.C.D., Dublin 4.

Hepatitis C virus (HCV) has recently been recognised as an important cause of non-A, non-B hepatitis (NANBH), as a result of the development of several reliable anti-HCV test kits.

The aim of this study was to analyse the prevalence of anti-HCV among 1,132 patients in various categories and risk-groups.

Analysis was made of anti-HCV tests performed from August 1989 through November 1991. Patients were categorised according to risk-group or clinical status. Sera were tested on one or two commercial systems, as they became available (Ortho, Abbott).

Of the 1,132 patients in the study, 24% were positive for anti-HCV, and 76% were negative. The highest risk group was found to be intravenous drug abusers (68% positive), while 62% of haemophiliacs (A or B) tested were positive. A comparably low level was found among the group receiving blood transfusions (13%).

We conclude that HCV is responsible for a considerable proportion of hepatitis cases in an Irish population, additional to that contributed by hepatitis A and hepatitis B in these Irish groups[1].

Reference

1. Shattock, A. G., Jones, L., O'Mahony, M., Hillary, I. B. Changes in incidence of hepatitis B in Ireland from 1970-1987. Irish J. Med. Sci. 1989: 158, 8, 210-214.

NEUROPSYCHIATRY/PHARMACOLOGY

CLINICAL APPLICATION OF OCULAR MICROTREMOR

C. Bolger, N. Sheehan, M. Hutchinson*, J. P. Phillips*, D. Coakley, J. Malone.
Mercer's Institute for Research in Ageing; *Adelaide Hospital, Dublin; *Beaumont Hospital, Dublin.

Ocular Microtremor (O.M.T.) is a constant, physiogical high frequency tremor of the eye. Eye movement is generated at brainstem level and it is postulated that O.M.T. may be a useful indicator of brainstem dysfunction. We have developed an accurate method of recording O.M.T., which unlike previous systems has

a flat frequency response between 20 and 200 Hz and is highly portable. A recording session takes between 10-15 mins from setup. Using replication reliability statistics we have demonstrated that as little as 1 second of record is required to provide an estimate of eye tremor frequency which is more than 90% reliable. Several other parameters of O.M.T. activity may be measured reliably from a 5 second trace. Records are obtained at the patient's bed side on audio tape and analysis performed later either by peak counting or spectral analysis. To date we have successfully obtained records from normal subjects, patients with Multiple Sclerosis, Parkinson's disease, in coma and brain dead subjects. The frequency of O.M.T. is significantly greater in normal subjects than from those with Multiple Sclerosis ($P<0.001$: n=100), patients with Parkinson's ($P<0.001$: n=44), patients in coma ($P<0.001$) and is absent in brain dead subjects. O.M.T. may provide an objective and portable neurophysiological means for assessing these patients.

CREUTZFELDT-JAKOB DISEASE IN THE UNITED KINGDOM 1985-90

T. F. G. Esmonde, R. G. Will.
Department of Clinical Neurosciences, Western General Hospital, Edinburgh EH4 2XU.

Epidemiological surveillance of Creutzfeldt-Jakob disease (CJD) in the United Kingdom was undertaken following the emergence of a new spongiform encephalopathy in cattle, bovine spongiform encephalopathy, in order to ascertain whether there had been any change in the incidence or characteristics of the human disease. Cases were identified through death certificates and by direct notification from clinicians. In the period 1/1/85 to 30/4/90, the average annual incidence was 0.43 cases per million. Mean age at onset was 61.5 years (SD=12.0), with an average illness duration of 6.5 months (SD=7.7). Eleven cases with a course of greater than 12 months, and 5 iatrogenic cases, two familial cases, and 4 cases with a family history of other dementia were found. No excess of employment in medical, paramedical, farming or food industries occurred. Dementia was seen in all except three cases, myoclonus in 80%, and a characteristic electroencephalogram in 71%. No spatio-temporal clustering of cases occurred. A prospective case-control study has identified 39 further cases between 1/5/90 and 31/10/91. No changes in age of onset or duration of illness were seen. Odds ratio for employment in medical, paramedical, food or animal-related industries was 1.16 (95% CI = 0.44-3.05) between cases and controls. Mutation in the PrP "prion" gene was seen in three cases. As yet, there has not been any change in the epidemiological characteristics of CJD.

REGULATION OF CHLORIDE TRANSPORT IN BRUSH BORDER MEMBRANE VESICLES FROM HUMAN PLACENTA

D. Faller, M. P. Ryan.
Department of Pharmacology, University College Dublin, Belfield, Dublin 4.

The basic defect in cystic fibrosis is associated with defective chloride transport in epithelial tissue. Membrane vesicles prepared from epithelial cells provide useful model systems to study regulation of chloride transport. Human placenta is an available source of human epithelial tissue. We have used brush border membrane vesicles (BBMV) from human placenta to investigate regulation of chloride transport. The purity of the BBMV was assessed by marker enzymes, electron microscopy and flow cytometry. We have previously reported effects of valinomycin, N-phenylanthranilic acid (NPA), 4,4,diisothiocyanostilbene-2-2'-disulphonic acid (DIDS), bumetanide and fatty acids on ^{36}Cl uptake using assay conditions of an outwardly directed Cl gradient. The present studies were carried out using conditions of an inwardly-directed K gradient which facilitates addition of putative Cl channel activators. Valinomycin (5 μM), DIDS (100 μM) and bumetanide (100 μM) were used to distinguish between conductive and other forms of chloride transport. Incorporation of ATP-γ-S (0.8 mM) into the BBMV significantly reduced total ^{36}Cl uptake. However, the DIDS and bumetanide-insensitive components of ^{36}Cl uptake were significantly increasaed ($p<0.05$) by incorporation of ATP-γ-S. These findings suggest that chloride channel activity in these vesicles may be regulated by cAMP dependent protein kinase. This model may aid in development of new therapeutic strategies for chloride channel activation in cystic fibrosis.

A NOVEL DIAGNOSTIC ASSAY FOR AUTOIMMUNE CHRONIC ACTIVE HEPATITIS

B. Manning, F. Martin.
Department of Pharmacology, University College Dublin, Belfield, Dublin 4.

The hepatic asialoglycoprotein receptors (ASGP-R) has been shown to be a significant immune target in the disease autoimmune chronic active hepatitis (AI-CAH), with over 90% of patients having circulating high titre autoantibodies which recognise the protein, with disease severity correlating with anti-ASGP-R antibody titre. Previous studies have employed purified ASGP-R protein from rabbit liver in radioimmunoassay of AI-CAH patient sera. This approach was limited, however, due to species non-cross-reactivity, and difficulty in protein purification.

We have employed the bacterial T7 RNA polymerase expression system, to overproduce a fragment of human ASGP-R from its cDNA in *E. coli*. The cloned protein was immunologically equivalent to natural ASGP-R as determined by Western blot analysis using antisera raised against the native protein.

The protein was purified and incorporated into an ELISA detection system for anti-ASGP-R autoantibodies in AI-CAH sera. Autoantibody was detected in AI-CAH patients with active disease, while patients in steroid induced remission from AI-CAH, or with unrelated autoimmune disorders (rheumatoid arthritis) had levels equivalent to normal healthy control serum.

Due to the simplicity and rapidity of this technique, this ELISA could significantly contribute to the diagnosis and management of AI-CAH in the future.

PATIENT AND PRESCRIBER KNOWLEDGE OF DRUG THERAPY

P. M. E. McCormack, A. McGrath, R. Lawlor, C. Donegan, C. Boyce, D. O'Neill, S. Smith, C. Moloney, J. Feely, J. B. Walsh, D. Coakley.
Departments of Pharmacology & Therapeutics and Medicine for the Elderly, St. James's Hospital, Dublin 8.

It is held that increasing patient knowledge of drug therapy

improves compliance. We assessed patient knowledge of prescribed drugs in 50 out-patients (OPD) and in elderly patients on admission (n=129) and on discharge (n=100) from hospital.

Results indicate that 88% in OPD, 40% elderly admissions and 41% elderly discharges knew the indication for therapy; only 40% OPD patients, 8% elderly admissions and 12% elderly discharges could name their medications. Patient information was derived mainly from the prescriber.

In a further study we assessed doctor, nurse and patient ability to discriminate between commonly prescribed white tablets; doctors made errors in discriminating tablets on 25% occasions, nurses on 40% and patients on 61% occasions – young patients 67% and elderly 55% occasions.

These studies indicate that both in- and out-patients have poor knowledge of their medications. In addition their main source of knowledge i.e. the prescriber has poor ability to tell tablets apart. These studies suggest the patients and prescribers' knowledge needs to be improved.

ANTIHYPERTENSIVE DRUG EFFECT ON THE RELATIONSHIP BETWEEN MEAN BLOOD PRESSURES AND CIRCADIAN PRESSURE CHANGES

A. Stanton, N. Atkins, E. O'Brien, K. O'Malley.
The Blood Pressure Unit, Beaumont Hospital and Department of Clinical Pharmacology, Royal College of Surgeons in Ireland, Dublin.

The results of studies on the effects of antihypertensive agents on circadian blood pressure patterns have been inconclusive. The positive association between mean blood pressure level and circadian changes in untreated subjects has been ignored. This study was designed to investigate the influence of current first-line drug therapies and mean pressure on circadian blood pressure alterations by means of analysis of covariance.

The 24-hour ambulatory blood pressure records of 1893 subjects on no medication and 509 subjects on single drug therapy (thiazide diuretics 87, cardioselective ß-blockers 213, calcium antagonists 104, ACE-inhibitors 105), were examined retrospectively. Systolic and diastolic mean 24-hour pressures and circadian alteration magnitudes (CAM), quantified by a cumulative sums technique, were determined from each record.

Regression of CAM on mean 24-hour SBP and DBP for each treatment group, summarized by the regression co-efficients (standard error), and the results of analysis of covariance are shown in the table.

Group	mean 24-hour SBP	mean 24-hour DBP
No medication	0.193 (0.013)	0.083 (0.016)
Thiazide diuretics	0.004 (0.067)	0.068 (0.080)
Cardioselective ß-blockers	0.144 (0.043)	0.110 (0.054)
Calcium antagonists	0.064 (0.060)	0.178 (0.070)
ACE-inhibitors	0.216 (0.068)	0.268 (0.089)
Analysis of covariance F (p-value)	45.3 (0.0001)	9.64 (0.0001)

The regression coefficients differ significantly, indicating that interactions occur between drug treatment effects and mean pressure effects on CAM. These interactions warrant further prospective investigation, as recent studies have suggested that the pattern of 24-hour blood pressure quite apart from absolute pressure levels, appears to contribute to morbidity and mortality in hypertension.

CRITICAL CARE/ANAESTHESIOLOGY/ NEPHROLOGY

IMPAIRED IMMUNITY IN EXPERIMENTAL ABDOMINAL SEPSIS AND THE EFFECT OF INTERLEUKIN-2

D. B. Gough, A. Jordan, J. A. Mannick, M. L. Rodrick.
Department of Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, M.A.

In critical illness cell mediated immunity (CMI) is often impaired and bacterial translocation and sepsis are common. It is unknown whether bacteria are the cause or result of associated impaired CMI. The effects of experimental abdominal sepsis on CMI were investigated.

At days 1, 4 and 7 following septic challenge i.e. caecal ligation and puncture (CLP) and sham CLP, the *in vitro* responses of mouse spleen cells to phytohaemagglutinin (PHA) and concanaval A (Con A) were assessed together with the effects of *in vitro* IL-2 on these responses and *in vivo* IL-2 on survival following CLP.

At day 1 post CLP, mean PHA response was enhanced (43.8%±17, n=9) compared to sham CLP (n=10, $p<0.04$). By day 4, the responses to both Con A and PHA were suppressed (45.5%±4.4 and 57.5%±5.6 respectively, $p<0.005$ for both compared to sham CLP). Responses at day 7 approached those of sham CLP controls. *In vitro* IL-2 restored suppressed PHA responses at 4 days post CLP, 61,052±3,407 cpm to those of sham injured animals 64,643±4,727 cpm.

When mortality after CLP was compared, both IL-2 and vehicle therapy were associated with identical mortalities in the first 24 hours, thereafter those receiving IL-2 fared better ($p<0.05$). Bacteria may suppress immune function in critical illness. IL-2 may have a role in preventing sepsis related immunosuppression and mortality.

CANNULA SEPSIS DURING T.P.N.: SEVERITY OF ILLNESS AND ACUTE PHASE PROTEIN (FERRITIN) RESPONSE

E. McCarthy, C. M. Cooney, J. Bourke, D. M. Phelan.
Department of Anaesthesia & Intensive Care, Mater Misericordiae Hospital, Dublin 7.

C-reactive protein has been used as a diagnostic test of sepsis[1]. Ferritin is also an easily measured acute phase protein[2]. This study analysed whether cannula sepsis is related to severity of illness and elevated serum ferritin levels. Severity of illness was assessed using the Simplified Acute Physiology Score (SAPS). Over 30 months, 120 patients having TPN had twice weekly serum ferritin determinations and SAP Score estimations. 80% of these patients had undergone G.I. surgery. Cannula sepsis was found to be increased in patients with a SAP Score over 12, as opposed to those with a SAP Score less than 12 (43% : 24%). Serum ferritin was increased in patients with cannula sepsis and no patients with low serum ferritin levels had cannula sepsis. 20% of patients with raised serum ferritin levels did not have associated sepsis. Serum ferritin determinations have a sensitivity of almost 100% and a specificity of 85% for cannula sepsis. Cannula sepsis has a greater incidence in the critically ill.

References

1. Matson, A., Soni, N., Sheldon, J. Anaesth. Intens. Care. 1991: 19, 182-186.
2. Stahl, W. M. Crit. Care Med. 1987: 15, 545.

THE INCIDENCE OF GASTRO-OESOPHAGEAL REFLUX DURING ANAESTHESIA

A. M. Robertson, A. J. McShane.
Department of Anaesthesia, St. Vincent's Hospital, Elm Park, Dublin 4.

Gastro-oesophageal reflux may occur in patients undergoing general anaesthesia. When associated with tracheal aspiration it increases post-operative morbidity and mortality. The layrngeal mask is a new device for maintaining the airway during anaesthesia allowing 'hands off' control without the need for intubation. The purpose of this study is to determine the incidence of reflux with this new technique, and to compare it to conventional mask anaesthesia.

Following informed consent 26 patients having general anaesthesia for elective surgery were studied. In group A (N=13) anaesthesia was maintained using a standard face mask. In group B (N=13) laryngeal masks were used. Prior to induction oesophageal electrodes were placed in all patients. Continuous pH recordings were taken until thirty minutes after surgery and subsequently analysed using Synectics from Gastrosoft.

The overall incidence of regurgitation was 38.4%. In group A (face mask) it was 15.4% but in group B (laryngeal mask) it was higher at 61.5%. These results suggest that the use of the laryngeal mask may increase the incidence of silent regurgitation.

LIPOPROTEIN(a) AND TREATMENT OF END STAGE RENAL FAILURE

D. Buggy, A. Breathnach*, B. Keogh*, T. Coole*, J. Feely.
Departments of *Nephrology, Meath Hospital, *Biological Sciences, D.I.T. and Therapeutics, Trinity Medical School, St. James's Hospital, Dublin 8.

Patients with end stage renal failure (ESRF) are especially prone to cornary heart disease (CHD). This is in part due to hyperlipidaemia as a consequence of increased hepatic production of lipids particularly apolipoprotein B. Lipoprotein (Lp(a)) combines elements of apolipoproteins B and (a) whch is structurally similar to plasminogen and is a strong independent risk factor for CHD. We measured Lp(a) on fasting serum samples in 44 ESRF patients and 20 age matched control subjects by an Eliza technique (Tint-Elize Biopool). Lp(a) concentrations (mg/dl, mean ± SEM) compared with controls (14 ± 2) were higher ($p<0.01$) in patients on contiuous ambulatory peritoneal dialysis ((CAPD) 40 ± 6, n=8) but normal in patients on haemodialysis (n=18) or following renal transplantation (n=18). Of importance given the inhibitory regulatory effect of albumin on lipoprotein production in hepatocytes albumin levels were lower in patients on CAPD ($p<0.01$). Treatment related differences in lipid metabolism in patients with ESRF extend also to Lp(a) possibly predisposing to CHD. The inverse relationship between Lp(a) and serum albumin, in CAPD patients suggests increased hepatic production of lipoproteins and gives further insight into the regulation of Lp(a) concentrations.

PLENARY SESSION

INCREASED LEVELS OF CALSEQUESTRIN mRNA IN PATIENTS WITH POSTVIRAL FATIGUE SYNDROME

P. O. Behan, H. M. A. Cavanagh, J. W. Gow, K. Simpson, W. M. H. Behan.
University Department of Neurology, Institute of Neurological Sciences, Southern General Hospital, 1345 Covan Rd., Glasgow C43 2TZ.

A variety of viruses have been implicated in the actiology of the postviral fatigue syndrome. (PFS); also known as myalgic encephalomyelitis (ME) or chronic fatigue syndrome (CSF). In the majority of epidemics numerous clinical symptoms but few clinical signs have been reported. There is as yet no diagnostic test available but a working diagnosis has been established; diagnosis by exclusion of all other causes of fatigue. We have previously demonstrated the presence of enteroviral genomes in muscle biopsies of 53% of PFS patients. We have now found a relationship between PFS and high levels of transcription of the cellular, calcium binding protein, calsequestrin (CSQ). Levels of expression of CSQ mRNA are increased in patients as compared with normal controls. This abnormality is the first measurable organic change to be found in this group of patients. In addition, computer analysis demonstrates a similarity, at the nucleic acid level, between the CSQ gene and the enteroviral genome. We have also noticed an abnormality in the level of transcription of CSQ in other autoimmune and virally induced disorders, e.g. rheumatoid arthritis and systemic lupus erythematosus. These disorders are also associated with fatigue highlighting the importance of abnormal CSQ mRNA levels.

INSULIN DEPENDENT DIABETES IN PREGNANCY: 10 YEAR EXPERIENCE, 300 PATIENTS

M. Foley, R. Firth, J. Stronge.
National Maternity Hospital, Holles Street, Dublin 2.

Between 1981 and 1991, three hundred patients with pregestational insulin dependent diabetes were managed at the National Maternity Hospital. The objective was to reduce macrosomia and other fetal complications by careful glycaemic control and to manage diabetic patients without complications in the same way as the non-diabetic patients. There has been a progressive reduction in the incidence of macrosoma (birth weight > 4500g) over the study period from an average incidence of 18% to 5%. The incidence of babies greater than 4000gm has fallen and in the last four years 90% of babies born weighed less than 4000gm. The caesarean section rate increased from 24% to 32%, the need for induction has halved from 33% to 17% and spontaneous labour has increased from 45% to 54% in the past four years. The percentage of patients delivering after 40 weeks gestation increased from 26% to 44% at the end of the study period. In the past four years 83% of patients delivered after 38 weeks. This has been achieved without compromise in fetal outcome. There was one perinatal death and no case of cerebral dysfunction (in the past four years). These results suggest that meticulous glycaemic control can allow the vast majority of diabetic mothers to anticipate a similar pregnancy outcome to those of non-diabetics.

EXCESSIVE MENSTRUAL BLEEDING – WHO NEEDS TREATMENT?

J. Bonnar, B. L. Sheppard.
T.C.D. Department of Obstetrics and Gynaecology, Sir Patrick Dun Research Centre, St. James's Hospital, Dublin 8.

Excessive menstrual bleeding is a serious problem in gynaecology often resulting in hysterectomy. In this study 500 women complaining of excessive menstrual bleeding were recruited from gynaecology clinics. Objective measurement of menstrual blood loss (MBL) of 416 of these women showed 227 (55%) to have a normal MBL of < 80 ml x 39 ml, range 1-77) and 189 (45%)

to have excessive MBL > 80 ml per cycle (x 182 ml, range 80-1,059). No correlation was found between haemoglobin levels, duration of bleeding, number of sanitary towels used, age, parity of the woman's perception of her blood loss and the objectively measured MBL. Hysterectomies were undertaken in 140 of these women; 48 (35%) had normal MBL and 92 (65%) had excessive MBL. Histological examination of this latter group showed 35 (38%) to have minor pathology (e.g. focal adenomyosis, small fibroids) but 57 (62%) had no pathology and were classified as dysfunctional uterine bleeding. The results show that the objective measurement of MBL would be valuable in the diagnosis of excessive menstrual bleeding. This would allow patients with normal MBL to be reassured and reduce by at least 50% the number of hysterectomies being carried out in women complaining of excessive menstrual bleeding.

Supported by the Health Research Board (Ireland).

THE EFFECTIVENESS OF NEONATAL HEARING SCREENING

R. J. McClelland, D. R. Watson, V. Lawless, H. G. Houston*, D. Adams.
Queen's Univeristy, Belfast; *Royal Belfast Hospital for Sick Children.

The aim of the study was to establish the reliability and utility of hearing screening using brainstem auditory evoked potentials in high risk neonates.

The project consisted of a 9 year prospective study of 405 neonates admitted to the Special Care Baby Unit, Royal Maternity Hospital, Belfast in the period October 1982 to March 1987 (mean follow-up 5 years). Outcome measures were type and severity of hearing impairment and mortality.

The incidence of bilateral severe sensorineural impairment for Northern Ireland in the period of the study was 0.96/1000 live births. The incidence of severe bilateral sensorineural impairment among graduates from the Special Care Baby Unit was 12.5/1000 live births. The incidence of all forms of hearing impairment for the unit requiring intervention was 45/1000 live births. The sensitivity of the screening method was 100%, the specificity 88%.

It has been shown that if the procedure was introduced into routine clinical practice the mean age at diagnosis for all children with severe perinatal hearing impairment would be 11 months (median 1 month). This compares with the present Health Visitor screening service in which the mean age at diagnosis is 23 months (median 19 months) (mean difference 10 months CI 6 to 16 months, P<0.0001).

OBSTETRICS/PAEDIATRICS

CHILDREN'S DISCLOSURE OF SEXUAL ABUSE DURING FORMAL INVESTIGATION

C. Fitzpatrick, K. Keary*.
Department of Child Psychiatry, Our Lady's Hospital for Sick Children, Crumlin, Dublin 12; *St. Clare's Unit, The Children's Hospital, Temple Street, Dublin 1.

This study set out to examine the hypothesis that children rarely disclose sexual abuse for the first time durng formal child sexual abuse investigation. The study was carried out in a sexual abuse assessment unit based in a children's hospital, staffed by a multi-disciplinary team, and receiving referrals from community child protection agencies, paediatricians, general practitioners and the police.

The case notes of 358 children seen over a twelve month period were reviewed. Children were divided into two groups – a) those who had previously told someone about their abusive experiences prior to investigation; b) those who had not. There was a strongly positive correlation between having previously told someone about sexual abuse and disclosure of such abuse during formal investigation. There was also a strongly positive correlation between not having previously told someone and not disclosing during formal investigation. Age was an important variable, the under-fives being least likely to disclose abuse during formal investigation, irrespective of whether they had previously told someone about abuse. Disclosure of sexual abuse during investigation was strongly positively correlated with abuse being regarded as confirmed.

These results call into question the value of formal sexual abuse investigation in children who have not previously told someone about abuse. Approaches which may enable children to initially talk to someone in their family or community network are discussed.

THE EPIDEMIOLOGY OF PERTUSSIS IN THE REPUBLIC OF IRELAND (1940-1989)

F. Howell, S. Jennings.
Eastern Health Board, Community Care Area 7, Aras Daimhin, Jones's Road, Dublin 3.

Although epidemiological data have been gathered on pertussis annually since 1941, no detailed analysis of this data has been carried out. Notifications show a similar pattern to that observed elsewhere. Between 1941-1989, 15 epidemics occurred (mean interval 3.12 years). After the introduction of a vaccine in the 50's annual pertussis notifications declined from 175.1/100,000 in 1956 to 7.6/100,000 in 1972. Following the adverse publicity surrounding the vaccine in 1973 uptake fell to 30% in 1976. Although vaccine uptake increased in recent years it has plateaued at 40-45% and large epidemics have occurred again in 1985 (109.4/100,000) and in 1989 (57.2/100,000). Mortality from pertussis has fallen from 7.38/100,000 in 1940-1944 to 0.03/100,000 in 1980-1984 as has case fatality from 16.5% in 1942 to 0.1% in the 80's. Females are affected more than males (male/female ratio 0.9) and most cases occur in children > 1 year. If the accelerated programme on vaccination was introduced whereby children get the vaccine at 2, 3 and 4 months was introduced, 45% of cases occurring in those < 1 year could be avoided.

AUTONOMIC FUNCTION IN INFANTS AT RISK OF THE SUDDEN DEATH SYNDROME (S.I.D.S.)

T. G. Matthews, S. Gormally, *M. O'Regan.
Rotunda Hospital, Dublin 1 and *Trinity College, Dublin 2.

The purpose of this study was to assess autonomic function in a group of infants at increased risk of a S.I.D.S. compared to a control group of infants. Autonomic function was measured in two groups: (1) 54 healthy infants who had sustained an acute life threatening episode (A.L.T.E.) which required vigorous resuscitation and was unexplained; (2) 27 healthy age matched control infants. In all infants autonomic function was assessed during quiet sleep, by the long term heart rate beat to beat variability

and the heart rate and blood pressure response to a change from the supine to the upright posture. Autonomic function was markedly different between the 2 groups studied with the A.L.T.E. group having a diminished heart rate variability [16.02 v 24.1, P<0.001] and a postural fall in blood pressure [BP response A.L.T.E. group - 8.97 mmHg; BP response control group + 6.48 mmHg]. The heart rate response to posture change was not different between the 2 groups. Infants who have suffered a severe A.L.T.E. have increased risk of S.I.D.S. (of 20-40/1,000 compared to 2.6/1,000 for all Irish infants) and markedly abnormal autonomic function. It is suggested that poor autonomic function predisposes an infant to A.L.T.E.s and S.I.D.S.

SUDDEN INFANT DEATH SYNDROME (SIDS) COUNSELLING: DOCTORS' TIME WELL SPENT

O. C. Ward.
Children's Research Centre, Our Lady's Hospital for Sick Children, Dublin 12.

In Dublin SIDS infants are brought to the children's hospitals. The remains are identified to the Gardai and a coroner's post-mortem is carried out. In 1986 100 families were visited to ascertain their perception of how the hospitals had catered for their needs. 1. Serious deficiencies were identified. A crisis intervention programme was set up in Our Lady's Hospital for Sick Children based on paediatric, nursing, social work and chaplaincy inputs. An explanatory booklet was prepared for parents. 2. After two years a further sample of 28 families was reviewed. Seven had moved, but 21 were visited. Whereas in 1986 50% of parents felt that their grieving had been aggravated by all hospitals' handling of their bereavements, in 1988 all 21 families in Our Lady's Hospital catchment area felt that they had been helped. An independent review has identified a group of parents suffering from prolonged abnormal grieving. No parents who had received medical crisis intervention counselling fell into this group. 3. Another 15 families were visited in 1990. Greater privacy in the casualty departments and a full written autopsy report for parents are now priorities.

References

1. Ward, S., McNamara, D., Ward, O. C. Irish Med. J. 1986: 79, 209-211.
2. Ward, O. C. The Hospital and Cot Death. Children's Research Centre, O.L.H.S.C.
3. Powell, M. Ir. J. Med. Sc. 1991: 160, 282-285.

THE EFFECTS OF SURGERY ON CELL-MEDIATED IMMUNITY IN PATIENTS WITH OVARIAN CARCINOMA

S. Kehoe[1,2,3], D. Luesley[2], K. Chan[3], K. Ward[2].
[1]Cancer Research Campaign, Queen Elizabeth Medical Centre, Birmingham, England; [2]Dept. Obs. and Gynae., Dudley Rd. Hospital, Birmingham; [3]The Women's Hospital, Birmingham.

The effects of surgery on cell-mediated immunity in 12 patients with histologically proven ovarian carcinoma and 10 control patients was examined. The mean age of cancer patients was 63 yrs [range 44-86] as compared to controls at 42 yrs [range 31-51]. Two patients had stage I, one stage II and 9 stage III/IV disease. Successful excision of all tumour was achieved in 9 cases. In the control group 7 had hysterectomies and 3 ovarian cystectomies. The total T cell, T helper [Th], T suppressor/cytotoxic [Ts] and natural killer cells [NK] were measured on the morning of operation and for 7 days post-operatively. A fasting venous blood sample [10 mls heparinised] was obtained and analysed using monoclonal antibodies and a Coulter Profile II flow cytometer. In patients with malignancy a significant fall [$p<0.05$] occurred in Ts from 19.37 (SE 4.2) on Day 0 to 8.67 (SE 2.39) on Day 2 in conjunction with a fall in NK cells from 17.5 (SE 7.3) to 4.5 (SE 1.6) [$p<0.05$]. These values returned to normal by Day 7. The total T cell count also fell but not to statistically significant level. In the control group a significant fall in both Ts and NK cells was recorded similar to that of the patients with malignancies. The fall in total T cell in the controls was significant by Day 2. The Th/Ts ratio did not alter significantly in either group, but the trend in the control group was to have a ratio above 2 [i.e. above normal ratio] whereas in the cancer patients this fell below 2 in 5 of the 7 post-operative days. The decreases in Ts and NK cells with the resultant imbalance in cellular immunity would be expected to have more sinister sequelae for patients following surgery for malignant rather than benign conditions.

ENDOCRINOLOGY/LIPIDS

OESTROGEN FAILS TO REGULATE CHOLESTEROL METABOLISM IN DIABETIC WOMEN

M. Cox, J. Caird, D. Owens, S. Gilligan, S. McBrinn, P. Collins, A. Johnson, G. Tomkin.
The Adelaide Hospital, Dublin and The Royal College of Surgeons in Ireland, Dublin 2.

The protective effect of oestrogen against the development of atherosclerosis is lost in diabetes. We have examined the relationship between oestrogen, progesterone, serum lipoproteins and cellular cholesterol metabolism in pre-menopausal diabetic women.

Five female non-diabetic control subjects were compared with 5 age- and sex-matched Type 1 diabetic patients. Ethics committee approval was obtained and fasting blood samples were taken weekly for four consecutive weeks. Cholesterol synthesis was measured by [^{14}C]acetate incorporation into cholesterol in peripheral blood mononuclear leucocytes (PBMC), cellular cholesterol by an enzymatic fluorometric assay and cholesterol ester transfer protein (CETP) activity by transfer of [^{14}C] cholesteryl oleate from low density lipoprotein (LDL) to high density lipoprotein (HDL). The compostion of lipoproteins, isolated by ultracentrifugation, were measured and serum lipoprotein levels were determined.

Serum cholesterols of 5.3±0.7 and 4.9±0.6 mmol/l, HDL cholesterols of 1.76±0.22 and 1.62±0.23 mmol/l and serum triglycerides of 0.88±0.16 and 0.75±0.10 mmol/l for controls and diabetic patients were similar and did not change during the menstrual cycle. There was a significant negative correlation ($p<0.05$) between both oestrogen and progesterone and [^{14}C]acetate incorporation into cellular cholesterol in control subjects but not in diabetic patients. The LDL esterified/free cholesterol ratio decreased from 2.14±0.08 to 1.44±0.16 ($p<0.05$) at mid-cycle in controls subjects only. CETP was significantly higher in diabetic patients (184±11 vs 143±6.5 nmol/ml/h for controls) ($p<0.05$). Cellular cholesterols of 27.4±2.1 and 26.1±3.2 μg/mg cell protein and Lp(a) levels of 10.5 and 6.6 mg/dl for control and diabetic were similar and remained unchanged during the menstrual cycle.

These findings suggest an alteration in endocrine regulation of cholesterol synthesis in diabetes which could be associated with increased risk of atherosclerosis in the female diabetic patient.

IMPACT OF PROGESTOGEN AND OESTROGEN ON LH PULSATILITY IN POLYCYSTIC OVARY SYNDROME

T. M. Fiad, M. Culliton, T. J. McKenna.
Department of Endocrinology and Diabetes Mellitus, St. Vincent's Hospital, Dublin 4.

The present study is designed to examine the effect of progestagen and oestrogen on the pattern of pulsatile LH secretion in polycystic ovarian syndrome (PCOS). Venous sampling at 15 minute intervals was performed over 6 hours followed by LH-RH administration. Sampling was performed under basal conditions, following exposure to the progestagen medroxyprogesterone (MPA), 10 mgs daily for 5 days, and following exposure to both MPA and clomiphene citrate (an anti-oestrogen), 50 mg daily for 5 days. The mean LH levels declined significantly from 8.5 ± 2.7 IU/L (mean ± SD) in untreated patients to 4.8 ± 2.1 IU/L following exposure to MPA, $p<0.001$. Although the mean LH pulse amplitude and the mean LH pulse frequency over 6 hours, declined following MPA treatment, the differences observed were not statistically significant. However, there was significant suppression of the maximum LH incremental response to LH-RH administration following MPA. The addition of clomiphene produced no further change. These findings suggest that progesterone deficiency which occurs in PCOS as a consequence of ovulatory failure, plays an important role in the LH hypersecretion observed in PCOS. Blunting of the LH response to LH-RH following exposure to progesterone suggests that the predominant effect of progesterone is on pituitary sensitivity.

THE INFLUENCE OF DIET, HYPERCHOLESTEROLAEMIA AND DIABETES ON SERUM LP(a) LEVELS

S. Gilligan, P. B. Collins, G. H. Tomkin*.
Department of Biochemistry, Royal College of Surgeons in Ireland, Dublin 2 and *The Adelaide Hospital, Dublin 8.

Lipoprotein (a) is an independent risk factor for coronary heart disease. This study investigated LP(a) levels in relation to hypercholesterolaemia and diabetes. Four categories of patients were examined: normocholesterolaemic controls (NC, n=42), hypercholesterolaemic controls (HC, n=23), normocholesterolaemic Type II diabetic subjects (DNC, n=21) and hypercholesterolaemic diabetic subjects (DHC, n=18). Plasma Lp(a) levels were measured using the Tint-Elize Kit (Biopool, Uema, Sweden), and low-density lipoprotein (LDL) fractions were prepared by standard ultracentrifugation. Due to the skewed nature of the Lp(a) distribution, all four groups showed great variation in plasma Lp(a) levels and this variation was greatest in the HC group. The DHC and HC categories were found to have an increased incidence of elevated Lp(a) levels (>30 mg/dl), when compared to both normocholesterolaemic groups (51% versus 22% respectively). The incidence of raised Lp(a) levels in the DNC group was comparable to that of the NC group. Short-term effects of high-fat or high carbohydrate feeding on Lp(a) levels in these patient categories indicated no major effects of diet on total serum Lp(a) levels, but evidence of altered ultracentrifugal distribution of Lp(a) between diabetic and non-diabetic subjects was apparent. The data suggests an association between elevated serum Lp(a) levels and diabetes only in the presence of co-existent hypercholesterolaemia.

REVERSE CHOLESTEROL TRANSPORT IN DIABETIC AND NON-DIABETIC SUBJECTS

S. McBrinn, A. Johnson, G. Tomkin*, P. Collins.
Department of Biochemistry, Royal College of Surgeons in Ireland, Dublin 2 and *The Adelaide Hospital, Dublin 8.

Reverse cholesterol transport identifies a series of metabolic events resulting in the transport of cholesterol from peripheral tissues to the liver and plays a major role in maintaining cholesterol homeostasis in the body.

The aims of this study were to investigate reverse cholesterol transport in diabetic and non-diabetic subjects by measuring cellular cholesterol content (μg/mg protein), leicithin: cholesterol acyl transferase (L.C.A.T.) activity and cholesteryl ester transfer protein (C.E.T.P.) activity (nmol/ml plasma/hr). The following subjects were examined: Group 1 normocholesterolaemic (n=8), Group 2 hypercholesterolaemic (n=14), Group 3 diabetic normocholesterolaemic (n=18), Group 4 diabetic hypercholesterolaemic (n=14). Cellular cholesterol was estimated flourimetrically and L.C.A.T. activity using a colorimetric method. C.E.P.T. activity was estimated using [^{14}C] cholesteryl-ester labeled LDL.

Cellular cholesterol content (μg/mg protein) was significantly lower ($p<0.01$) in Group 1 (26.4±2.3) compared to Groups 2, 3 and 4 (40.5±3.6; 37.2±3.9 and 35.1±3.4 respectively). In non-diabetic subjects there was a significant correlation between serum and cellular cholesterol ($R=0.68$; $p<0.0001$) but not in diabetic subjects ($R=0.099$; NS). L.C.A.T. activity was significantly lower ($p<0.05$) in Group 2 subjects (116.0±27.3) than in Group 4 subjects (271.5±64.5). No other significant differences were recorded regarding L.C.A.T. activity. Group 3 subjects had significantly lower ($p<0.05$) C.E.T.P. activity (25.9±2.9) than Groups 1, 2 and 4 (39.6±4.9; 40.1±4.3 and 34.3±4.5 respectively).

We conclude that serum cholesterol content reflects cellular cholesterol content in non-diabetic subjects. We also conclude that reverse cholesterol transport may be altered in diabetes. This alteration is in part due to the activities of C.E.T.P. and L.C.A.T., the two major enzymes involved in reverse cholesterol transport.

THE EFFECT OF ALPHA BLOCKADE ON CHOLESTEROL REGULATION *IN VITRO* AND *IN VIVO*

D. Owens, G. H. Tomkin.
Department of Metabolic Medicine, The Adelaide Hospital, Dublin.

Beta blockers have been used for many years in the treatment of hypertension, yet studies have failed to demonstrate a benefit in the prevention of cardiovascular events. This study evaluates the effect of doxazosin, an alpha blocker on cholesterol metabolism at cellular level. The effect of doxazosin on low density lipoprotein (LDL) binding to mononuclear leucocytes was examined in a series of *in vitro* experiments to evaluate the results of the clinical study. Ten hypertensive patients were examined in the clinical study. LDL composition and cholesterol synthesis as measured by [14C]-acetate incorporation were compared before and after treatment with doxazosin and cellular cholesterol and LDL receptor binding were also measured. Mean serum triglycerides fell from 2.32±0.38 to 1.89±0.42 mmol/l, $P>0.05$. Serum cholesterol did not change significantly but LDL receptor-mediated binding fell from 15.7±3.0 to 6.7±1.5 ng/mg cell protein ($p<0.002$). [^{14}C]-acetate incorporation rose sgnificantly from 10.9±1.1 to

14.4±1.0 nmol/mg cell protein ($p<0.03$) and cellular cholesterol fell from 61.4±7.8 to 23.4±2.5 ng/mg cell protein ($p<0.001$). In an *in vitro* cell system doxazosin had no effect on LDL receptor binding or on cellular cholesterol synthesis.

We conclude that doxazosin has an inhibitory effect on LDL binding and causes a reduction in cellular cholesterol in the peripheral cell which may have a beneficial influence on delivery of cholesterol to the atheromatous plaque.

A METHOD FOR DETERMINING CHOLESTEROL SYNTHESIS RATES IN HUMAN LIVER BIOPSIES

J. C. Stinson, D. Owens, P. Collins, A. Johnson, G. H. Tomkin.
Departments of Medicine, Adelaide Hospital and Department of Biochemistry, Royal College of Surgeons in Ireland.

Research into cholesterol synthesis in humans usually involves mononuclear cell or cell culture models. The aim of the study was to develop a system for measuring cholesterol synthesis rates in human liver biopsies obtained at laparotomy. Ethical committee approval was obtained. This technique was developed in the rat and rabbit initially before human tissue was studied.

Patients undergoing laparotomy for non-cancerous conditions gave informed consent to wedge biopsy of liver. Once obtained this biopsy was placed in RPMI medium containing penicillin and streptomycin at 4°C. This sample was then manipulated on ice. The capsule was stripped off and using a 3mm "punch biopsy" cylinders of 3mm diameter were bored. These cylinders were cut into 2mm lengths and excess fluid removed with filter paper. Dry weights were recorded and cholesterol synthesis rates were measured by incubating these biopsies in lipoprotein deficient medium containing ^{14}C acetate. The radioactive cholesterol produced was extracted, separated by chromatography and quantified by scintillation counting. Results were expressed as pmol/min/mg protein. Production remained linear for up to 7 hours of incubation. For the rat the synthesis rate was 573±43.6, for the rabbit 236±51.1 pmol/min/mg protein.

For man the synthesis rate (6 patients) was 288±48 pmol/min/mg protein. This compared to a value of 1497±385 pmol/min/mg for these patients' mononuclear cell cholesterol synthesis rates. As a pilot study 4 patients were given 40 mgs of simvastatin daily for 3 days prior to surgery. Cholesterol synthesis rates were almost completely suppressed in the liver (18.5 pmol/min/mg protein) but the synthesis rates in their mononuclear cells did not seem to be effected (1550±375 pmol/min/mg protein) after the 3 days therapy (these numbers are too small for statistical analysis). This technique may be used for assessing other synthetic processes in the liver and their therapeutic manipulation.

PUBLIC HEALTH/EPIDEMIOLOGY/ GERONTOLOGY

EVALUATION OF NEONATAL BCG VACCINATION IN IRELAND

L. Clancy, A. Shannon, M. Lucey, M. Cooney, J. Stinson, P. Corcoran, P. Kelly.
Peamount Hospital, Newcastle, Co. Dublin and North Western Board, Co. Donegal.

To assess the usefulness of neonatal BCG in Ireland we looked at its protective effect in the general population and in a mini-epidemic. We used the National TB Survey of 1986 (Ir. Med. J. 1988: 81, 7-10) and the National Census of Population (1986). We divided the country into 3 populations with respect to BCG policy: (a) neonatal BCG, (b) BCG at age 12-14 years, (c) no routine BCG. We compared the incidence and spectrum of TB in each of these populations using X^2 analysis.

Results: Total number of cases of TB was 756 (21.4 per 100,000). Incidence of TB in people ≤ 15 years is significantly lower ($p=<0.0001$) in areas that have a routine policy of neonatal BCG compared to the other 2 populations. We estimate that 86 cases of TB were prevented by neonatal BCG.

In a large second level school outbreak of TB (1160 teenagers at risk) we studied the protective effect of neonatal BCG vaccination and showed that children with neonatal BCG vaccination were significantly less likely ($p<0.001$) to contract TB compared with children who had never received vaccination.

Conclusion: In Ireland neonatal BCG vaccination offers significant protection against TB in the under 15 year old age group. This effect was seen both in the general population and in a major school mini-epidemic.

UTILISATION OF HOSPITAL BEDS BY ELDERLY PATIENTS - A COHORT STUDY

C. Hayes.
Community Care Area 8, Eastern Health Board, Cromcastle Road, Coolock, Dublin 5.

The use of hospital beds by 200 elderly patients admitted to a Dublin Teaching Hospital was examined. Using objective predetermined criteria[1] each day of hospital stay was evaluated in terms of whether the services provided or the patients' condition justified hospitalisation on that particular day. For days where the predetermined criteria were not met, an attempt was made to identify the principal causative factor[2]. Of a total of 2,724 days of care reviewed, 792 (29.1%) were considered inappropriate. Female sex, age and over 75 years, single status, residence with another adult, or visits by the public health nurse prior to admission, and medical card entitlement, were associated with inappropriate days of care. Self-referral to hospital, admissions to medical wards, admissions for observation, social and multiple reasons and an admission diagnosis of cerebrovascular disease, were also associated with misutilisation. Patients who remained in hospital longer than 3 weeks had twice the proportion of inappropriate days compared with those who were discharged within 10 days of admission ($P<0.001$). Patients receiving rehabilitation services in the absence of other services, accounted for one quarter of all inappropriate days of care identified. Responsibility lay with the hospital for 27.8% of barriers identified, while the patients' physician was considered responsible for 20.5%.

In the light of these findings, it is recommended that review of the structures and processes of care provided for elderly patients be undertaken.

References
1. Gertmann, P. M., Restuccia, J. D. The Appropriateness Evaluation Protocol: A technique for assessing unnecessary days of hospital care. Med. Care 1981: 19(8), 856-71.
2. Restuccia, J. D., Holloway, D. C. Barriers to appropriate utilisation in an acute facility. Med. Care 1976: 559-67.

CHILDHOOD ACCIDENTS IN THE HOME - A CASE-CONTROL STUDY

M. Laffoy.
Eastern Health Board and Our Lady's Hospital for Sick Children, Crumlin, Dublin.

The study compares sociodemographic data on cases and

controls, details injuries sustained, ascertains home safety awareness among parents and recommends where prevention strategies should be introduced or modified. Over a three month period, 174 cases were randomly selected from children attending the Accident & Emergency Department due to accidents at home. Cases and controls were pair matched for age and sex. One hundred and seventy-four controls were randomly selected from Health Board Birth Registers. Using a structured questionnaire, parents of both groups were interviewed at home.

Regarding cases: the majority (66.1%) were under 5 years and were boys, families were more likely to belong to social classes 4-6 ($P<0.01$), parents were less likely to have completed second level education ($P<0.01$) and mothers were less likely to be employed ($P<0.01$). Falls accounted for 50.5% of injuries. Most accidents occurred in the kitchen (32%), 50% of children were unsupervised. The majority of injuries were minor, yet 42% require further care. Pre-school children[1], boys[2] and lower social class groups[3] are at greatest risk of home accidents. It is these groups towards which preventive strategies should be targeted.

References

1. Troop, P. Accidents to Children: An analysis of in-patient admissions. Public Health 1986: 100, 278-285.
2. Rivara, F. *et al.* Epidemiology of Childhood Injuries. Sex differences in injury rates. American Journal of Diseases of Children 1982: 166, 502-6.
3. Working Party on Inequalities in Health Report. London: DHSS, 1980: (Black Report).

ALCOHOL INTAKE IN PATIENTS ADMITTED ACUTELY TO A GENERAL MEDICAL UNIT

J. A. McKnight, D. R. McCance, F. O'Hare, B. Wisdom, J. R. Hayes.
Department of Medicine, The Queen's University of Belfast, Level 6, Belfast City Hospital, Belfast, N. Ireland.

The role of alcohol in causing acute medical admissions is recognised but not well quantified. We have prospectively studied alcohol intake in patients aged 18-60 yrs admitted to a medical unit using a questionnaire and have analysed the contribution of alcohol to their admission. During nineteen 24h "take-in" periods 372 patients were admitted. One hundred and six of these (61M:45F) who fulfilled our pre-set age criteria were studied. Alcohol intake (mean + SEM) was 9+1 and 12+1 units on average and heavy drinking days respectively, and 38+6 units during their last drinking week. Gamma glutamyl transferase (GGT) was > 60 U/l (upper limit of normal) in 28 (n=92). Eighteen (30%) men had drunk >50 units and 7 (16%) women had taken >36 units in their last drinking week. In 25 (41%) men and 11 (24%) women alcohol intake was felt to contribute to their admission. Intake was 15+2 and 20+1 units on average and heavy drinking days respectively and 87+13 units in the last drinking week in this subgroup. GGT was available in 29 and abnormal in 18. Admission diagnoses were drug overdose (n=16), alcohol withdrawal symptoms (n=7), liver disease (n=6), haematemesis (n=4) and others (n=3). Fifteen (42%) felt they had a definite alcohol problem.

The use of abuse of alcohol contributes significantly to the general medical workload in the age group studied.

RISK OF HEPATITIS A FOLLOWING CONTAMINATION OF A PUBLIC WATER SUPPLY

L. Thornton, J. Fogarty, C. Hayes, M. Laffoy, D. O'Flanagan, R. Corcoran.
Eastern Health Board, Naas, Co. Kildare.

In October 1991 an episode of sewage contamination occurred affecting the water supply of approximately half the population of a town of 12,000 people.

Salivary antibody testing was used (i) to determine the baseline prevalence of immunity to Hepatitis A in this population and (ii) to establish if evidence existed of an outbreak of Hepatatis A associated with this water contamination.

Using the electoral register, a random sample of 200 households was selected, and each household member was included in the sample. Of selected households 84% participated in the study, yielding 496 analysable salivary samples. Repeat testing (to establish seroconversion) six weeks later from 90% of initial participating households yielded 368 samples, results of which could be paired with an earlier sample.

On the initial test the prevalence of immunity to Hepatitis A from past infection was 42.9% (213/496) : 56.3% (279/496) of subjects were susceptible (non-immune). Only 3 subjects showed evidence of recent infection.

This study is the first to demonstrate the feasibility of using salivary antibody tests for Hepatitis A immunity in a population-based study in Ireland. Results showed that overall immunity to Hepatitis A was 43.3% and confirmed the absence of an outbreak of Hepatitis A associated with this episode of water contamination.

EVOKED POTENTIALS AS DIAGNOSTIC MARKERS IN DEMENTIA

D. O'Mahony, M. Rowan*, J. Feely*, J. B. Walsh, D. Coakley.
Mercer's Institute for Research on Ageing, St. James's Hospital, Dublin. *Department of Pharmacology, Trinity College, Dublin

So far, no reliable non-invasive marker of dementia has been found. The aim of the present study was to examine the value of combined auditory P300 and visual evoked potential testing in detecting mild, established senile dementia. We studied the P300 and combined pattern-reversal (PRVEP) and flash visual evoked potentials (FVEP) in 17 healthy elderly and 13 age-matched patients with early dementia (9 with Alzheimer's disease, 4 with multi-infarct dementia). Using one-way ANOVA (group x evoked potential latency), we found significant delays in the dementia group for the P300 N2 ($p<0.0005$) and P3 ($p<0.0002$) latencies, the FVEP latency ($p<0.03$) and the (FVEP-PRVEP) latency difference ($p<0.05$). Using these 4 measures in a discriminant function analysis, 15/17 controls and all 13 dementia patients were correctly classified (sensitivity 100%, specificity 88.2%). The discriminant score was applied prospectively to 12 newly diagnosed early dementia cases. Eleven of these patients were correctly assigned to the dementia category (sensitivity 91.7%). We conclude that combined P300 and VEP analysis is a quick, non-invasive clinical technique which reliably detects mild dementia on an *individual* basis.

ONCOLOGY/HAEMATOLOGY

PROSTATE SPECIFIC ANTIGEN IN PATIENTS UNDERGOING TRANSURETHRAL RESECTION, IS IT OF VALUE?

M. G. Clyne, M. J. Duffy, A. O'Brien, M. Davis, D. G. Kelly, D. M. Quinlan.
Departments of Urology, Nuclear Medicine and Pathology, St. Vincent's Hospital, Elm Park, Dublin 4.

Prostate Specific Antigen (PSA) is a protease produced selectively by prostate epithelial cells. The aims of this study were: (a) to determine if a preoperative PSA measurement would differentiate those patients with prostate cancer from those with benign hyperplasia, (b) to determine if any correlation exists between preoperative PSA and volume of tissue resected, and (c) to investigate any relationship between preoperative PSA and Gleason Grade of tumour. One hundred patients had preoperative PSA levels measured by radioimmunoassay. Histological review and volume measurements of specimens were also done. Patients with cancer underwent Technetium bone scans. PSA was elevated (i.e. >10 ng/ml) in 13% of the 63 patients with benign hyperplasia, the mean value being 4.7 ng/ml. PSA was elevated in 63% of the 27 patients with localised cancer, the mean value being 26.6 ng/ml. PSA was elevated in 100% of the 10 patients with metastatic disease, the mean value being 82.6 ng/ml. A statistically significant difference was found to exist between patients with prostate cancer and benign hyperplasia ($p<0.0005$). No correlation was found between PSA and volume or between PSA and Gleason Grade. Hence, it is suggested that patients being considered for transurethral resection should have routine preoperative PSA levels measured. Those with a PSA greater than 10 ng/ml most likely have cancer and should be biopsied. Young patients with localised cancer may be better served by a radical prostatectomy and those with metastatic disease may benefit from hormonal manipulation.

Bcl-2 REARRAGEMENT IN HODGKIN'S DISEASE AND REACTIVE LYMPH NODES

N. Corbally, M. M. Keane, L. Grogan, P. A. Dervan, D. N. Carney.
Departments of Medical Oncology and Pathology, Mater Hospital, Dublin 7.

The t(14;18) chromosomal translocation involving the *bcl-2* oncogene is demonstrated frequently in patients with low grade non-Hodgkin's lymphoma (NHL). It involves the juxtaposition of the *bcl-2* oncogene (chromosome (Chr.) 18) next to the joining region (JH) of the immunoglobulin heavy chain gene (Chr. 14). The aim of this study using the polymerase chain reaction (PCR) was to determine the incidence of the t(14;18) chromosome translocation (major breakpoint region (MBR)) in histologically confirmed lymph nodes from patients with reactive hyperplasia (n=34), Hodgkin's disease (n=60) and low grade NHL (n=14). Using the PCR and primers directed towards opposing sides of the t(14;18) translocation (MBR) we found the *bcl-2* translocation in 57% (8/14) of low grade NHL, in 11% (7/60) of Hodgkin's disease, and in 10% (3/34 of reactive lymph nodes. Those samples found to be positive for the *bcl-2* translocation contained no histological evidence of coexisting low grade NHL. There was no correlation between the histological subtypes of Hodgkin's disease, or reactive lymph nodes and the presence of the translocation. The incidence of the *bcl-2* translocation in lymph nodes in Hodgkin's disease and the reactive lymph nodes were similar. These results suggest that the detection of the *bcl-2* oncogene translocation in Hodgkin's disease may reflect its presence in the reactive component of the disease rather than in the Reed Sternberg cells. Reactive hyperplasia and Hodgkin's disease are not associated with a marked increase in incidence of low grade NHL. This suggests that the occurrence of the *bcl-2* translocation may not be a definitive genetic change associated with lymphoproliferative oncogenesis.

Supported by CRAB, Irish Cancer Society.

PROGNOSTIC VALUE OF c-erbB-2 ONCOPROTEIN IN BREAST CANCER AS DETERMINED BY ELISA

K. Duffy, A. Nugent, E. W. M. McDermott, N. J. O'Higgins, J. J. Fennelly, M. J. Duffy.
Departments of Nuclear Medicine, Surgery and Medical Oncology, St. Vincent's Hospital, Dublin 4.

Amplification of the c-erbB-2 gene is implicated in the pathogenesis of different types of adenocarcinomas, including breast cancer. Present assays to detect gene amplification involve Southern blotting while increased protein expression is usually detected using immunocytochemistry. In this investigation c-erbB-2 protein was measured by an ELISA. High levels of the oncoprotein (>10 u/ug protein) were found in 25/161 (16%) of primary breast cancers and in 3/6 (50%) of breast cancer metastases. High levels were not found in normal breast tissue or benign breast tumours. C-erbB-2 protein was positive more often in estradiol receptor (ER) negative than in ER positive tumours (chi-square = 4.6, $p<0.05$) and in progesterone receptor (PR) negative than in PR positive tumours (Chi-square = 8.7, $p<0.005$). C-erbB-2 protein level was positively correlated with the number of involved axillary nodes ($r=0.28$, $p<0.001$).

Patients with tumours containing high levels of c-erbB-2 protein had a significantly shorter disease-free and overall survival (chi-square = 11.3, $p<0.001$; Chi-square = 10.9, $p<0.001$, respectively) than those with low levels. It is concluded that assay of c-erbB-2 protein by ELISA is simple, rapid, quantitative and offers significant prognostic information in breast cancers.

EPSTEIN-BARR VIRUS DNA INTEGRATION IN HODGKIN'S DISEASE AND NON-HODGKIN'S LYMPHOMA

M. M. Keane, N. Corbally, P. A. Dervan, D. N. Carney.
Departments of Medical Oncology and Pathology, Mater Misericordiae Hospital, Dublin.

Integrated Epstein-Barr virus (EBV) DNA is found in malignant tissue from patients with Hodgkin's disease (HD) and certain subtypes of non-Hodgkin's lymphoma (NHL), in particular diffuse large cell (DLC) NHL. We used the polymerase chain reaction (PCR) to analyse snap-frozen and formalin-fixed paraffin-wax embedded tissue from patients with HD (n=54) and NHL (n=145) for the presence of integrated EBV DNA. All tissue was analysed using two sets of primers, the first amplifying a 387 base pair segment of the highly conserved coding domain of the EBV nuclear antigen-1 and the second amplifying a 240 base pair segment of the EBV IR3 region. EBV DNA was amplified from 31 (57%) cases of HD and 48 (33%) cases of NHL including 21/64 (33%) cases of DLC NHL. EBV DNA was amplified from

21/71 (30%) cases of NHL with B cell immunophenotype and 8/27 (30%) cases with T cell immunophenotype.

These results confirm the association of integrated EBV DNA with HD and with NHL. No correlation was found between histological subtype of HD and the presence of integrated EBV DNA. The results show an association between integrated EBV DNA and both B and T cell immunophenotype in NHL, however no particular increased incidence of integrated EBV DNA was found in association with DLC NHL.

Supported by CRAB, The Irish Cancer Society.

IN VIVO AND *IN VITRO* PRODUCTION OF TRANSFORMING GROWTH FACTORS IN OESOPHAGEAL CARCINOMA

F. O'Brien, G. O'Sullivan, J. K. Collins.
Department of Microbiology, University College, Cork and Department of Surgery, Mercy Hospital, Cork.

We have found that oesophageal carcinoma cells secrete mitogenic growth factors and transforming growth factors. While other groups have shown increased epidermal growth factor receptor (EGF-R), this is the first report on autocrine growth factor production by oesophageal carcinomas, which are particularly lethal and, metastatic tumours, and suggests that these factors are important in the genesis and progression of the tumour. TGFs were produced by nude mouse xenograft and primary tumour explants, suggesting that autocrine growth factor production is not a tissue culture selected artifact specific to the cell lines. More significantly we have detected and measured TGF presence in the urine, serum and malignant ascites of oesophageal cancer patients.

Preliminary biochemical characterisation of oesophageal derived TGFs suggest these to be heat and acid stable proteins which are disulphide bond dependent for biological activity. On the basis of antibody neutralisation studies and molecular weight the TGFs were not any of the common TGFs, i.e. TGFa, TGFb, PDGF, FGF or EGF.

Further characteristisation of these factors and their receptors opens up new avenues for the diagnosis, tumour typing and, ultimately, the development of new molecular therapy strategies for the containment/treatment of this highly aggressive and lethal disease.

POSTER PRESENTATIONS

ENDOCRINOLOGY

AN AUDIT OF DIAGNOSTIC METHODS IN 21 CASES OF PRIMARY HYPERALDOSTERONISM

A. B. Atkinson, C. G. Ferrett, J. A. McKnight, H. Leslie, E. M. McIlrath, C. M. Ritchie, *C. F. J. Russell, **B. Sheridan.
Metabolic Unit, **Supraregional Endocrine Laboratory and *Endocrine Surgery Unit, Royal Victoria Hospital, Belfast, BT12 6BA.

Over a 12 year period 21 patients (13 male, 8 female) have been diagnosed as having hypertension and primary hyperaldosteronism. Mean systolic and diastolic blood pressures at presentation were 180 ± 9 and 108 ± 5 mmHg respectively, and serum potassium was 3.4 ± 0.1 mmol/l (mean ± SEM). Normal ranges for serum aldosterone were established at 0800h (supine) and 0945h (erect and ambulant) and after a 4 hour 2L normal saline infusion between 1000h and 1400h. The maximum normal values (mean + 2SSD) were 457 pmol/l (n=95), 501 pmol/l (n=84) and 137 pmol/l (n=34) respectively. In 7 of the 21 patients only basal serum aldosterone values were obtained while 14 patients also had saline suppression tests. Nine of the 21 had normal supine aldosterone and 5 had normal erect aldosterone at some stage during their evaluation. Serum aldosterone was elevated following saline infusion in 13 of 14 cases. On CT scanning 11 patients were reported as having definite evidence of an adenoma, 10 were reported as either suspicious of adenoma (n=8) or bilaterally abnormal (n=2). Adrenal venous sampling further elucidated the differential diagnosis and on the basis of venous sampling and CT scan findings 13 thus far have undergone surgery, all of whom have had confirmed histological evidence of an adenoma. Two of the 13 patients operated upon have not required long-term antihypertensive medication. Mean blood pressure (n=13) at follow-up (43±8 months) was 140±3 / 88±2 mmHg. In most cases of primary hyperaldosteronism the combined use of both CT scanning and adrenal venous sampling remains extremely valuable.

MICROALBUMINURIA IN NON-INSULIN-DEPENDENT DIABETES

M. Bashyam, N. O'Sullivan, H. Baker, P. F. Duggan, T. H. Mitchell.
Department of Medicine, Cork Regional Hospital.

Most cases of chronic renal failure in diabetes occur in patients with non-insulin-dependent diabetes. Microalbuminuria in the latter is predictive of clinical proteinuria and early mortality. Microalbuminuria is defined as urinary excretion rates between 30 and 300 mg/24hr (20-200 mg albumin/litre or 3-30 mg/mmol creatinine). We have assessed the prevalence of microalbuminuria in non-insulin-dependent diabetes (stabilised on diet + or – tablets for at least 1 year), whose urine was negative on routine albustix testing. Microalbuminuria was measured on three occasions over a six-month period in overnight urine samples from 95 patients. The microalbumin was measured qualitatively by Micro-Bumintest Reagent tablets (Ames) and the Micral-test (Boehringer Mannheim) and quantitatively by an immunoturbidimetric assay. Microalbumin ≥20 mg/litre (≥3 mg/mmol creatinine) by immunoturbidimetric assay was found on two or more occasions in 13 patients. The Micro-Bumintest was positive in 51%, false negatives occurred in 49% and the false positive rate was 6%. The Micral-Test was positive in 70% with 30% false negatives and no false positives. Our results suggest that the qualitative tests might not be a useful alternative to screening by quantitative assay.

MICROALBUMINURIA: IS IT A USEFUL PREDICTOR OF ISCHAEMIC HEART DISEASE IN GENERAL PRACTICE?

O. Beatty, J. Browne, K. Clarke, A. B. Atkinson, B. Sheridan, P. M. Bell.
Metabolic Unit, Royal Victoria Hospital, Belfast and Carryduff Health Centre, Belfast.

Recent studies have suggested that microalbuminuria is relatively common (9.4%) in non-diabetic subjects and that it is a

marker for increased cardiovascular risk. In an attempt to assess the prevalence of microalbuminuria in Northern Ireland where there is a high incidence of coronary heart disease, we studied 400 males, age 35-65 years, chosen at random from a Belfast general practice. There was a 73% response rate (n=273). Thirteen subjects (4.7%) had an albumin excretion rate of 20 ug/min^{-1} or more. Sixteen per cent of the population had ischaemic heart disease. After exclusion of subjects with diabetes mellitus or renal diseases, the group with microalbuminuria (n=8), was compared to those without microalbuminuria (n=256). There was no significant difference between the two groups, nor did the group of vascular risk factors, apart from triglyceride (1.8±0.2 v 1.3±0.0 mmol/l^{-1}, p<0.05) and glucose (5.5±0.3 v 5.1±0.3 mmol/l^{-1}, p<0.05) levels. We conclude that the prevalence of microalbuminuria in a Belfast general practice, at high risk of ischaemic heart disease, was low and was not helpful in predicting subjects at risk of ischaemic heart disease.

THERAPY WITH RECOMBINANT GROWTH HORMONE IN ADULTS WITH GROWTH HORMONE DEFICIENCY

J. G. Devlin, P. Collins*, J. Laski, S. O'Neill, F. Redington.
Department of Endocrinology, Beaumont Hospital, Dublin 9 and *Department of Biochemistry, Royal College of Surgeons in Ireland, Dublin.

Adult growth hormone deficiency has been associated with an increase in cardiovascular and cerebrovascular disease. Assuming this to be due to unfavourable lipid changes, this study examines the effects of recombinant growth hormone therapy on lipid profiles in adult patients with growth hormone deficiency. Initial results show these transient changes: LDL - initial mean 4.205±1.053, three months mean 3.279±0.751, (p=0.0002), nine months mean 3.938±1.248, (p=0.2562), total cholesterol initial mean 6.03±1.266, three months mean 4.997±1.57, (p=0.0002), nine months mean 5.608±1.397 (p=0.4). Sustained statistically significant changes are seen in apolipoprotein A2 levels (59.9±16.921 to 39.417±6.244 at nine months, p=0.0328), triglycerides (1.231±0.6227 to 1.012± 0.517 at nine months, p=0.0432), ratio of apolipoprotein A1/A2 increases after the third month, (p=0.0009), IGF_1 levels show sustained increases in all patients. HDL and apolipoprotein B and apolipoprotein A1 are not significantly changed. The previous reported increases in lean body mass and decreases in % body fat and improved sense of well-being are demonstrated in this study.

DIABETIC PERIPHERAL NEUROPATHY AND FOOT ULCERATION: EARLY IDENTIFICATION OF PATIENTS AT RISK

A. V. Dominique, P. Scanlan, R. G. R. Firth.
Department of Diabetes and Endocrinology, Mater Misericordiae Hospital, Dublin.

The diabetic neuropathic foot is a major cause of morbidity and an expensive burden on health resources worldwide. It is due to motor, sensory and intrinsic foot muscle pathology. The aims of this study are to assess peripheral nerve and autonomic function as well as dynamic foot pressure/time relationships using a state of the art pedobarograph in newly diagnosed NIDDM patients in an effort to identify patients at risk of foot ulceration at an early stage. Patients were assigned a neuropathic disability score from history (modified Dyck symptom score) and underwent a standard battery of clinical tests including biothesiometry, cardiorespiratory reflexes and pedobarograph analysis. Results indicated that in this group of newly diagnosed NIDDM patients, 50% had symptoms of neuropathy at diagnosis and up to 60% had objective evidence of peripheral neuropathy including autonomic neuropathy depending on the variable assessed. 12.5% of the group had elevated maximum foot pressures during normal gait. With follow-up, we hope to establish which variables best correlates with development of subsequent foot ulceration. This study forms the basis for early intervention trials using Aldos Reductase inhibitors and/or special foot wear.

MICROALBUMINURIA IN INSULIN-DEPENDENT DIABETES MELLITUS: PREVALENCE AND RELATIONSHIP TO RISK FACTORS

T. Fiad, R. Freaney, B. Murray, M. J. McKenna.
St. Vincent's Hospital, Elm Park, Dublin 4.

We sought to define the prevalence of microalbuminuria (MA) in a clinic-based population of patients with insulin-dependent diabetes mellitus (IDDM).

Patients selected for study had IDDM for at least 5 years without history of macroproteinuria. The following information was collated: body mass index, presence of diabetic retinopathy, history of hypertension, average of two blood pressure readings, and average of two glycosylated haemoglobin levels. A 24-hour urine was obtained. Creatinine clearance was determined. Urine albumin excretion was measured by an immunoturbidometric method with a sensitivity of 1.8 µg/ml. Albumin excretion rate (AER) was expressed in µg/min.

Preliminary findings in 63 patients showed that 33% had MA (AER between 20 to 200 µg/min); 2 patients had macroproteinuria. The relationship between AER and risk factors will be presented.

We have found that MA is common in a sample of Irish patients with IDDM. Both the natural history and the effect of intervention need elucidation. For the present, based on our study and other reports, we suggest that AER be determined as part of routine care in Irish patients.

---

cDNA PROBES FOR THE INVESTIGATION OF GLUCOCORTICOID MODULATION OF APOPROTEIN mRNA TRANSCRIPTION

M. MacMahon, J. Murphy, Wm. C. Love.
Departments of Biochemistry, Trinity College and St. James's Hospital, Dublin.

Decreasing LDL cholesterol (LDL-C) and increasing HDL cholesterol (HDL-C) are integral components of strategies to prevent or minimise cardiovascular disease. However, the curious anomaly exists that glucocorticoid treatment in rheumatoid arthritis and other diseases is associated with accelerated atherosclerosis despite causing a prolonged increase in HDL-C and no increase in LDL-C. To examine this phenomenon at a fundamental level, we have examined the influence of synthetic glucocorticoid on the production and secretion of the apoprotein components of HDL and HDL in hepatic and intestinal tissue. cDNA probes for

apoprotein AI, AII, E and AIV were isolated and labelled using random hexanucleotide primers and DNA polymerase (Klenow). Dot blotting and Northern analysis were used to assess apoprotein mRNA levels. A 2-fold increase in apoprotein AI, a key component of HDL, mRNA has been detected in response to dexamethazone. This confirms our previous data, where an *in vitro* translation system incorporated S^{35}-methionine. To determine whether glucocorticoids increase apoprotein AI mRNA as a result of direct effect on the liver or enterocytes, HepG2 and CaCO2 cells are being studied, along with a detailed examination of the lipoprotein particles secreted under these conditions.

ADRENAL ANDROGEN AND GLUCOCORTICOID PRODUCTION IN CUSHING'S SYNDROME

T. J. McKenna, S. K. Cunningham.
Department of Endocrinology and Diabetes Mellitus, St. Vincent's Hospital, Dublin 4.

While ACTH may modulate adrenal androgen production, there is evidence that other factors are required[1]. Cushing's disease and ectopic ACTH secretion provide an opportunity to examine adrenal androgen levels in conditions of ACTH excess. We observed elevated plasma cortisol values in 9 of 14 adult patients with Cushing's disease. In contrast, plasma androstenedione was elevated in only 2 patients (range, 4.1-11.3 nmol/l; normal range, men 2.1-7.7 and women 3.3-9.9 nmol/l). Plasma dehydroepiandrosterone sulphate (DHEAS) was elevated in only 3 patients and plasma dehydro-epiandrosterone (DHEA) was normal or low in all 14 patients. One of two patients with ectopic ACTH syndrome had markedly elevated androstrenedione (80 nmol/l) but suppressed DHEA and DHEAS; the second subject had normal androgen levels. The association of normal adrenal androgen with elevated cortisol levels in Cushing's disease indicates that ACTH alone is not sufficient to modulate adrenal androgen levels. However, the finding of markedly elevated androstenedione levels in a patient with ectopic ACTH suggests that all factors necessary for the modulation of adrenal androgens may be derived from pro-opiomelanocortin, the ACTH parent polypeptide.

Reference

1. McKenna and Cunningham. J. Endocrinol. 1991: 129, 1.

LONGTERM OCTREOTIDE FOR ACROMEGALY: EFFECT ON SERUM GROWTH HORMONE AND TREATMENT OF GALLSTONES

J. A. McKnight, D. R. McCance, J. G. Crothers, E. McIlrath, B. Sheridan, A. B. Atkinson.
Metabolic Unit, Royal Victoria Hospital, Belfast BT12 6BA, N. Ireland.

Ten patients with resistant acromegaly were treated with the somatostatin analogue Octreotide. Two had treatment withdrawn within one month, one due to persistent diarrhoea and another due to concurrent illness. Serum growth hormone (GH) was assessed during 24h profiles. Mean GH basally was 36.0±9.6 mU/l (±SEM: n=8), after one year was 7.5±1.6 mU/l (up to 500 mcg octreotide three times daily), and was 11.9±2.7 and 8.6±1.9 mU/l after 2 and 3 years respectively (200 mcg three times daily). Somatomedin C was 122±8 nmol/l basally and was normal (>48 nmol/l) in 3 patients after 1 year, and in 5 patients after 2 and 3 years. Abdominal ultrasound was normal before commencement of octreotide in 7 patients, but revealed multiple gallstones in one patient after 4 months (no basal scan). One patient developed new gallstones after 6 months, 2 others after 1 year, and another after 2 years of treatment. All 5 were asymptomatic. Medical gallstone dissolution therapy with chenodeoxycholic acid (7.5mg/Kg/day) and ursodeoxycholic acid (5.0mg/Kg/day) was initiated in these 5 patients while octreotide was continued. Repeat ultrasound examination after 6 months showed no evidence of gallstones in 2 of the cases.

Octreotide reduces serum growth hormone longterm in resistant acromegaly, and the major side effect of gallstones may sometimes be successfully treated without cessation of octreotide.

MODERATE EXERCISE, AND ACTH AND PGE_2 BLOOD LEVELS IN MAN

F. Ni Chiardha, E. M. Gebruers, W. J. Hall, D. A. Hegarty.
Department of Physiology, University College, Cork.

Induction of the ACTH response in stress conditions in the laboratory animal appears to occur by activation of the arachidonic acid cascade system by cytokinase such as Interleukin-1. In this study we have investigated the effects of moderate exercise on blood levels of ACTH in man and on a stable metabolite of PGE_2, the main product of the arachidonic acid cascade in muscle.

Subjects were asked to carry out sustained handgrip (35% maximum) for 5 mins in the seated position. In the test arm blood flow, measured by the method of venous occlusion plethysmography increased from 1.4 to 12.7 ml/min/100 ml forearm ($P<0.01$). This was accompanied by significant changes in pH ($P<0.01$) and in the blood gases (PO_2, $P<0.02$ and PCO_2, $P<0.01$) in the venous blood draining active limb. ACTH values measured before and in the last minute of exercise did not differ. However, the 30 min post-exercise value was significantly less. This reduction probably reflects the diurnal decrease which occurs at about the time in which the experiments were carried out. Control and test values for the PGE_2 metabolite were not significantly different.

We conclude that this level of exercise in humans is not stressful enough to lead to activation of the ACTH response either through PGE_2 production or any other mechanism.

CIGARETTE SMOKING PROMOTES GRAVES DISEASE

J. O'Hare, M. Geoghegan.
Department of Medicine, Limerick Regional General Hospital.

Our objective was to determine whether cigarette smoking (CS) plays a role in the development of Graves Disease (GD). Eighty-three patients with GD were age and sex matched with 168 euthyroid subjects attending orthopaedic clinics. There were 70 female and 13 males with GD aged 42 ± 13 years. Fifty-five (66%) with GD smoked at any time prior to the diagnosis of GD, compared to 86 (51%) of controls, odds ratio: 1.87 (95% c.i. 1.04 - 3.38, P=0.024). Forty-six (55%) with GD were smokers in the year prior to presentation compared to 58 (35%) of controls - odds ratio 2.36 (95% c.i. 1.32 - 4.21, P=0.0016). Patients with GD did not smoke more on average nor have a heavier total smoking history (by pack years). Thirty-four (41%) of cases had ophthalmopathy and these patients smoked significantly more than those without ophthalmopathy ($P<0.01$). We conclude that CS plays a role in the development of Graves Disease and heavier smoking promotes ophthalmopathy.

PREVALENCE OF DIABETIC NEUROPATHY COMPLICATIONS

J. O'Hare, F. Abuaisha, M. Geoghegan.
Departments of Medicine, Limerick Regional General Hospital

We studied prospectively the prevalence of symptomatic complications of diabetic peripheral and autonomic neuropathy in a diabetic clinic population. Six hundred and seventy-eight patients (291 type 1 and 387 type 2 DM) with a mean DM duration of 9±8.5 yrs were studied by structured interview and examination. Symptomatic neuropathy of any type affected 34%. Painful polyneuropathy 13%; restless feet syndrome 9%; diminished sensation 6%; amyotrophy 0.9%; extra ocular nerve palsy 0.1%; peroneal nerve palsy 0.1%. Symptomatic autonomic neuropathy resulted in total erectile impotence in 20% (males <65 yrs); diabetic diarrhoea 1.2% and postural hypotension 1.2%. Neuropathy was significantly related to older age ($p<0.01$), proliferative retinopathy ($p<0.001$), proteinuria ($p<0.03$) and less smoking ($p<0.05$). Neuropathy was not significantly related to sex, duration of DM, DM type, alcohol intake, glycosylated haemoglobin, ischaemic heart disease or hypertension.

We conclude that the complictions of peripheral neuropathy are a greater burden than those of autonomic neuropathy both of which are commoner in older patients who have other diabetic complications.

THE METABOLIC EFFECTS OF CYCLOPENTHIAZIDE IN HYPERTENSIVE TYPE II DIABETICS ARE DOSE DEPENDENT

A. P. Passmore*, E. M. Whitehead, V. Crawford*, G. D. Johnson.
Department of Therapeutics & Pharmacology and *Geriatric Medicine, The Queen's University of Belfast, Northern Ireland.

In two previous studies we demonstrated that 125 μg of cyclopenthiazide was as effective as 500 μg for lowering blood pressure in mildly hypertensive patients and had fewer adverse biochemical effects. This study was undertaken to determine if these advantages also applied to patients with type II diabetes. Twenty-four non-insulin dependent diabetics with mild to moderate hypertension were randomised to receive 125 or 500 μg of cyclopenthiazide as part of a crossover design in which active treatment periods lasted 12 weeks and placebo periods 6 weeks. Patients were stabilised on diet and/or oral hypoglycaemic agents throughout the study. Blood pressure was measured and a fasting blood sample taken for estimation of glucose, $Hb_{A_{1c}}$, fructosamine, lipids, urate and potassium during the placebo run-in and at the beginning and end of each treatment period. The changes in diastolic blood pressure were the same for both doses. The increase in fasting blood glucose (21.4%), $Hb_{A_{1c}}$ (8.1%) and fructosamine (5.2%) were greater with the 500 μg dose than with the 125 μg dose (4%, 2.3%, 1%) $p<0.05$. Fasting triglycerides and serum urate were also higher ($p<0.05$) but no differences were observed with cholesterol or apolipoproteins. The decreases in serum potassium (–9.41 mmol/l) were greater with the 500 μg dose than with the 125 μg dose (–0.16 mmol/l) $p<0.001$.

LIPOPROTEIN (a) AND MYOCARDIAL INFARCTION

R. Sheahan, D. Foley, G. D'Arcy, M. Gibney, T. Cooke, G. Gearty, P. Crean, M. Walsh
Department of Biological Sciences, Kevin Street, Department of Cardiology, St. James's Hospital, Dublin 8.

A strong association between elevated lipoprotein (a) (Lp(a)) concentration and increased risk of coronary artery disease has been established. The close structural homology of Lp(a) and plasminogen has been reported as an important link between lipoprotein metabolism and the coagulation/fibrinolytic systems. A potential association between Lp(a) and myocardial infarction (MI) was examined in 94 patients with angiographically proven coronary artery disease. Patients with a history of MI in the previous 4 weeks were excluded. Thirty-five patients with previous MI as evidenced by a consistent history, documented cardiac enzyme rise and ECG changes, were compared with 59 CAD patients with no previous MI. Forty-six patients with normal coronary arteries were used as controls.

	No.	Mean Lp(a) (mg/L)	SEM
Previous MI	35	473	64.3
No previous MI	59	376	44.9
Normal controls	46	183	43.6

There is a significant trend ($p=0.21$) towards higher Lp(a) levels in those patients who had a previous MI, while both patient groups have significantly higher levels of LP(a) than controls (p less than 0.001).

This study does not confirm a definite association between elevated Lp(a) and myocardial infarction.

ENDOCRINOLOGY/NUTRITION

ORAL REHYDRATION THERAPY – A THIRD WORLD SOLUTION FOR INTENSIVE CARE?

C. M. Cooney, H. G. Gallagher, D. M. Phelan.
Department of Anaesthesia & Intensive Care, Mater Misericordiae Hospital, Dublin 7.

Diarrhoea is common in intensive care, occurring in up to 26% of all aminoglycoside-treated subjects and in 20% of nasogastrically-fed patients[1]. Mortality can be as high as 40%.

Three post-operative adult males developed severe diarrhoea and intravascular volume depletion. Fluid management consisted of a brief period (3 hours) of intravascular replenishment with crystalloid followed with a mean of 2.2 l/day of oral rehydration therapy (ORT) by the nasogastric route for 6-10 days. Renal and metabolic function was maintained or improved in all. ORT maximises intestinal sodium and water uptake using the phenomenon of glucose-stimulated water and solute absorption[2], a co-transport system which is maintained during secretory diarrhoea. It is also effective in the treatment of this common ICU problem in that it maintains volume status and renal and metabolic balance. It is less invasive than intravenous therapy. It should, in conjunction with standard diagnostic methods, be evaluated as a general supportive and enteral preparation for intensive care diarrhoea.

Table: Serum values in ORT-treated patients (mmol/l)

	Na+	K+	Urea	Creat.
Pre	133	3.8	10.2	389
Post	134	4.5	9.2	165

References
1. Dobb, G. J. Intensive Care Med. 1986: 12. 113-5.
2. Rolston, D. D. K., Zinzuvadia, S. N., Mathan, V. I. GUT 1990: 31, 1115-9.

DEXA - A NEW WAY TO MEASURE BODY COMPOSITION

M. Stokes*, L. Plank, G. Knight, S. Mitra, G. Hill
Departments of *Surgery, St. Vincent's Hospital, Elm Park, Dublin and Auckland Hospital, Auckland, New Zealand.

Dual Energy X-ray absorptiometry (DEXA) measures bone density and has been adapted to measure body composition. To establish its precision and accuracy, we performed studies on one volunteer, five phantoms and 40 patients, comparing it with anthropometry, bioelectrical impedance (BIA) and *in vivo* neutron activation analysis (IVNAA)

The volunteers showed the precision for the various components to be – fat 2.5%, lean 1.1% and bone mineral 0.5%. Phantom studies showed that DEXA measures of fat were within 5% of those achieved using chemical analysis and IVNAA. The table shows the results of body fat measurements in the 40 patients. Standard error (s.e.) and c.v. were tabulated by factor analysis; values are in kgs.

	Mean	S.D.	s.e.	c.v.
IVNAA	13.16	8.85	± 1.15	8.7%
DEXA	15.53	10.44	± 1.66	10.7%
Anthrop.	15.65	9.34	± 2.73	17.4%
BIA	14.13	7.71	± 3.00	21.2%

Fifteen of these patients were restudied after two weeks of nutritional support. Using factor analysis the errors on the changes were calculated at - IVNAA ±1.73 kg, DEXA ± 0.25 kg, Anthropometry ± 1.17 kg and BIA ± 1.96 kg.

DEXA is not as accurate as IVNAA in measuring body composition, but that because its error is systematic, it is the best method to follow changes in patients.

NUTRITION/NEUROSCIENCES/PSYCHIATRY

PROLONGED T2 RELAXATION TIME ON MRI: EVIDENCE FOR BASAL GANGLIA DYSFUNCTION IN SCHIZOPHRENIA

P. Buckley, E. O'Callaghan, O. Redmond, J. T. Stack, J. T. Ennis, J. L. Waddington, C. Larkin*.
*Cluain Mhuire Family Centre, Blackrock, Co. Dublin.

Recent investigations employing magnetic resonance imaging (MRI) attest its superior anatomical resolution and sensitivity to detect subtle abnormalities in cerebral structure in schizophrenia. In addition, the relaxation parameters, T1 and T2, may provide valuable quantitative information on tissue functional characteristics and metabolism. This approach was applied here to derive basal ganglia T2 estimations from a double-echo axial sequence of representative images obtained from cranial MRI examination (1 5T, Siemens Magnetom). Comparisons were made between 37 patients with DSM III schizophrenia and 22 age/sex matched normal volunteers. T2 values for left and right caudate nuclei did not distinguish patients from controls. However, those in the left ($p=0.1$) and particularly the right (74.7±3.6 vs 72.2±3.5 ms, $p<0.02$) putamen were prolonged in schizophrenia; a similar pattern was evident in the globus pallidus, particularly in the right hemisphere (62.9±3.5 vs 60.8±3.1 ms, $p<0.03$). These findings compliment current neuroimaging and neuropathological research which assert an organic causation for schizophrenia and implicate basal ganglia dysfunction in its pathogenesis.

Supported by the St. John of God Order and the Health Research Board.

ABNORMAL CREASES IN THE HAND-PRINTS OF SCHIZOPHRENIC PATIENTS

M. Cannon, M. Byrne, D. Cotter, P. Sham*, C. Larkin, E. O'Callaghan.
St. John of God Psychiatric Services, Newtown Ave., Blackrock, Co. Dublin and *Institute of Psychiatry, London.

Recent neuropathological and epidemiological studies have implicated disturbance of fetal development during the second trimester in the aetiology of schizophrenia. The distal upper limb develops during this period and structural abnormalities of the palms and fingers may reflect deleterious intrauterine experience.

Using an inkless method, we took finger and palm prints from 46 ICD-9 schizophrenic patients and 43 healthy controls. The prints were examined "blindly" by four raters and 7 sets of prints were judged by all four raters to have extensive, "net-like" secondary creases over the fingers and palm. These unusual prints were all from the schizophrenic group ($p<0.05$). The patients who displayed the abnormality had a greater number of hospital admissions ($p<0.01$), were on higher amounts of neuroleptic medication ($p<0.05$) and tend to have an earlier age of onset of illness ($p=0.07$), than the remainder of the patient sample. This finding may implicate prenatal factors in the aetiology of schizophrenia.

Supported by the St. John of God Order, HRB and the Stanley Foundation.

EVIDENCE FOR CONFINEMENT OF WINTER BIRTH EXCESS IN SCHIZOPHRENIA TO URBAN BORN

D. Cotter, K. Colgan, C. Larkin, J. L. Waddington[1], D. Walsh[2], E. O'Callaghan.
St. John of God Psychiatric Services, Newtownpark Avenue, Blackrock, Co. Dublin; [1]R.C.S.I. and [2]St. Loman's Hospital.

Schizophrenics are more often winter born. This may be explained by the association between prenatal exposure to viral infections and later schizophrenia. Because viral infections are more prevalent in the winter and in urban areas, we hypothesised that the winter birth excess would be more marked in the urban born.

The birth dates of 3553 schizophrenic (ICD8/9) patients born in Ireland between 1900 and 1970 were examined. No significant season of birth effect was found for the overall sample. However, patients born in urban areas were significantly ($p=0.015$) more likely to be winter born than the general population. A spring birth excess was found for female – rural-born patients ($p=0.042$).

These findings are consistent with the view that exposure to prenatal viral infections may be relevant to the aetiology of schizophrenia.

Supported by St. John of God Order, H.R.B. and the Stanley Foundation.

NEUROSCIENCES

LYMPHOCYTE EXPRESSION OF THE AMYLOID PRECURSOR PROTEIN

A. M. Gillian, N. Byrne, K. C. Breen.
Department of Pharmacology, University College, Belfield, Dublin 4.

The amyloid precursor protein (APP) is a membrane bound glycoprotein which consists of at least three isoforms, and is

abnormally broken down by proteolysis in Alzheimers to the 42 amino acid bA4 polypeptide present in the characteristic pathological senile plaques. APP has been well characterised in the nervous system, where it has been demonstrated to play a role in the mediation of cell - cell substrate adhesion (Breen *et al*, 1991). APP has also been detected on a number of other tissues.

The aim of this study was to examine the expression of APP on peripheral blood lymphocytes subsets. Peripheral blood mononuclear cells (PBMCs) were isolated on a ficoll gradient. These were labelled for double fluorescence flow cytometry with PE-conjugated antibodies specific to lymphocyte subtypes, and FITC-labelled antibodies to APP.

APP was shown to be expressed on both B and T lymphocyte subtypes, as well as on the HuT 78 human T-lymphoma cell line. This finding may be used to examine a possible alteration in APP isoform expression in Alzheimers patients and which may prove useful as an early diagnostic tool.

This work was supported by the Health Research Board of Ireland. K. B. is a H.J. Heinz Newman Scholar.

EVIDENCE FOR INCREASED FERTILITY IN MARRIED MALE SCHIZOPHRENICS

A. Lane, M. Byrne, F. Mulvaney, C. Larkin, J. L. Waddington[1], D. Walsh[2], E. O'Callaghan.

St. John of God Psychiatric Services, Newtownpark Avenue, Blackrock, Dublin, [1]R.C.S.I. and [2]St. Loman's Hospital.

Although a genetic component to the aetiology of schizophrenia is established, the mode of transmission is unclear. The effect of gender on genetic risk and transmission is now being questioned. We examined gender effect on marriage and fertility among 1224 schizophrenics.

The marital rate of the group, 39%, was significantly lower ($p<0.001$) than that of the general population (58%). Marital rate of males was significantly lower ($p<0.001$) than general population males (27% versus 54%) with similar findings for females (53% v. 63%, $p<0.001$). Male schizophrenics were significantly less likely ($p<0.001$) to marry than female counterparts.

The mean number of children for the group (3.3±2.2) did not differ from the general population (3.3). However, males had significantly more children (3.8±2.6, $p<0.05$) and females had significantly less (2.9±1.9, $p<0.001$) than the population average. Within the schizophrenic group, males had significantly more children ($p<0.001$) than females.

Increased fertility in schizophrenic males may ensure transmission of the disorder.

Supported by St. John of God Order, H.R.B. and the Stanley Foundation.

SELEGILINE AND BEHAVIOURAL SYMPTOMS IN ALZHEIMER'S DISEASE

B. A. Lawlor.

Department of Psychiatry, Section of Old Age Psychiatry, St. James's Hospital, Dublin 8.

The effect of selegiline hydrochloride on behavioural symptoms in patients meeting NINODS criteria for Alzheimer's disease (AD) was studied. Ten AD patients received selegiline (10mg p.o.) and placebo in a double-blind, placebo-controlled, crossover study, counterbalanced for order. Selegiline treatment resulted in a significant decrease in behavioural symptoms, particularly in depression-related items, compared to placebo. In two separate studies, cerebrospinal fluid (CSF) levels of the dopamine metabolite, homovanillic acid (HVA) were found to be inversely correlated with depression scores in AD patients. These studies suggest that selegiline can improve depression in AD, and that this effect may be related to modulation of dopaminergic function in this population.

ARE OBSTETRIC COMPLICATIONS CAUSALLY RELATED TO LATER SCHIZOPHRENIA?

E. O'Callaghan, H. A. Colohan, P. Buckley, D. Walshe, T. Gibson, *J. L. Waddington, C. Larkin.

St. John of God Psychiatic Services, Newtownpark Avenue, Blackrock, and *Royal College of Surgeons in Ireland.

The aetiology of schizophrenia remains obscure. Although genetic factors play a role, environmental factors must also contribute to the disorder since monozygotic twin studies reveal only 50% concordance rates.

Obstetric complications (OC's) have been implicated as a possible causal factor. The present study is a case controlled investigation using contemporaneous birth records of a representative sample of schizophrenic patients.

The birth records of 65 ICD-9 (35M, 30F) schizophrenic patients were identified at two maternity hospitals in Dublin. The previous same sex live birth of each case was taken as control. The data was extracted verbatim and rated blindly by two independent raters using the Lewis and Murray Scale (LMS) and the Parnas Scale (PS).

No differences were noted between patients and controls in terms of maternal age, socio-economic group or birth order. Schizophrenic patients had significantly more OC's than controls [LMS: $p<0.02$, PS: 0.03]. Males had significantly ($p<0.018$) more OC's than females. Patients with a history of OC's had a significantly ($p<0.035$) younger age of onset than those without OC's.

These data indicate that OC's are overrepresented in the birth histories of those later diagnosed as schizophrenic.

PHARMACOLOGY AND THERAPEUTICS

THE EFFECT OF ALBUMIN ON PROTEIN EXPRESSION IN A NEUROBLASTOMA CELL LINE

E. Ronayne, T. M. Maguire, K. C. Breen.

Department of Pharmacology, University College, Belfield, Dublin 4.

Alzheimer's disease is characterised by two distinct pathological lesions. Neurofibrillary tangles are intracellular and are composed of cytoskeletal elements including the heavy neurofilament (NF-H) and the microtubule-associated protein Tau. Neuritic plaques are extracellular deposits consisting of an aluminosilicate core and b-A4 amyloid fibrils which consist of a 42 amino acid A4 polypeptide derived from a larger amyloid precursor protein (APP).

Aluminium is a potent neurotoxin in high doses, and its presence in the senile plaques of Alzheimer's disease has suggested a possible aetiological role. A recent study also demonstrated a correlation between the incidence of Alzheimer's disease and the aluminium content in the drinking water.

The aim of this study was to examine the effects of aluminium treatment on the expression of proteins implicated in Alzheimer pathology including the cytoskeletal components tau and NF-H,

and the amyloid precursor protein, using the Neuro 2A cell line as a model neural system. Control and differentiated cells were cultured in the presence of aluminium salts. This, however, had no effect on the levels of expression of APP, tau or NF-H in either the differentiated or undifferentiated cells.

While these results question the direct role of aluminium in Alzheimer's aetiology, its participation in a multi-factorial event cannot be discounted.

This work was supported by EOLAS, and the Sandoz Institute for Gerontological Research. K. B. is a H. J. Heinz Newman Scholar.

NEOCORTICAL FIELD POTENTIALS IN FOCAL EPILEPSY

H. Staunton, A. Coughlin, P. Shu Ming, J. Phillips.
The Richmond Institute for Neurology and Neurosurgery, Beaumont Hospital, Dublin 9.

The standard temporal lobectomy performed for the treatment of intractable epilepsy includes removal of the mesial structures, amygdala and hippocampus. However, one may see a curative response to neocorticectomy, with preservation of deeper structures. Further, the spike potential (paroxysmal depolarization shift - PDS) seen on surface ECGs, correlating with focal epilepsy, cannot be explained as an electrical potential generated in mesial structures and conducted through the brain by passive volume conduction. It was decided to establish through field potentials recorded at surgery, whether or not there is a neocortical sink-source basis for the PDS which would generate local epileptic activity. Four patients were studied. A grid of 8 contact surface recorded the PDS on the exposed superior, middle and inferior temporal gyrus. An 8 contact (tips separated by 0.5 mm) multichannel electrode was inserted a distance of 4 millimetres into the cortex at the site of a positive depolarization shift. In all cases studied it was possible to record phase reversals indicating a sink-source relationship in the grey matter of the neocortex. The foregoing indicates that, while the grey matter of the neocortex may be influenced in terms of epileptogenesis by the mesial structures, it itself is potentialy epileptogenic in focal epilepsy.

NATURE OF DECLINING INCIDENCE OF SCHIZOPHRENIA IN A RURAL CATCHMENT AREA

J. L. Waddington[1], H. A. Youssef[2].
[1]Department of Clinical Pharmacology, Royal College of Surgeons in Ireland, Dublin 2 and [2]St. Davnet's Hospital, Monaghan.

Variations in rate of occurrence characterise virtually all known diseases and provide important clues to etiology, but are little investigated in schizophrenia; this study addresses the controversy over temporal variations. As detailed in relation to geographical variations[1], all cases of DSM-IIIR schizophrenia with an address within a catchment area of 25,178 persons were sought, and morbid risk [MR] for schizophrenia examined by quinquennium of birth. MR for schizophrenia was essentially constant [8.3±1.33/1000 risk-lives-exposed] for persons born 1920-39 but fell for those born 1940-1969; decline in MR was confined essentially to females [–56%; P<0.05] and to cases with onset after age 25 [–66%; P<0.02]. Regarding the neurodevelopment hypothesis, decline in MR over 1920-69 was unrelated to changes in early neonatal mortality but preceded a comparable decline in infant mortality by one quinquennium. These data suggest the secular 'purification' of schizophrenia towards a disorder of early onset, male preponderance, and direct attention to factors regulating sexual dimorphism in cerebral development.

This work was supported by the Health Research Board.

Reference
1. Youssef, H. A., Kinsella, A., Waddington, J. L. Arch Gen. Psychiatry 1991: 48, 254-258.

MENSTRUAL CYCLE AND SODIUM-LITHIUM COUNTER-TRANSPORT: A PRELIMINARY REPORT

G. Adebayo, G. Feely.
Department of Pharmacology & Therapeutrics, T.C.D. Medical School, St. James's Hospital, Dublin 8.

Sodium dependent lithium efflux from lithium loaded red cells, sodium-lithium counter-transport (SCL) is a marker for hypertension. As its value is lower in females and increased by oral contraceptives, we studied SLC during normal menstrual cycles in 8 healthy, non-medicated and non-obese volunteers, aged 34.4 ± 9.5 years (mean ± SD). Blood was taken on three occasions for the determination of SLC[1]. SLC value (mmol/l cell.h) at midcycle (0.170±0.082) was lower than at day 1-4 (0.204±0.107; p<0.05) and at day 21-24 (0.199±0.074; p<0.05) (ANOVA). Sitting diastolic pressure (random zero sphygmomanometer) at midcycle (70±6) was modestly but insignificantly lower than at day 1-4 (75±6 mmHg) and day 21-24 (73±8); and so was the systolic pressure: 111±8, 114±12 and 113±12 respectively. Our data suggest changes in SLC during normal menstrual cycle, possibly a reflection of similar changes in blood pressure reported by others[2].

References
1. Smith, J. B., Price, A. L., William, R. R. *et al.* A reproducible sodium-lithium countertransport assay: the outcome of changing key laboratory parameters. Clin. Chim. Acta 1982: 122, 327-335.
2. Kelleher, C., Joyce, C., Kelly, G., Ferriss, J. B. Blood pressure alters during the normal menstrual cycle. Br. J. Obstet. Gynecol. 1986: 93, 523-6.

THE ATYPICAL ANTIPSYCHOTIC CLOZAPINE AND D-1 VERSUS D-2 DOPAMINE RECEPTOR-MEDIATED FUNCTION

S. A. Daly, J. L. Waddington.
Department of Clinical Pharmacology, Royal College of Surgeons in Ireland, St. Stephen's Green, Dubin 2.

The action of typical antipsychotic [neuroleptic] drugs to block dopamine [DA] receptors in the brain is well-recognised, and usually takes the form of non-selective blockade of both D-1 and D-2 receptors or selective blockade of D-2 receptors. Clozapine, an atypical antipsychotic with greater efficacy and fewer motor side effects, has been studied in these terms. Young adult rats were challenged with the selective D-2 agonist RU 24213 [15.0 mg/kg] or the selective D-1 agonist A-68930 [0.25 mg/kg] following pretreatment with vehicle or 4.0-36.0 mg/kg clozapine, and the resultant behavioural responses assessed. Clozapine exerted weak antagonism of RU 24213-induced sniffing [–31%, p<0.01] and locomotion [–41%, p<0.05]. Conversely, clozapine failed to exert any significant antagonism of A-68930-induced sniffing or vacuous chewing [which was somewhat potentiated] but readily blocked A-68930-induced intense grooming [–98%, p<0.01]. These data

suggest that clozapine preferentially blocks D-1 receptor-mediated function, but only in terms of some D-1 agonist-induced behaviours; thus, it may interact only with systems involving putative sub-types of D-1 receptor.

This work was supported by the Wellcome Trust.

A RETROSPECTIVE STUDY OF DELIBERATE DRUG OVERDOSE IN AN IRISH HOSPITAL

J. S. Fennell, F. Coakley, C. Hayes, Z. Johnson.
St. Columcille's Hospital, Loughlinstown.

Drug overdoses constitute a significant proportion of admissions to a general medical unit[1]. This study was carried out to determine the clinical features of deliberate drug overdoses. A retrospective study of all available hospital charts of drug overdose cases between January 1986 and December 1990 was performed. Information sought included demography, timing, method, motivation, treatment and clinical outcome. Four hundred and sixty-seven cases were studied. The male : female ratio was 1 : 1.5. The peak age group was 15-24 years for both sexes. There was a history of depression in 32% and alcohol dependence in 17%. Drug overdoses usually occurred between 6 pm and 6 am. A seasonal variation was seen only in female patients with a peak in summer months. 70% of patients took more than one drug and alcohol was involved in 44% of all cases. The average duration of hospitalisation was only two days and morbidity was low, although one death from Tricyclic overdose did occur. It is concluded that drug overdoses constitute a significant clinical workload in our unit, morbidity is low but occasional mortality can occur.

Reference
1. Murphy, G. *et al.* Drug overdoses – A three year study at Altnagelvin Hospital, Londonderry. Ulster Medical Journal 1984: 53(2), 131-139.

DOCTORS' ABILITY TO RECOGNISE COMMONLY PRESCRIBED DRUGS

M. Hall, P. M. McCormack, J. Feely.
Department of Pharmacology and Therapeutics, Trinity College Medical School and Medicines Evaluation Unit, St. James's Hospital, Dublin 8.

Many medications are not easily identified by patients[1]. The aim of this study was to ascertain hospital doctors' ability to recognise and name commonly prescribed drugs in Ireland. Twelve of the most commonly prescribed drugs were selected from the GMS and Hospital list: cimetidine, bendrofluazide, diazepam (Roche), diazepam (D5), digoxin, ferrous sulphate, frusemide, mefenamic acid, paracetamol, prednisolone, temazepam and theophylline were chosen. Doctors were asked to identify these and name the top 5 prescribed drugs in Ireland. Eighty doctors participated; 76/80 recognised mefenamic acid and 71/80 recognised cimetidine despite the fact that the names were on both these drugs; diazepam 5mg (Roche) 62/80, paracetamol 43/80, bendrofluazide 36/80, temazepam 34/80, theophylline 23/80, D5 17/80, prednisolone 11/80, ferrous sulphate 7/80 and both frusemide and digoxin 5/80. The best overall score 10/12 was achieved by only two doctors. Generic drugs were poorly recognised.

For the top five drugs prescribed (amoxycillin, salbutamol, mefenamic acid, ampicillin and the combined oral contraceptive pill) the best score was 3/5; 4/80 doctors achieved this score, 36/80 scored 1/5 and 13/80 scored 0/5.

We conclude that many doctors cannot easily recognise the commonly prescribed drugs and this in turn may affect patient education and accuracy of drug histories.

Reference
1. McCormack, P. *et al.* Can the elderly discriminate between their medications? Br. J. Clin. Pharmac. 1991: 31, 608P.

TRANSDERMAL NARCOTIC DELIVERY – *IN VITRO* AND *IN VIVO* EVALUATION

M. Martin, M. O'Connor, P. Curley, Y. O'Connell, G. Mulryan, E. Meenan, J. Kelly.
Elan Corporation, plc., Monksland, Athlone, Co. Westmeath.

Hydromorphone is widely used for the relief of post-operative or severe chronic pain. Narcotic analgesics such as hydromorphone have a low systemic bioavailability following oral administration due to significant first pass metabolism. Severe pain relief therefore often requires parenteral administration, either by injection or infusion, thereby allowing an element of patient control (Patient Controlled Analgesia/PCA). Passive transdermal narcotic delivery has been demonstrated for fentanyl. However, few narcotics readily permeate the skin unassisted. Electrical assistance will often enhance the delivery of such drugs.

We report the successful transdermal delivery of hydromorphone. Experiments were carried out both *in vitro* an *in vivo* using an electrically assisted drug delivery system. Using the hairless mouse skin as an *in vitro* model, transdermal hydromorphone delivery was observed in the presence of an electric field in a manner proportional to the current and cycle employed (0.5 to 6 mg/hr, 0.05-0.6 MA/cm^2). The data were confirmed *in vivo* in the rabbit where the rate and extent of drug delivery and the resulting physiological response were proportional to the electrical conditions employed.

From our *in vitro* and *in vivo* data it appears that therapeutically relevant amounts of hydromorphone can be delivered using an electro-transdermal system.

BETA ADRENOCEPTOR FUNCTION WITH AGEING IN THE MRC-5 FIBROBLAST

P. M. E. McCormack, S. Kilfeather, T. Cotter, K. O'Malley.
Department of Clinical Pharmacology, Royal College of Surgeons in Ireland, Dublin 2 and Department of Biology, St. Patrick's College, Maynooth.

Beta adrenoceptor (BADA) responsiveness has been shown to decline with age both *in vivo* and *in vitro*. The fibroblast (FB) has been proposed as a model for studying age related events. We studied the effect of *in vitro* ageing on BADR responsiveness in MCR-5 FB.

The BADR was studied at receptor (R) level, at the level of the regulatory protein (N) and at the catalytic subunit (C) using isoprenaline, cholera toxin and forskolin respectively as the stimulants. Response is measured as cyclic AMP / mg protein. There was a significant decline in maximal responsiveness at R ($n=9$, $r=-0.516$, $p<0.05$); but not at N ($n=14$, $r=-0.04$) or C ($n=15$, $r=-0.48$, $P<0.1$). Mean maximal responsiveness also declined with in vitro ageing at R [413±53 pmol cyclic AMP ($n=8$) vs 269±28 pmol cyclic AMP ($n=7$)] but not at N or C.

Our studies show that BADR responsiveness declines with *in vitro* ageing in MRC-5 fibroblasts. These studies suggest that the defect is at the level of the receptor.

MODELS AND MECHANISMS OF GENTAMICIN NEPHROTOXICITY IN CULTURED PRIMARY RAT RENAL CELLS

H. McGlynn, M. P. Ryan.
Department of Pharmacology, University College, Belfield, Dublin 4.

The kidneys are major targets for toxicity by drugs and other chemicals including those of environmental interest. Toxic nephropathy leading to renal failure is believed to be a significant contributor to end-stage renal disease. There is a need to develop better molecular and mechanistic models for investigating nephrotoxicity. We have previously reported findings on gentamicin nephrotoxicity using *in vivo* animal models and renal cell culture systems. The present report extends the *in vitro* investigations and provides further evidence for amelioration of gentamicin nephrotoxicity by magnesium asparate hydrochloride. Renal proximal tubular cells were isolated from male Sprague Dawley rats by means of collagenase digestion and percoll separation. Cells were cultured for 5 days. Cells were exposed to gentamicin in concentration range 10^{-5} - 10^{-3}M for various times up to 48 hours. Gentamicin was found to enhance lactate dehydrogenase leakage from cells. Morphological alterations resulting from gentamicin administration included formation of myeloid bodies and mitochondrial disruption. Gentamicin impaired both ^{45}Ca uptake into the efflux from the cells. Kinetic analysis of ^{3}H-gentamicin binding revealed a single class of non-interacting binding sites with a K_D of 3.4±1.0 μM and a B_{max} of 18.2±1.2 fmoles/mg protein. Gentamicin was displaced from the binding sites by magnesium-asparate-hydrochloride. These findings indicate that membrane-mediated events are early manifestations of gentamicin toxicity. Magnesium-L-asparate may be a useful compound in ameliorating gentamicin nephrotoxicity.

PHARMACOLOGY AND THERAPEUTICS/ GENONTOLOGY

RECENT FINDINGS ON THE EFFECTS OF SOLVENT VAPOURS ON THE MEMBRANE BOUND ACETYLCHOLINESTERASE OF HUMAN ERYTHROCYTES

F. Ó Gharbháin, P. L. Chambers.
Department of Pharmacology and Therapeutics, University of Dublin, Trinity College, Dublin 2.

Some solvents and their vapours inhibit erythrocyte membrane-bound acetylcholinesterase (EMBAchE) *in vitro*[1]. This may be due to trauma and not true inhibition. Initially a Cobe CML Lung and later a more efficient silicone/rubber membrane lung have been used to expose undiluted whole human blood to solvent vapours in air at 37°C. The EMBAchE activity was determined using Ellman's technique[2]. Initially the results suggested that EMBAche increased over time with the concentrations used[3]. Slightly different results from these were produced with the later model. Several solvents have been studied. To find an explanation for these findings, the relationship between the Mean Corpuscular Volume (M.C.V.) of the erythrocyte and the EMBAchE activity has been investigated. The M.C.V. was determined using a Coulter Counter T890. Red blood cells in reduced plasma volumes were also used to remove the possible "cushioning effects" produced by plasma lipids or other constituents. The results indicate that non-halogenated solvents produced first an increase in EMBAche activity followed by a decrease. The M.C.V. showed an increase which correlated with the decrease in enzymatic activity.

References
1. Chambers, P. L., Healy, F. The effect of solvent vapour on the membrane bound acetylcholinesterase of the erythrocyte. Ir. Chem. News, Spring 1988, 19.
2. Ellman, G. L., Courtney, E. D., Andrews, V., Featherstone, R. A. A new rapid determination of acetylcholinesterase activity. Biochem. Pharmacol. 1961: 7, 89-95.
3. Ó Gharbháin, F., Chambetrs, P. L. An improved method to study the effects of solvent vapours on the membrane bound acetylcholinesterase of human erythrocytes. Ir. J. Med. Sci. (in press).

DEPENDENCY OF ELDERLY PEOPLE LIVING IN THE COMMUNITY IN RELATION TO SOCIAL SERVICES SUPPORT

V. Crawford, H. Campbell, R. W. Stout.
Department of Geriatric Medicine, The Queen's University of Belfast, Whitla Medical Building, 97 Lisburn Road, Belfast BT9 7BL.

In order to assist future planning for care of elderly people, a survey was designed to assess dependency levels and social circumstances of those aged 75 and over in South Belfast and to determine the support provided by social services. The survey instrument used to measure dependency was the Clifton Assessment Procedure for the Elderly. The requirement for and provision of social services support was assessed by questionnaire. A total of 390 persons randomly sampled from the total elderly population were assessed (282 female, 109 male, mean age 80.6 years). 71% were classified as independent and 21% as having low dependency. Medium dependency accounted for 6% of the sample while the remaining 2% were highly dependent. With respect to social services support it was determined that while 20% of those in the high dependency groups were supported by home help, 36% of those who were independent and 60% of the low dependency group were also supported. A similar pattern occurred for other support services measured. Thus, the proportion of very dependent elderly people living in the community is very small but a large proportion of independent elderly people are receiving support which may be unnecessary. This finding has important implications for future planning.

DIFFERENTIAL ADHERENCE TO MORAXELLA (BRANHAMELLA) CATARRHALIS IN SYMPTOMATIC AND ASYMPTOMATIC ELDERLY

V. Hegarty, T. Scott, C. T. Keane, J. B. Walsh, D. Coakley.
Mercer's Institute for Research on Ageing and Dept. of Clinical Microbiology, St. James's Hospital, Dublin.

Moraxella (Branhamella) catarrhalis is the third commonest

organism isolated from patients with respiratory tract infection (after *Streptococcus pneumoniae* and *Haemophilus influenzae*). Infection with this organism has a particular predeliction for the elderly. Colonisation and consequent infection have been associated with the adherence characteristics of microorganisms, highly adherent bacteria being more likely to colonise epithelial surfaces.

The aim of this study is to compare the adherence characteristics of *Branhamella catarrhalis* organisms isolated from the sputum of elderly patients with clinical evidence of respiratory tract infection with those of *Branhamella catarrhalis* from the oropharynx of asymptomatic elderly in the community. The adhesion test used was haemagglutination of human Group O red blood cells.

Branhamella catarrhalis organisms were collected from two groups. Group 1 (n=36), elderly patients with clinical evidence of respiratory tract infection. Group 2 (n=12), asymptomatic elderly in the community whose throat swab contained *Branhamella catarrhalis*. A Chi Square (incorporating Yates' correction for continuity) found the two groups to be significantly independent (X=17.09, p<0.001), group 1 having greater ability to cause haemagglutination.

The *Branhamella catarrhalis* organisms from elderly patients with clinical evidence of respiratory tract infection are shown to be more adherent than the *Branhamella catarrhalis* organisms from the oropharynx of asymptomatic elderly in the community. This suggests that the adherence capacity of *Branhamella catarrhalis* organisms may play a role in respiratory tract infection in the elderly.

SMALL INTESTINAL BACTERIAL OVERGROWTH AND ALIPHATIC AMINE EXCRETION IN THE ELDERLY

M. MacMahon, M. Healy, R. R. O'Moore, D. G. Weir, C. T. Keane, J. B. Walsh, D. Coakley.
Mercer's Institute for Research on Ageing, Depts. of Biochemistry, Gastro. and Microbiology, St. James's Hospital, Dublin.

Bacterial by-products of choline metabolism are absorbed in the duodenum and excreted via the kidneys. It has been suggested that small intestinal bacterial overgrowth (SIBO) may interfere with this process, producing methylamines; toxic metabolites of choline. These alipathic amines have the potential to produce carcinogen precursors, and to alter the bioavailability of certain orally administered drugs.

However, the excretion of these toxic metabolites has never been studied in relation to quantitative and qualitative small bowel bacteriological analysis.

Urinary dimethylamine (DMA), an end product of choline metabolism, was measured after choline ingestion in a group of elderly patients; 18 culture proven SIBO (bacterial counts > 10^5) including strict anaerobes in 12, and 7 culture negatives. The presence of certain species was studied in relation to DMA excretion.

DMA values: (1) did not differ between controls and each patient group (P>0.05), and (ii) did not correlate significantly with total bacterial counts (r=0.2), or, strict anaerobic counts (r=0.1). Hence, methylamine excretion in this group of patients was independent of the total bacterial and strict anaerobic count in the small bowel. Therefore, the toxic metabolic side-effects due to methylamine production are unlikely to occur as a consequence of SIBO, in the elderly.

GERONTOLOGY

CHANGES IN ARGININE VASOPRESSIN (AVP) DURING ATRIAL NATRIURETIC PEPTIDE (ANP) INFUSION

E. Mulkerin, A Brain*, D. Hampton*, M. Penney*, K. Woodhouse.
University Department of Geriatric Medicine, Cardiff.
*Department of Chemical Pathology, Newport, Gwent.

The exact role of ANP in modulating AVP is unknown. It has been suggested that ANP suppresses AVP release, thus enhancing its direct natriuretic effect[1]. Since advancing age is associated with elevation of ANP levels and alterations in AVP release[2], we assessed the effects of a physiological infusion of ANP on the plasma AVP levels of young and elderly healthy volunteers.

Six young (mean age 27 years) and 6 elderly (mean age 73 years) male volunteers were recruited. After an overnight fast, baseline plasma ANP and AVP and serum electrolyte levels were assessed at 10.00 hrs and repeated 1 hour later. Thereafter, a 2-hour ANP infusion (5 ng/Kg/min) was commenced. Biochemical and hormonal parameters were assessed hourly during the infusion and continued for a further 2 hours.

The increment in plasma ANP during infusion[29(10) vs 34(11)] and baseline plasma AVP levels [0.35(0.10) vs 0.30(0.08)] were similar in the young and elderly volunteers (all values pmol/l, mean (1sd). Plasma AVP levels failed to alter significantly in either group throughout the study.

We conclude that physiological infusion of ANP does not alter plasma AVP levels in either young or elderly healthy subjects.

References
1. Fujio, N. *et al.* Clin. Endocrinol. 1986: 25, 181-187.
2. Helderman, J. H. *et al.* J. Gerontol. 1978: 33, 39-47.

BLOOD GLUCOSE IS NOT RELATED TO MORTALITY IN ACUTE STROKE

F. Treacy, V. Crawford, R. W. Stout.
Department of Geriatric Medicine, The Queen's University of Belfast, Whitla Medical Building, 97 Lisburn Road, Belfast BT9 7BL.

Blood glucose concentration has been observed to be elevated in acute stroke. Hyperglycaemia has been associated with a poorer outcome. It is not known whether it is due to a stress response to the severe illness or whether glucose is toxic to ischaemic nervous tissue. Patients hospitalised with acute stroke were recruited if they had no history of diabetes mellitus, no acute illness and were not on drugs likely to cause hyperglycaemia. Sixty-eight patients had fasting blood glucose, fasting cortisol, noradrenaline, insulin and HbAlc estimations performed on samples taken within 24 hours of the onset of symptoms. They were followed up for three months. These measurements, together with age and sex, were related to mortality, using discriminant analysis. Only age and Log-10 cortisol concentration were independently related to mortality (p<0.0001 and p=0.0001 respectively). This result would suggest that mortality is related to the severity of the stroke and the age of the patient and that the relationship of hyperglycaemia to mortality reflects the stress of a severe illness. It does not support the view that blood glucose levels are toxic to ischaemic nervous tissue at levels encountered in the clinical situation.