

INAUGURAL NATIONAL SCIENTIFIC MEDICAL MEETING (contd. from Feb. 1993)
Friday, 13th & Saturday, 14th March, 1992

GERONTOLOGY/ONCOLOGY

THE IMPACT OF LIFELONG CARING IN IRELAND

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Throughout Ireland, many parents continue to provide primary care for their adult sons or daughters with mental handicap even when this is no longer the preferred option. The carers themselves experience their own ageing while they remain active parents and companions¹. This study was undertaken to chart the experiences of older mothers in Ireland providing care to adult children. A total of 280 mothers in Ireland and Northern Ireland were interviewed in their homes. Their perceptions of the formal services needed or received, their informal supports from family and friends, their expectations and their own health and characteristics were explored. The results suggest that (1) the mothers have more constrained social networks; (2) many feel anxious about the future "when I'm not here"; (3) the impact on mother's health is associated with perceived stress as well as a number of demographic variables.

Reference

1. Seltzer, M. M., Kraus, M. W. Aging parents with mentally retarded children: Family risk factors and sources of support. *American Journal on Mental Retardation* 1989; 94, 303-12.

COMPARATIVE VALUE OF MORPHOMETRY IN THE PROGNOSIS OF OVARIAN EPITHELIAL TUMOURS

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The role of morphometry as a prognostic indicator in ovarian tumours has been widely acknowledged. The aim of this study is to compare morphometry with other prognostic indicators - clinical staging and histological grading.

In this study forty (40) primary epithelial tumours ovary (20 mucinous, 15 serous and 5 endometrioid) were selected. They included 20 benign and 20 malignant tumours. Patients with the same clinical stage received similar treatment. Clinical follow-up was available for all the patients.

The morphometric features investigated included mitotic activity index (MAI), volume percentage of epithelium (VPE) and volume corrected mitotic index (M/V Index).

Using relative risk and 95% confidence interval to analyse our results, it was shown that risk of death in any unit of time goes up on average by 7% (95% confidence interval 1.1 - 13.3%) for each unit increase in VPE. This risk is maintained even when analysis is corrected for the effect of stage or grade.

THERAPEUTIC IMPLICATIONS OF PRIMARY BREAST CANCER C-erb-2 ONCOPROTEIN EXPRESSION

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C-erb-2 oncoprotein expression detected immunohistochemically in primary breast cancer is a potent poor prognostic variable for patients including Irish women^{1,2}. Also primary C-erb-2

expression indicates hormone resistance in recurrent breast cancer and relative tumour resistance to low intensity chemotherapy with mitoxanthrone (data in press). Forty young women (median age 41 years) had staining for C-erb-2 in their primary tumours; 11 showed positive staining and 29 did not. All subsequently had recurrences of breast cancer and were then given intensive chemotherapy with doxorubicin 40 mg/m² intravenously and ifosfamide/mesna 5 g/m² by intravenous infusion over 24 hours, with mesna alone for 8 hours. Cycles repeated at 21 day intervals to a total of 4 cycles in patients with responsive tumours. Response rates in recurrences (82% C-erb-2+VE vs 72% C-erb-2-ve) median response durations, and post-treatment survival were no different between patients on the basis of primary tumour C-erb-2 expression. This strongly suggests that young women with operable breast cancer and expression of C-erb-2 should be selected for intensive doxorubicin based neo-adjuvant/adjuvant chemotherapy.

References

1. Wright *et al.* *Cancer Res.* 1989; 49, 2087-2090
2. McCann *et al.* *Cancer Res.* 1991; 51, 3296-3303.

LYMPHOKINE ACTIVATED KILLER CELLS IN OESOPHAGEAL SQUAMOUS CARCINOMA

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In this study, we report that three human tumorigenic cell lines derived from both squamous and adenocarcinomas of the oesophagus were resistant to natural killer (NK) cell activity but were sensitive to lymphokine activated killer (LAK) cell activity. These oesophageal carcinoma cell lines were LAK cell sensitive when grown both as anchorage dependent monolayer cultures and as 3-dimensional (3-D) tumourids. The relative abilities of tumor node lymphocytes (TNL), reference node lymphocytes (RNL) and peripheral blood lymphocytes (PBL) from oesophageal squamous carcinoma patients to generate LAK cell activity was investigated. While RNL and PBL exhibited high LAK cell activity, we were unable to generate LAK cell activity from TNL in the same patients. The addition of an oesophageal tumour derived immunosuppressor factor (ISF) to interleukin 2 (IL2) stimulated TNL, RNL and PBL inhibited the generation of LAK cell cytotoxicity. Similar inhibition of LAK cell cytotoxicity by ISF was observed with PBL from normal control donors. Inhibition occurred in a dose dependent fashion and was irreversible. The suppressive effect of ISF was most significant during the early stages of LAK cell generation and no inhibitory effect was seen when ISF was added directly to preformed LAK cells. ISF mediates its effect by inhibiting DNA synthesis which we have shown to be essential for LAK cell generation. The elaboration by tumour cells of ISF may partially explain the failure of LAK/IL2 therapy in some clinical and experimental protocols.

CHANGING TRENDS IN THYROID CARCINOMA

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We reviewed the relative incidence of histological sub-types of thyroid carcinoma at St. Vincent's Hospital between 1970 and

1991 and compared survival rates. The findings were compared with previous reports between 1946 and 1970.

Patients with thyroid carcinoma from 1970 through 1991 were identified and pathological and clinical data retrieved.

Of 141 patients identified, 113 were female and 28 male. Fifty-seven patients had papillary, 41 follicular, 24 anaplastic and 6 medullary carcinoma. There were 10 lymphomas and 3 thyroid metastases. The 10-year actuarial disease-free survival for papillary carcinoma was 93%, follicular 80% and medullary 37%. The median overall survival for anaplastic carcinoma was 5 months. The number of cases seen increased from 2.2 per year between 1946-1965 to 7.6 per year between 1982-1991. From 1946 to 1991 the relative incidence of papillary carcinoma increased from 19% to 57%.

Of interest is the change in relative incidence of the histological sub-types. Follicular carcinoma is associated with endemic goitre and increased iodine intake may explain its reduced incidence. Increased radiation may explain the increase in papillary carcinoma. There is a need for a National Tumour Registry to see if this local trend is reflected nationally.

PROTEOLYTIC ENZYMES AS PROGNOSTIC MARKERS IN BREAST CANCER

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Considerable evidence from animal tumour systems suggest that proteolytic enzymes are involved in cancer invasion and metastasis. Levels of specific proteases in primary human cancers might thus be markers for metastatic potential of these tumours. The aims of this investigation were therefore to investigate a number of different proteases as prognostic markers in breast cancer. Of six different proteases studies, two, i.e. cathepsin D (CD) and urokinase plasminogen activator (u-PA) correlated significantly with both shortened disease-free interval and patient survival. Using univariate analysis, u-PA as a prognostic marker was of similar value to axillary node status but stronger than that of tumour size, estrogen receptor (ER) status or CD. In multivariate analysis, u-PA as a prognostic marker was independent of nodal status, tumour size and ER status. In addition, using overall survival as end point, u-PA was a significant prognostic marker in both axillary node-negative and node-positive patients. We conclude that u-PA is a new and independent prognostic marker in breast cancer.

PROGRESSIVE MOLECULAR CHANGES IN THE DEVELOPMENT OF CANCER

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The discovery of oncogenes and tumour suppressor genes provides a molecular basis for studying the pathogenesis of malignant disease. A number of molecular defects have been described in several types of cancer, notably retinoblastoma, Wilm's Tumour, colorectal cancer and breast cancer. In our own time we have described allele loss on chromosome 17q in ovarian cancer. This loss of genetic material is thought to represent inactivation of a

tumour suppressor gene. Ovarian cancer is ranked as the fifth commonest neoplasm in women with a 5 year survival of 28 percent.

These studies have been taken a stage further by Vogelstein's group in the USA with the discovery of a series of progressive molecular changes in the development of colo-rectal cancer from benign adenomatous polyps to frank malignancy. We have examined the changes in various types of ovarian tumours ranging from benign lesions to borderline tumours, through advancing clinical stages of malignancy. By combining the clinical and molecular results from three centres in Belfast, Edinburgh and Aberdeen, over 150 cases have been accumulated. It is now possible to discern a progressive pattern of molecular changes in the transition from benign to malignant disease (Table).

Allele loss in ovarian cancer (%)

Normal tissue	0
Benign tumour	7
Borderline tumours	11
Malignant: Stages I & II	40
Stages III & IV	67
Anaplastic	100

TRANSFORMING GROWTH FACTORS IN BIOLOGICAL FLUIDS OF CANCER PATIENTS

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Using the NRK (normal rat kidney fibroblast) bioassay we have detected TGFs in the serum, malignant ascites and urine of patients with a variety of epithelial malignancies. We were unable to detect these factors in sera or urine from age-matched control non-cancer patients. Levels of TGF activity appeared to correlate for a given tumour type. Biochemical and immunological characterisations showed TGFs detected in urine and sera to be heat stable proteins, disulphide bond dependent for activity and differing from the well characterised TGF α and TGF β . Gel filtration analysis revealed a complex profile, however a TGF activity of 15kD was consistently observed. Urine may provide a convenient, readily accessible material for the detection of biologically active tumour markers, such as tumour derived TGFs.

CHARACTERIZATION OF CELL LINES DERIVED FROM HUMAN OESOPHAGEAL CARCINOMAS

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The objective of this project was to establish human tumour derived cell lines, to investigate the fundamental biological properties of oesophageal carcinoma and to correlate their properties with the invasive metastatic character and consequent poor prognosis of this neoplasm. Such cell lines are rare on a worldwide basis and reports of their establishment are confined to high disease incidence areas. A number of such cell lines have been established during the course of this study and two cell lines derived from human oesophageal squamous carcinomas and one cell line from an adenocarcinoma of the oesophagus have been subjected to further investigation, including cell growth, gene expression, tumour

derived factors and response to potential therapeutic agents. These cell lines exhibit the following characteristics:

- (1) tumourigenic in nude mice and invasive using the chick heart invasion assay,
- (2) produce and secrete transforming growth factors and immune suppressor factors,
- (3) exhibit clonogenic growth in serum free medium,
- (4) are cytokeratin positive and coexpress vimentin, keratin expression is responsive to retinoid morphogenesis,
- (5) lack HLA antigen expression which can be included on interferon treatment,
- (6) exhibit oncogene amplification,
- (7) are sensitive to LAK cell therapy.

Despite the common tissue of origin, these cell lines differed in their response to chemotherapeutic agents and radiation sensitivities. Using this system factors have been identified which may, at least in part, account for the refractory nature of this tumour to conventional therapy. In addition these cells will facilitate the development of new therapeutic strategies including biotherapy/immunotherapy.

IMMUNOSCINTIGRAPHIC ASSESSMENT OF OVARIAN CARCINOMA TREATMENT RESPONSE

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We evaluated immunoscintigraphy to assess treatment response after surgery and chemotherapy in epithelial ovarian carcinoma (21 pts). C.A.T. scan and ultrasound were insensitive. Histological assessment by laparotomy or laparoscopy was invasive and unsuitable for some patients. The monoclonal antibodies used were HMFG (15 pts), H₁₇F₂ (3 pts), AUA, 3 patients. DTPA - monoclonal antibody was radiolabelled with ¹¹¹Indium and serial planar and tomographic images obtained after intravenous infusion. Results were compared with C.A.T. scan and/or ultrasound, serum CA 125 and where possible histological assessment. Radioimmunoscans located tumour in 9 of 13 patients with residual ovarian carcinoma. Serum CA 125 was elevated in 11 of these patients but did not localize tumour. All positive immunoscans were associated with elevated serum CA 125. Techniques which may increase imaging sensitivity in ovarian carcinoma are discussed.

ONCOLOGY/PATHOLOGY

THYROID ENLARGEMENT AND BREAST CANCER

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Observations on the concurrence of thyroid disease and breast cancer have yielded conflicting results. One hundred and eighty consecutive patients with breast cancer (mean age 57.5±1.0 yrs.) were investigated in this study; 100 after therapeutic intervention (Retrospective Group) and 80 at the time of excision biopsy (Prospective Group). A Control Group consisted of 150 non-hospitalised females (mean age 51±0.65 yrs.). Hypert thyroidism

and hypothyroidism were not significantly different between the groups but palpable goitres were present in 18/180 (10.0%) of breast cancer patients compared to 9/150 (6.0%) of controls. Ultrasound measurement emphasised this difference in that thyroid volume was significantly enlarged (>18.0 mls) in 67/180 (37.2%) of breast cancer patients compared to 13/150 (8.6%) of controls (p<0.001) and the mean volume of 20.2±1.9 mls. was significantly greater than that of 12.9±1.2 mls. in controls (p<0.01). Patients with breast tumours graded T3 had a greater mean thyroid volume than T1 (23.8±2.8 v 16.45±1.4 mls, p<0.01) and were associated with a greater number of enlarged thyroids (T3: 64% v T1: 24%). To exclude therapeutic intervention as a cause for thyroid enlargement, 80 patients subsequently diagnosed as having breast cancer had thyroid scans at the time of excision biopsy. Neither mean thyroid volumes (20.0±1.2 mls. v 20.2±1.6 mls.) nor the % of thyroid enlargements (39% v 35%) were significantly different between Retrospective and Prospective Groups. The results indicate a direct relationship between the two disorders perhaps involving a common growth stimulus.

DISULFONATED STILBENES CAUSE CALCIUM-MEDIATED EXCITATORY EFFECTS IN T84 CELLS

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Previously, the outwardly-rectifying chloride channel (ORDIC) was believed to be involved in the pathogenesis of cystic fibrosis. It has now been discredited in favour of a small conductance linear chloride channel, recently located in cells transfected with the gene coding for the Cystic Fibrosis Transmembrane Regulator. The ORDIC but not the linear channel is sensitive to the stilbene, DIDS. Apical additions of DIDS (0.5mM) to T84 monolayers mounted in Ussing chambers were without effect on cAMP-stimulated short-circuit current (I_{sc}), thus confirming lack of involvement of the ORDIC in electrogenic chloride secretion. Basolateral additions of DIDS (10-160µM) caused large concentration-dependent and bumetanide-sensitive increases in I_{sc}. These responses were occlusive with those of the calcium-elevating agent, thapsigargin, but they were synergistic with those of cyclic nucleotide-elevating agents. These results suggested a common intracellular pathway for DIDS and thapsigargin. Further, DIDS responses were blocked by calcium removal from the basolateral side. In whole-cell patch clamp experiments DIDS caused an increase in chloride conductance with characteristics similar to those of thapsigargin and ionomycin. Therefore, in T84 monolayers and single cells, DIDS elevates intracellular calcium. The resulting conductance changes depend on the degree of cell differentiation.

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PATHOLOGY

THE PROGNOSTIC VALUE OF PLOIDY IN BREAST CARCINOMA

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Despite the documented prognostic value of nuclear or his-

toxicological grading systems, very little evidence is given to such systems in therapeutic decision making. This is largely because such systems lack objectivity and consequently would appear to be inaccurate assessors of histological behaviour in carcinomas. Hence the search for more objective prognosticators such as ploidy. Our study involves 252 patients assessed and treated in one centre over a five year period. All patients were treated initially with lumpectomy and radiotherapy. The mean patient age was 57 years and 71% were post-menopausal. Pathologic grade, necrosis and amount of in-situ tumour component were assessed on H/E sections. Histological grade was assessed using the Bloom and Richardson method. Ploidy was assessed via flow cytometry and image analysis. Findings suggest that pathologic grade is strongly associated with ploidy status. When the individual components of pathologic grade are examined, the correlation is greatest of the nuclear components. Ploidy also exhibited a strong positive correlation with the presence of tumour necrosis and an inverse correlation with the presence of in-situ tumour component. In multivariate analysis, however, ploidy lost its prognostic value. In conclusion, ploidy is of limited value in the light of a full rigorous histopathological assessment.

THE POLYMERASE CHAIN REACTION (PCR) AND HISTOPATHOLOGY – SOME PRACTICAL PROBLEMS ENCOUNTERED

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Amplification failure using the polymerase chain reaction is encountered by those using archival fixed paraffin wax-embedded histopathological material^{1,2}. Such "failures" may not be due to absent target DNA sequences in the tissues, but may be a direct effect of the type of fixative, fixation time and/or fixation temperature used. In this study, the effect of nucleic acid preservation in tissues and its suitability for use in the polymerase chain reaction according to fixative type, time and temperature were evaluated. 100 mg pieces of tonsillar tissue were fixed in formal saline, 10% formalin, neutral buffered formaldehyde (NBF), Carnoy's, Bouin's buffered formaldehyde sublimate, Zenker's, Helly's and glutaraldehyde at 0-4°C, room temperature and 37°C fixation temperature and for fixation periods 6, 24, 48, 72 hrs and 1 week. Primers for B. globin gene were used to amplify a 110 bp. fragment of this gene using PCR3. NBF and Carnoy's fixed tissue yielded amplified product primarily yet variably. Room and 37°C fixation temperature and 6-48 hour fixation times favoured amplification.

References

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HAEMATOLOGY/RHEUMATOLOGY

EFFECTS OF IL-2 ON IN-VITRO RHEUMATOID FACTOR PRODUCTION

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IgM rheumatoid factor (IgM RF) production is a characteristic feature of rheumatoid arthritis (RA). However little is known of the mechanisms which initiate and sustain RF synthesis. The aim of this study was to determine the effects of several cytokines on in vitro IgM RF synthesis. Two groups were studied: (A) 10 untreated patients with active RA; (B) 16 healthy controls. PBMCs were cultured with and without mitogen (SAC) for 2 days. After washing, the cells were cultured for a further 5 days in the presence of IL-2, IL-4 or IL-6. Immunoglobulins and rheumatoid factors were measured by ELISA.

Experiments were performed after SAC and cytokine doses giving IgM synthesis were determined. IgM synthesis was stimulated by SAC in both control and RA groups as IL-2, but not IL-4 or IL-6, led to a further increase in IgM synthesis ($p < 0.001$). SAC also induced IgM RF synthesis in control cultures but, in contrast to IgM, IL-2 produced no further enhancement of synthesis. In RA cultures IgM-RF was produced spontaneously and at levels which were not increased by either SAC or SAC and IL-2. No stimulation or enhancement of IgA RF was observed under the same culture conditions.

In this study IL-2 enhanced SAC induced IgM, but not IgM RF, synthesis. Thus, factors regulating IgM RF synthesis may not necessarily be the same as those regulating IgM.

RHEUMATOLOGY

EXPRESSION OF HOMING RECEPTORS ON RHEUMATOID SYNOVIAL FLUID LYMPHOCYTES

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Leucocyte function associated antigen 1 (LFA-1) and pgp-1 (CD44) molecule are homing receptors for peripheral blood leucocytes. LFA-1 binds to the ligand ICAM-1 and pgp-1 has recently been identified as the hyalauronic acid receptor. LFA-1 expression is normally biphasic on peripheral blood leucocytes but uniphasic on activated lymphocytes. We studied the patterns of expression of LFA-1 and CD44 in both peripheral blood (PB) and synovial fluid (syn) T cells of 18 patients with active rheumatoid arthritis (RA) and compared this to expression in normal peripheral blood T cells using two colour FACSCAN analysis. CD44 was expressed on all T cells in both PB and syn. The density of expression (mean fluorescence intensity [MFI]) of CD44 in peripheral blood T cells did not differ between RA and controls. However, the density of expression of CD44 was significantly enhanced on CD3+ cells in the RA synovial fluid relative to RA PB (181 ± 20 vs 126 ± 13 , MFI, mean \pm SE, $p < 0.01$). All but one patient had an increase in synovial lymphocyte CD44 expression ranging from 19 to 425% (mean 115). 14/18 RA patients and 9/10 control subjects (CS) had a biphasic pattern of LFA-1 expression in PBLs. By contrast 15/18 RA patients had a uniphasic pattern of LFA-1 hi expression on synovial lymphocytes. These findings are

consistent with the concept that cells expressing high density of homing receptors selectively home to the rheumatoid synovium. An alternative explanation may be that local T cell activation induces enhanced expression.

RELATIONSHIPS IN ADULTS WITH ARTHRITIS SINCE CHILDHOOD

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Chronic arthritis in childhood may cause substantial social, psychological and physical impairment. This study examined family and peer relationships in adults with chronic arthritis since childhood using the Mother-Father-Peer Scale (MFPS) which measures the patient's perception of these relationships compared to population norms.

Forty-six patients were evaluated: 25 female, mean age 26.8 yrs and mean disease duration 17.5 yrs. The MFPS scores revealed a sizeable feeling of rejection among the patients: 14 (30%) felt rejected by at least one parent and 14 felt rejected by peers. Males tended to feel more rejection by their peers than female patients. In addition, mothers tended to either over- or under-protect the patients but fathers tended to do this with their daughters only. The median AIMS psychological score was 2.32, the AIMS social activity score was 3.0 and the AIMS pain score was 3.5 (scale 0-10). These values were disproportionately high when compared with clinical measurements (duration of morning stiffness, Ritchie articular index) and the AIMS physical score (median values 10 mins, 1.5 and 1.0 respectively).

In conclusion, this study demonstrated that a substantial number of patients with chronic arthritis since childhood perceived that they had been rejected by parents and peers.

GASTROENTEROLOGY

THE PROGNOSTIC SIGNIFICANCE OF GENETIC CHANGES IN DUKES B COLORECTAL CARCINOMA

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Colorectal carcinoma (CRC) presents as the second most common human malignancy in the Irish population. Discrete genetic changes associated with colorectal carcinoma progression have been observed. The aim of this retrospective study is to determine the role of such changes in tumour genetic material in the assessment of the prognosis of Dukes B colorectal carcinoma patients.

The study population consisted of 60 patients with Dukes B CRC divided into two groups based upon known outcome. Group 1 : 30 patients dying of their disease within 3 years of surgery and Group 2 : 30 patients known to be alive at least 5 years after surgery. Archival tumour specimens underwent analysis by means of the polymerase chain reaction (PCR) to detect the occurrence of c-Ki-ras point mutation, amplification of the c-erb B2 oncogene and loss of heterozygosity at the p53 locus.

Forty four per cent of cases exhibited point mutation of codon 12 of the c-Ki-ras oncogene; 42% in group 1 and 46% in group 2 (p=ns). Amplification of the c-erb B2 oncogene was not detected to any significant extent in either group. Fifty per cent of the patients in each group were heterozygous for the p53 polymorphism and loss of heterozygosity was detected to an approximately equal extent in both groups.

While these genetic changes are not independent prognostic variables for Dukes B CRC, it is possible that, in conjunction with other genetic changes, these may form the basis of a multivariate prognostic system for the assessment of colorectal tumours.

CI-INHIBITOR AND INHIBITION OF THE INFLAMMATORY RESPONSE IN SLE AND RA

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CI-inhibitor (CI-INH) is an important inhibitor of the inflammatory response. Measurement of the interaction of CI-INH with activated inflammatory mediators may give clues as to the involvement of these mediators in processes. In this study a sensitive assay which can detect interactions between CI-INH and activated inflammatory mediators is applied to patients with SLE and RA. The assay is based on antibody capture of CI-INH from plasma. Plasma from 20 normal controls, 18 patients with SLE, and plasma and synovial fluid from 7 patients with RA were examined for the presence of cleaved CI-INH and CI-INH protease complexes. In nine of the 18 patients with SLE an increase in the amount of CI-INH complexes and in the quantity of cleaved CI-INH was found. This is consistent with increased utilisation of CI-INH by activated complement components. However, there was no apparent increase in either cleaved or complexed CI-INH in synovial fluid of patients with RA in comparison with their plasma suggesting that CI-INH consumption is not increased at the site of active inflammation in RA. These results are very surprising in view of the widely held view that immune complexes formed in the joint are involved in the inflammatory process in RA. Employment of this assay may yield important information on the function of CI-INH in health and disease.

VITAMIN C REDUCES COLONIC CRYPT CELL PROLIFERATION

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Epidemiological studies have shown that vitamin C intake is inversely correlated with the incidence of colorectal carcinoma. Colonic crypt cell proliferation is used as an indicator of risk of colorectal cancer. This study assessed the effect of vitamin C supplementation on the colonic crypt cell proliferation of patients with adenomatous polyps. Twenty patients with adenomatous polyps were recruited. Ten were supplemented with 750 mg of vitamin C daily for one month. Ten received no supplementation. Four colonic biopsies were taken before and at the end of the trial period. These were assessed for colonic crypt cell proliferation using the bromodeoxyuridine immunohistochemical technique. The mean labelling index percent (LI%) is calculated as the percentage ratio of the mean number of proliferating cells to the total number of cells in the crypt.

	TOTAL LI%	
	Pre supplement	Post supplement
Normal	2.9	
No supplement	7.1	6.6
Vitamin C	5.4	2.5* p<0.001

All adenomatous polyp patients had significantly increased LI%

compared to normals. Vitamin C supplementation significantly decreased the total LI%. 750 mg of vitamin C daily for one month significantly decreases the colonic crypt cell proliferation in patients with adenomatous polyps.

ADIPOSE TISSUE PROFILES IN INFLAMMATORY BOWEL DISEASE

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Dietary fat may be a risk factor in the aetiology of inflammatory bowel disease (IBD). Adipose tissue fatty acid composition is a reliable indicator of the quality of fat consumed and was used to investigate the relationship between the quality of fat consumed and IBD. Abdominal adipose tissue biopsies of 26 ulcerative colitis (UC) patients, 22 Crohn's disease (CD) patients and 24 controls were analysed by gas liquid chromatography. Results were expressed as mass percentage total fatty acids. The fatty acid composition of the three groups were similar with regard to i) the saturated fatty acids C14:0 and C18:0, ii) the major monounsaturated fatty acids C16:1 and C18:1 and iii) the major polyunsaturated fatty acid C18:2 (n-6). The principal abnormalities in the IBD were that i) CD patients had significantly higher levels of C16:0 (21.85% vs 20.62%) and lower levels of C20:1 (n-9) (0.78% vs 0.92%) than UC patients and ii) CD patients had significantly lower levels of C18:3 (n-3) (0.7% vs 0.98%) than controls. The major fatty acids found in adipose tissue were the same in IBD patients and controls, indicating similar patterns of fat consumption. Metabolism of some lipids is altered in the IBD population. The level of the eicosanoid precursor C18:3 (n-3), is reduced in the adipose tissue of IBD patients. This may reflect increased production of active mediators of inflammation in IBD.

A PROSPECTIVE EVALUATION OF LAPAROSCOPY AND IMAGING IN THE STAGING OF FOREGUT CANCER

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As part of a (larger) trial evaluating the optimum method of staging gastro-intestinal cancer, 72 patients with foregut cancer were examined. All had histological diagnosis of malignancy made on endoscopic biopsy. They were then entered into the trial after informed consent had been obtained. Ultrasonography (US) and computed tomography (CT) were performed, followed by laparoscopy (the results of imaging tests were not known by the surgeon at this stage). Biopsy of all suspicious lesions was undertaken at laparoscopy. The results of all tests were then discussed and further biopsies, as necessary, were obtained using imaging methods. Of the 72 people examined, laparoscopy confirmed metastases in 25, CT in 17, and US in 9. In addition CT gave one false positive and 2 equivocal results. In those with metastatic spread to the peritoneal cavity, laparoscopy was the only method that allowed assessment of response of these tumours to chemotherapy. Therefore we feel that for the cost of effective and accurate pre operative staging of gastric cancer, that CT with biopsy of suspicious areas should be the first method of staging. This should be followed by laparoscopy and biopsy in those that have negative CT scans. Laparoscopy is the best method for follow up of local responses of the tumour to chemotherapy.

LYMPHOCYTES IN THE NORMAL MUCOSA OF CROHN'S DISEASE

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Previous studies have shown that involvement of the gastrointestinal tract in Crohn's disease is more extensive than is revealed by conventional histology. In the apparently uninvolved tissue as judged by routine histology, neuronal abnormality and increased enzyme activity have been demonstrated. The object of this study was to assess the lymphocyte concentration in the histologically normal mucosa of patients with Crohn's disease.

Forty two patients with Crohn's disease and a similar number of age and sex matched controls with the irritable bowel syndrome (IBS) were studied. Rectal and descending colon biopsies were taken for histology and immunohistology. Using monoclonal antibodies to T cells, helper and suppressor cells and B cells, the lymphocyte concentration within the lamina propria and epithelium of the mucosa was characterised. A quantitative method of assessment was used.

The histology was reported as normal in 30 of 42 patients with Crohn's disease. All patients with IBS had normal histology. Similar densities of lamina propria and intraepithelial lymphocytes were found in the mucosa of patients with IBS.

It appears that histological normal mucosa of Crohn's disease is cellularly normal.

PATIENTS WITH HEARTBURN HAVE A SPECIFIC PERSONALITY PROFILE

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One hundred and four consecutive patients presenting with heartburn completed, (i) a hassles and uplifts scale, and (ii) the Crown-Crisp personality inventory. These questionnaires were also completed by 20 healthy age-sex matched controls. By endoscopy, patients were grouped as oesophagitis (OES, 32) other eg DU (OTH, 16) and normal (NOR, 52). Four patients with both OES and OTH were excluded.

Heartburn sufferers as a group (ALL) [$p \leq 0.002$] and more especially OTH [$p < 0.0001$], experienced both more hassles and more uplifts than controls. OTH also experienced more hassles and more uplifts than the other two patient groups [$p < 0.05$]. Compared with controls, ALL had significantly increased anxiety [$p < 0.05$], particularly NOR [$p < 0.05$]. OTH and NOR had significantly greater obsessiveness than controls [$p < 0.05$].

In conclusion, heartburn sufferers do have a personality profile which differs from controls. It is possible, on the basis of hassles, uplifts, anxiety and obsessiveness, to differentiate the different pathological groups within heartburn patients.

STRESS IMPEDES NORMAL OESOPHAGEAL FUNCTION

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The effects of psychological (Stroop test, ST) and physical (cold pressor, CP) stress on oesophageal motility were studied in 20

healthy volunteers (11m; mean age (SD) 44 (14.7) yr). Each period of stress was compared with its own rest period. Systolic blood pressure, heart rate and an analogue scale of stress assessed autonomic stress effects. Oesophageal pressure waves in response to 10 ml water swallows were measured for peristaltic amplitude (A), duration (D) and propagation velocity (V). Abnormal waves were counted (%ABN).

Both stressors induced significant changes in all parameter of autonomic function ($p < 0.05$ - 0.0001). Both significantly increased V (ST: 2.41-2.96 cm^{-1} , CP: 2.32-2.66, $p < 0.05$). ST increased %ABN (0.3-8.5% (median), $p < 0.05$). CP decreased A (111.0-100.6 mm Hg, $p < 0.01$) and D (4.1-3.7 s, $p < 0.05$).

Both psychological and physical stress reduce ability to propagate a bolus and to clear gastric refluxate.

IS OESOPHAGEAL MANOMETRY CLINICALLY BENEFICIAL?

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Our oesophageal laboratory serves a population of 1.5 million people. The purpose of this study was to examine referred patterns and assess the usefulness of manometry.

All 268 consecutive first referrals (119 male, mean age 51 (12-82)) in the four years 1988-1991 were reviewed. Manometry tracings and patient notes were examined. The reasons for referral were: dysphagia (50.4%), non-cardiac chest pain (NCCP) (23.1%), reflux disease (GORD) (14.2%), connective tissue disease (CT) (11.2%) and other (1.1%).

The results of manometry were: normal (49.3%), achalasia (17.9%), non-specific oesophageal motor disorder (11.9%), CT (7.8%) hypertensive lower oesophageal sphincter (4.5%), nut-cracker (2.6%), diffuse oesophageal spasm (1.5%) and other (4.5%).

A positive diagnosis was significantly more common when dysphagia was the referral reason (65.9 v 35.3% $P < 0.000001$). A manometric diagnosis was made in CT (60%), NCCP (30.6%) and GORD (21.1%). In CT a positive diagnosis was significantly more common if symptoms were present (85 v 10%, $P < 0.001$).

In conclusion, manometry gives a high diagnostic yield in NCCP, dysphagia and symptomatic connective tissue disease.

CUTANEOUS MANIFESTATION OF CROHN'S DISEASE

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This study documents the prevalence of cutaneous disease occurring in patients with Crohn's disease. Twenty-seven patients previously diagnosed as having Crohn's disease were assessed with a detailed history and examination, the cutaneous and systemic manifestations were documented and related to Crohn's disease extent and activity. The mean age was 36 years; 8 were males, 19 were females. Eight of the patients had active Crohn's disease. All patients had significant dermatological findings. Significant telogen effluvium was noted in 81%. Over half the patients had perianal changes; 26% had perianal violaceous discolouration and scarring, 48% had perianal tags, 2 patients had perianal abscesses, one patient had a perianal sinus, another had a fissure-in-ano. 26%

of patients had finger clubbing. 22% had Raynaud's phenomenon. 15% had a history of erythema nodosum. 26% had a history of mouth ulceration, with minor aphthous ulcers clinically evident in one patient. One patient with active disease had severe chelitis. Three patients had psoriasis. Four patients had dermatographism. A single patient had alopecia areata. 15% of patients either had or gave a history of conjunctivitis. Telogen effluvium, chelitis, and mouth ulcers were related to active Crohn's disease. This study outlines the importance of a full dermatological assessment of all Crohn's disease patients.

GASTROINTESTINAL CARCINOMA AND MONOCYTE ESTERASE DEFICIENCY

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Monocytes from 120 patients with gastrointestinal cancer (GIT Ca) have been examined for the presence of monocyte specific esterase activity using automated cytochemistry and/or manual cytochemistry on cytocentrifuge preparations of concentrated peripheral blood mononuclear cells. Thirteen patients (11%) showed monocyte esterase deficiency while 4 of 474 (0.8%) normal blood donors and 7 of 410 (1.7%) of patients with other cancers were similarly deficient.

The GIT Ca patients with esterase deficiency have been compared to those without in relation to white cell count, site, stage and age of presentation, presence or absence of tumour at time of monocyte assessment, the occurrence of multiple malignancies in the two cohorts and the likelihood of occupational exposure to organophosphates.

A familial occurrence of this deficiency has been previously demonstrated and esterase negative monocytes have been shown to have a deficiency of cytotoxicity. We therefore suggest that esterase deficiency is not only linked to gastrointestinal neoplasia but may indicate a predisposition to its development.

INCREASED TNF PRODUCTION AND MALNUTRITION IN CHRONIC INFLAMMATORY BOWEL DISEASE

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Chronic exposure to Tumour Necrosis Factor (TNF) in animal models leads to metabolic effects, affecting nutritional status. Nutritional disturbances associated with TNF are similar to those seen in chronic inflammatory bowel disease (CIBD). The aim of this study was to investigate the role of TNF in mediating the systemic effects of malnutrition in CIBD. Nutritional assessments, carried out on 17 CIBD patients, 7 ulcerative colitic (UC) and 10 Crohn's disease (CD) showed that patients had significantly lower triceps skinfold thickness values ($p < 0.05$) and mid-arm circumference values ($p < 0.001$) than their age- and sex-matched healthy controls (HC). Serum TNF levels, measured by the L929 assay were significantly higher in CIBD patients when compared to controls (CIBD, 134.7 pg/ml (27.9); HC, 55.9 pg/ml (30.5), χ (SEM), $p < 0.05$, but there was no significant difference between UC and CD patients. Supernatants from unstimulated PBMCs showed significantly higher TNF levels on ELISA in CIBD patients

than in controls (CIBD, 267.4 pg/ml (121); HC 32.9 pg/ml (13), x (SEM), $p < 0.05$, but there was no significant difference found after PBMC stimulation with anti-CD3 for 48 hours. The increase in TNF levels in serum and PBMC supernatants did not correlate with either malnutrition or disease activity, indicating that the increase in TNF production in CIBD is not responsible for the malnutrition associated with the disease.

ANXIETY AND DEPRESSION IN GASTROENTEROLOGY CLINICS

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The purpose of the study was to detect anxiety and depression in attenders at both medical and surgical gastroenterology (G.I.) clinics.

Consecutive attenders aged between 18 and 65 at the G.I. clinics were included in the study. Anxiety and depression was diagnosed using the Hospital Anxiety and Depression Scale (HAD). The HAD measures definite and borderline anxiety and depression. Patients completed the HAD in the out-patients clinic.

Thirty-seven medical patients participated in the study (11 male, 26 female, mean age 42.3, s.d. 12.7). Thirty surgical patients were included (11 male, 19 female, mean age 42.0, s.d. 15.8). Of the medical patients, 7 (18.9%) had definite anxiety and 13 (35%) had borderline anxiety. Two (5.4%) were depressed and 4 (10.8%) had borderline depression. Four (13.3%) of the surgical patients had definite anxiety and 7 (23.3%) were borderline. None were depressed but 2 (6.7%) were borderline. No statistically significant difference was found between the medical and surgical groups.

In conclusion, 53.9% of medical and 36.6% of surgical patients had definite or borderline anxiety. 16.2% of medical and 6.7% of surgical patients had definite or borderline depression. Further research is warranted.

GASTROENTEROLOGY/DERMATOLOGY

ERADICATION OF METRONIDAZOLE-RESISTANT *HELICOBACTER PYLORI* AND HEALING OF DUODENAL ULCER

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Metronidazole (MTZ) resistance in *H. pylori* may lead to treatment failure with this drug. The aim of this study was to 1) evaluate a triple therapy regimen; 2) assess interaction *in vitro* between MTZ and tetracycline (TE) against *H. pylori*. Thirty four patients with duodenal ulcer and *H. pylori* infection were treated with colloidal bismuth subcitrate (CBS) 120 mg q.i.d. for 4 weeks, MTZ 400 mg t.i.d. and TE 500 mg t.i.d. for the first week. *H. pylori* isolates from the patients were tested for susceptibility to MTZ and TE, and antral biopsies for histologic examinations at the first endoscopy. Interaction between MTZ

and TE for 23 isolates was measured using checkboard technique. All patients were rescoped and *H. pylori* status and histologic features redetermined at least 4 weeks after end of treatment. Among 25 patients with sensitive isolates, 23 (92%) became *H. pylori* negative while 5 of 9 (55.56%) with resistant isolates had *H. pylori* eradicated. This regimen was able to heal the ulcer among 88% (22/25) of the patients with sensitive isolates and 77.78% (7/9) of those with resistant isolates. *In vitro* synergism was observed between MTZ and TE from 7 of the 23 isolates. In conclusion, triple therapy with CBS, MTZ and TE is effective in eradicating both sensitive and resistant *H. pylori* and healing duodenal ulcer.

DERMATOLOGY

IS ALLERGY TESTING A WASTE OF TIME?

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Fifty men and 50 women with atopic eczema and 25 men and 25 women with recurrent urticaria filled in a detailed questionnaire to detect exacerbating factors in their condition. Intradermal (prick) testing was carried out with the standard series of food and inhalant allergens. Positive responses mainly to milk, eggs and wheat products were found in five of the atopic eczema patients and four of the recurrent urticaria. There was poor correlation between answers and the intradermal tests. It may be concluded that little helpful clinical information arises from the intradermal testing.

METABOLIC DISTURBANCE OF PORPHYRINS IN CHRONIC RENAL FAILURE AND MAINTENANCE HAEMODIALYSIS

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Patients with chronic renal failure on maintenance haemodialysis may develop blistering disorders occasionally attributable to photoactive medication or porphyria cutanea tarda (PCT) but more frequently idiopathic. Because of an increased incidence of PCT and abnormal porphyrin profiles in haemodialysis patients, patients in the national renal transplant centre were screened to establish a reference range for porphyrin levels.

Seventy patients were examined clinically and blood obtained for porphyrin fluorimetric assay.

Porphyrin levels in patients: 19.1 ± 13.5 nmol/l, were significantly higher than those of a normal population ($N=40$): 5.5 ± 3.2 nmol/l ($P < 0.05$, Mann Whitney test). One patient had high porphyrin levels 419 nmol/l. Clinically he had skin fragility, easy bruising and hypertrichosis with no blistering. Three patients with blistering on exposed skin, not on photoactive medication, had porphyrin values which were greater than the normal range but fell within the range for haemodialysis patients. Explanations for the elevated serum levels of porphyrins in haemodialysis include an acquired metabolic disturbance due to renal failure, or dialysis and poor clearance across the dialysis membrane. The pathogenesis of blistering in our patients on haemodialysis, though possibly light related, remains elusive.

CUTANEOUS LUPUS ERYTHEMATOSUS – A RETROSPECTIVE STUDY OF CLINICAL LABORATORY, THERAPEUTIC AND PROGNOSTIC FACTORS IN 65 PATIENTS

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Sixty-five patients were seen over a ten year period. The aims of the study were to divide them into clinical sub-groups; to determine prognostic factors from clinical and laboratory findings; to discuss treatment and to describe the pattern of referral to other specialities. Eighty-three percent were female with a sex ratio of 1 : 5 male to female. The mean age of onset of rash was 39.0 ± 16.9 years. It began at 14 and 22 years in two patients who developed systemic lupus erythematosus (SLE). The majority of patients reported spring/summer onset and sunshine was the most frequent aggravating factor. Three (4.6%) had a rash consistent with SLE at presentation and five had both chronic discoid LE (CDLE) and SLE at the outset; 57 had discoid LE (DLE). Two (3.5%) of the 57 developed SLE. The laboratory abnormalities preceding change to SLE included ANA, WCC, ESR and immunoglobulins. Most patients were managed with topical steroids and sunblock creams but antimalarials were used on occasion. The most frequent referral was to Rheumatology. Overall the prognosis for CDLE was good; clinical groupings provided useful prognostic information. The results compared well with those previously published in the world literature.

EPIDERMOLYSIS BULLOSA IN NORTHERN IRELAND

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(i) We set out to study the incidence and distribution of types and subtypes of epidermolysis bullosa (EB) occurring in Northern Ireland (NI).

(ii) Cases of EB diagnosed in NI during a 23 year period (1962-1984) were identified from dermatology clinic files, paediatric hospital notes and cases known by general practitioners. Patients were examined clinically and the clinical diagnosis was confirmed when possible by skin biopsy.

(iii) A total of 48 confirmed new cases of EB were diagnosed during the screening period. This involved 31 families with identification of 35 further cases. The distribution of incident EB subtypes was simplex 31 (65%), junctional 1 (2%), dystrophic 12 (25%) and acquisita 4 (8%). The incidence rate of new cases of EB diagnosed per year is 1.4 per million and prevalence of all forms estimated at 32 per million. The prevalence of simplex, junctional and dystrophic forms is 28, 0.7, and 3 per million respectively.

(iv) The prevalence of all types of EB in NI is comparable to the disease prevalence in Norway. However EB simplex and dominant dystrophic EB are more prevalent in NI but recessive dystrophic EB less common.

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LINKAGE OF EPIDERMOLYSIS BULLOSA SIMPLEX TO KERATIN GENE LOCI

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(i) Epidermolysis bullosa simplex (EBS) is characterised by intraepidermal blistering of the skin. It has been suggested that EBS-Koebner is linked to loci on chromosome 1¹. Others have found linkage of EBS to keratin gene clusters on chromosome 12 and 17². We have studied two families with Weber-Cockayne EBS to determine whether the disease is linked to these loci.

(ii) DNA from affected and non affected individuals was extracted. Polymorphisms were typed using both the Southern blotting technique and also the Polymerase Chain Reaction (PCR). Linkage analysis was carried out using a data management computer package.

(iii) In the first family, chromosome 1 loci, including the AT3 locus showed negative linkage. However linkage to chromosome 17 markers flanking the keratin 14 gene was found; D17S74 (Zmax = +2.45, O = 0.10), COL1A1 (Zmax = +0.97, O = 0.00). In contrast, the second family showed positive linkage to D12S17 (Zmax = +1.37, O = 0.08) and COL2A1 (Zmax = +0.33, O = 0.15).

(iv) In one family EBS-WC is linked to the keratin gene cluster on chromosome 17 and in the other family to the keratin gene cluster on chromosome 12. Abnormal epidermal keratin expression could result in abnormal intermediate filament formation and thus to fragility of the basal cell layer³.

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A PROSPECTIVE STUDY OF PULMONARY FUNCTION IN PATIENTS ON METHOTREXATE THERAPY

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Pulmonary toxicity occurs in 7.6%-33% of patients on high-dose methotrexate (MTX) chemotherapy, and in 3-4% of patients on low-dose MTX for rheumatoid arthritis. It is considered rare in patients on low-dose MTX for psoriasis but only one study has been carried out¹. There was no difference in the pulmonary function of 10 patients with psoriasis on MTX compared with 10 patients who had never had systemic therapy for psoriasis. We have initiated a long-term prospective study and report our preliminary results.

Prior to MTX therapy patients had full pulmonary function tests (PFTs), which were repeated yearly while on MTX. To date 10 patients have had pre- and follow-up PFTs. There was no significant deterioration in PFTs during or after MTX therapy, but there was a trend for gas transfer to improve. The results are

encouraging but more patients need to be studied to determine if pulmonary toxicity is a problem in patients with psoriasis treated with MTX.

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DARIER'S DISEASE AND CUTIS VERTICIS GYRATA

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A 75-year old lady presented with follicular, keratic rash affecting the upper trunk. Further examination revealed nodules behind both ears and on the scalp, palmar pits, white and red banding of the nails with v-shaped notching of the free margin and white papules on the palate. Skin biopsies from the rash on the trunk and a nodule on the scalp showed the changes of Darier's disease. Two years later she developed longitudinal folding and furrowing of the scalp extending from the occiput to the forehead typical of cutis verticis gyrata (CVG). One son has Darier's disease, but there is no family history of CVG.

This is the first report of Darier's disease and CVG occurring together. About 50% of cases of CVG are secondary to other disorders, the commonest being chronic inflammatory conditions of the scalp such as psoriasis and eczema. Scalp trauma and tumours, acromegaly and syphilis are other causes and have been excluded in this patient. We postulate that the chronic scalp inflammation of the Darier's disease contributed to her developing CVG. It is rare for CVG to start after the age of 30.

ERYTHROPOIETIC PROTOPORPHYRIA, TRANSFUSION THERAPY AND PROTOPORPHYRIN HEPATITIS

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A 28-year old man with erythropoietic protoporphyria (EPP) presented with increasing photosensitivity. Standard therapy was not helpful. He was then treated with 6 units of packed cells over a one month period to suppress photoporphyrin (PP) synthesis. Two weeks later his red cell PP level had doubled. Liver function tests showed a hepatic picture and the only cause found was the high PP level. On skin biopsy there were PAS positive deposits around dermal blood vessels. Direct immunofluorescence showed deposits IgA around the dermal blood vessels. A liver biopsy showed no fibrosis. In the Kupffer cells and hepatocytes were deposits of golden brown pigment. Under polarising light the pigment was bright red in colour with a central dark Maltese cross typical of PP crystals. Intense red fluorescence of hepatocytes was seen on fluorescent microscopy. Electron microscopy showed the ultrastructural features of EPP.

This is the first report of deterioration after blood transfusion therapy for EPP but there are 5 reports of deterioration after oral iron therapy. The iron load from the transfusion may have been responsible.

ICHTHYOSIS, DEAFNESS AND CAROTENAEMIA

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This 4½-year was born with mild erythroderma and absent scalp hair. At 3 months she developed dry scaling of the skin. At 20 months yellow discolouration of the skin was noted and serum carotene was 6.86 mmol/l (normal 0.74-3.72). Investigation, including a detailed dietary history, suggested the cause was an inborn error of carotene metabolism. There is no relevant family history. More recently she has developed hyperkeratotic plaques and nodules on the face, limbs and trunk. She also has palmo-plantar keratoderma and dysplastic nails. She has no keratitis. She has a bilateral neurosensory deafness but other neurological examination is normal. Serum phytanic acid was normal.

A skin biopsy showed acanthosis, hyperkeratosis and follicular plugging. On skin histochemistry there were no lipid vacuoles and alcohol dehydrogenase activity was normal.

The overall picture is in keeping with the keratitis, ichthyosis and deafness (KID) syndrome. Keratitis often develops later, usually by early adolescence. This is the first report of carotenaemia occurring in a patient with ichthyosis

PAPULAR MUCINOSIS, PARAPROTEINAEMIA AND ISCHAEMIC HEART DISEASE

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A 62 year old man presented with firm, flesh-coloured papules on his limbs and trunk. The rash developed 2 months after commencing nifedipine for ischaemic heart disease (IHD). The nifedipine was stopped and 6 months later the rash had almost disappeared. A coronary angioplasty had to be abandoned due to technical difficulty.

A skin biopsy showed an increase in fibroblasts in the dermis, and thickened collagen fibres separated by spaces with a basophilic tinge in keeping with papular mucinosis (PM). Alcian blue staining confirmed the presence of mucin. Serum electrophoresis showed a paraprotein band of type IgGL, the type commonly associated with PM.

There is debate about the frequency of other systemic manifestations, including IHD. One post mortem in a patient with PM showed mucinosis involvement of the coronary arteries. In this patient the unsuccessful angioplasty may have been due in part to infiltration of the coronary artery by mucin. This is the first report implicating a drug in the aetiology of PM, and only the second PM resolving without treatment.

IMMUNOLOGY/OBSTETRICS & GYNAECOLOGY

CELL MEDIATED IMMUNITY IN BREAST CANCER PATIENTS

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It is suggested that patients with advanced breast cancer exhibit more impairment of T lymphocyte function than those with early

disease. This hypothesis was examined in the following experiment. On first presentation peripheral blood mononuclear cells (10,000 cells/ml) from sixty-four patients with mammary carcinoma were stimulated with the mitogens Phytohaemagglutinin (PHA) and Concanavalin A (Con A) to yield an index of T cell function. To standardise for inter-assay variation, blood from a pool of ten controls (thirty observations) were also assessed. There was a highly significant correlation between Con A and PHA responses in all subjects tested ($r=0.757$, $p<0.0001$). In the controls (mean \pm standard error of the mean), PHA and Con A responses were 54574 ± 3543 cpm (counts per minute) and 51537 ± 3430 cpm respectively, and in patients 4729 ± 2348 cpm and 32949 ± 1844 cpm respectively. (Control *versus* patients; PHA - $p>0.05$, Con A - $p<0.05$)*. In patients, there was no significant difference* observed between PHA response in the different disease stages (Stage I: 51930 ± 3659 cpm, $n=24$; Stage II: 49242 ± 5819 cpm, $n=13$; Stage III: 45816 ± 9429 cpm, $n=6$; Stage IV: 41229 ± 3827 cpm, $n=14$). Con A results showed a similar trend (Stage I: 3617 ± 3195 cpm; Stage II: 32919 ± 4650 cpm; Stage III: 28904 ± 6844 cpm; Stage IV: 31890 ± 2747 cpm). Although T lymphocyte function appeared to be impaired in comparison to the control group, disease stage did not correlate with this impairment. In conclusion, we have found no evidence to suggest that cell mediated immune function is a significant factor in the progression of breast carcinoma.

*Student T Test.

OVARIAN HYPERSTIMULATION SYNDROME (O.H.S.S.)

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Ovarian hyperstimulation is a serious problem faced during the treatment of infertile females with gonadotrophins

The unpredictable response of patients to extraneous hormone is responsible for ovarian hyperstimulation syndrome (OHSS) which is a life threatening condition in its severe form. It is a complex syndrome of unknown aetiology. Gonadotrophin releases high levels of sex steroids resulting in ovarian enlargement, painful abdominal distension, ascites and pleural effusions with respiratory distress. There is electrolyte imbalance, oliguria haemoconcentration, and hypovolemic shock. OHSS is classified in three groups according to symptomatology: mild, moderate and severe (classification by W.H.O.).

Incidence of OHSS in A.I.H. and I.V.F. (Siddiqua Hospital)

	Mild	Moderate	Severe	Total	%
A.I.H.	15	3	7	146	5.8
I.V.F.	11	5	4	157	7.8

In our experience, induction of ovulation is carried out by injection of HMG 150-350U, HCG 5,000-10,000U. OHSS is commonly found in young women, polycystic ovarian syndrome, and anovulatory patients.

The management depends upon the severity of the syndrome, and includes hospitalization, correction of electrolyte imbalances, and tapping of the pleural cavity.

Careful monitoring of follicular growth by series of ultrasounds, can result in early detection of OHSS. Thus, discontinuation or reduction of gonadotrophin could prevent OHSS.

OBSTETRICS & GYNAECOLOGY

ALTERATIONS IN CELL-MEDIATED IMMUNITY FOLLOWING A SINGLE DOSE OF PLATIN IN PATIENTS WITH OVARIAN CARCINOMA

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The effects of cytotoxic drugs on lymphocyte subsets is still not fully understood¹. We examined the alterations in serum cell-mediated immunity associated with a single dose of platinum therapy. Eight patients with histologically proven epithelial ovarian cancer, 1 stage I disease, 1 stage II and 6 stage III/IV disease were included in the study. The median age was 50 yrs (range 50-75). All patients were platinum naive and not receiving any steroid therapy. Fasting venous blood samples (10mls heparinised) were obtained the mornings pre and post therapy. Analysis of T helper [Th], T suppressor/cytotoxic [Ts], total T cells and natural killer [NK] cells, was performed using monoclonal antibodies [Coulter] on a Coulter Profile II flow cytometer. Response was assessed according to UICC criteria. Four (50%) of patients responded, [1 complete and 3 partial responses]. There was disease progression or non response in 3 patients and response was not assessable in one patient. All patients showed a reduction in total T cells and Th cells. Six patients had a reduction in Ts cell. NK cell counts remained unaltered or reduced in 6 and rose in 2 patients. In those patients who responded to treatment the mean Th/Ts ratio rose from 1.4 [SE 0.22] to 1.87 [SE0.37], whereas in those who did not respond, a fall in Th/Ts from 1.21 [SE 0.08] to 0.93 [SE 0.04] was noted. This pilot study is the first report on such early immune changes following platinum therapy which, amongst other aspects, may have prognostic implications. Recruitment of patients to the study continues.

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FOETAL PROGRESS AND ONSET OF PARTURITION MONITORED BY PLASMA OESTROGEN LEVELS IN THE COW

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Total (conjugated and unconjugated) oestrogen (E) levels rise gradually throughout gestation, a fact well documented by urinary E assays in mammals. This bovine research review encompasses details obtained from the radioimmunoassay (RIA) of total and free (unconjugated) plasma E throughout gestation in cows (Friesians, $n=30$) in successive pregnancies. The designs of these 3 studies evolved as knowledge advanced from successive gestations. The total and free E were assayed (RIA) to investigate, (1) levels of E at monthly intervals as gestation progressed to term, (2) influences of twin- and single-bearers on the monthly E levels until delivery (c. day 280) and (3) daily E assays in latter gestation to detect any signals for parturition (E levels are expressed as ng oestrogen/ml plasma, mean sem). Primarily, in the pregnant cow total E rose (3.6 ± 0.6 to 11.3 ± 1.1) between days 130 and 250 while free E remained low (c. 0.3 ng/ml). A 3-fold and 10-fold

rise was noted in total and free E levels, respectively, in the last month. Secondly, the most significant ($P < 0.001$) rise between twin- (9.8 ± 0.03) and single- (5 ± 0.4) bearing cows was at mid-gestation (c. day 150). Thirdly, and finally, a significant ($P < 0.001$, $r = 0.83$, $n = 13$) correlation was noted between the day on which free E reached 2.0 ng/ml of plasma and the actual day (length of gestation from mating or AI) of parturition.

EFFECT OF ORAL CONTRACEPTIVES ON PLATELET AGGRAVATION

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Oral contraceptives increase the risk of thromboembolic complications in high risk women. This increased risk may be mediated by changes in the haemostatic system which are dependent on both the progestogen and the dose of oestrogen. Whole blood platelet aggregation was measured serially in 45 women randomly assigned to one of three different preparations.

Marviol® (30 ug ethinlyoestradiol (EE) 150 ug deogestrel (DES) Mercilon® (20 ug EE/150 DES) or Femodene® (30 ug EE/75 ug gestodene). Blood was taken before treatment and at 6, 12 and 24 weeks on treatment and at 6 weeks following treatment.

Platelet aggregation in response to collagen was increased significantly in women taking Mercilon and Femodene ($P < 0.03$; $P < 0.05$). Arachidonic acid (AA) induced aggregation was also increased in the Mercilon and Femodene groups ($P < 0.02$; $P < 0.03$). In the Marviol group, an increase in both collagen and AA induced aggregation was observed which was not significant ($P < 0.07$). ADP induced aggregation was increased following treatment with all three oral contraceptives; these changes were not significant. Oral contraceptive treatment did not alter adrenalin or PAF induced aggregation.

No significant differences in platelet aggregation was observed between the three different pill groups.

The results of this study indicate that oral contraceptive use is associated with an increase in whole blood platelet aggregation particularly in response to collagen and AA. This increase may be mediated by an increase in pro-aggregatory thromboxane A_2 . The dose of oestrogen, 30 ug or 20 ug and the type of progesterone did not significantly influence the levels of platelet aggregation found.

OBSTETRICS & GYNAECOLOGY/PAEDIATRICS

RELATIONSHIP OF MENSTRUAL BLOOD LOSS TO HISTAMINE AND MAST CELL CONCENTRATIONS IN THE UTERINE TISSUE

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We have studied if uterine tissue histamine and mast cell concentrations in women with normal menstruation are different from those suffering from dysfunctional uterine bleeding (DUB). Following recruitment and menstrual blood loss (MBL) estimations, the subjects were divided into two groups. Those with endocrine disorders or uterine pathology were excluded. Subjects with blood loss over 80 ml were grouped as DUB subjects, others were considered normal. Hysterectomies were carried out in the

menstrual phase of the menstrual cycle and samples of uterine tissue were estimated for histamine and mast cell numbers. The results of 18 subjects in the DUB and 12 in the normal group are given as mean \pm SEM. Women with DUB had MBL of 228.75 ± 52.83 ml and endometrial tissue histamine (ETH) value of 2.76 ± 0.39 μ g/g compared with MBL of 34.25 ± 3.31 ml and ETH value of 6.19 ± 1.77 μ g/g in the normal group ($p < 0.01$ and < 0.05 respectively). Mast cell count (mm^2) in the myometrium of women with DUB was 59.08 ± 11.76 compared with 91.53 ± 22.17 in the control group. Because of the irregular distribution of mast cells in uterine tissue, the difference is however not significant. These results suggest that DUB is associated with mast cell degranulation and/or destruction but its significance is not yet clear.

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RENAL MACROSOMIA IN THE INFANTS OF DIABETIC MOTHERS

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Sixteen infants (gestational age 33-38 weeks) born to diabetic mothers had ultrasound kidney measurements during the first week of life. The measurements were kidney length (KL) and transverse diameter (TSVD) at right angles to the renal pelvis. Body measurements included birthweight, bodyweight, and midarm circumference (MAC). Ponderal Index (PI) was calculated from the formula $PI = (\text{Birthweight (g)}/\text{Bodylength (cm)}^3) \times 100$. All mothers had at least two blood sugar profiles during pregnancy (range 2-28, mean 11). The mean for each of the profile times (fasting, 1030, 1530, 2030, 2330h) for each mother was calculated. Pearson correlation was performed between kidney measurements and a) body measurements and b) mean maternal profile blood sugar. Kidney measurements were compared to these from a normal population. Mean KL was 45.6 mm compared to 42.4 mm for full term infants, with TSVD 23.5 mm compared to 22.8. TSVD correlated very highly with MAC and PI ($r = 0.67$ and 0.81 respectively). TSVD also showed a significant relationship to most of the maternal mean blood sugar profile values: r values for left TSVD for each of the profile times were 0.42, 0.59*, 0.48*, 0.46, 0.48* (* $p < 0.05$). It is speculated that these relationships are related to adipose tissue.

PAEDIATRICS

CONTINUAL VERSUS CONVENTIONAL ASSESSMENT

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Clinical paediatrics is usually assessed by a written paper and a conventional clinical exam in the final year. These methods of assessment focus on "simple recall of information" and the testing of clinical skills by a method that lacks objectivity, thus failing to "meet the most important... educational function, namely that of providing feedback to learners". Continual assessment requires time-consuming effort. If it correlated well with the time-honoured methods of assessment it would be a more useful tool, since it can provide feedback. The purpose of this paper is to

see whether the continual assessment score allocated at the time of the paediatric clinical attachment accurately predicted how the student would do in the final paediatric examination.

In our department, 30% of the final paediatric examination marks are allotted to continual assessment during the 2 month clinical attachment. An assessment score is allocated using 3 different parameters: 1. a monthly assessment mark, based on performance at clinical tutorials; 2. a clinical exam at the end of each month (using both conventional exam and an OSCE); 3. completion of a case report and a project done during the attachment.

Over the past 5 years 43% of those with a poor assessment score failed the final paediatric exam, and 57% passed, while 1% of those with a high score failed, 73% passed and 26% got honours ($p < 0.001$).

This study confirms that continual assessment score accurately predicts the results of the final examination.

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INBORN ERRORS OF METABOLISM (IEM) AS A CAUSE OF ACUTE ENCEPHALOPATHY IN CHILDHOOD 1979-91

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Childhood encephalopathy is a devastating illness. The cause is often obscure. Our aim was to study patients with Reye's and related syndromes for IEM using inter alia the technique of gas chromatography - mass spectrometry (GC-MS) on urine. 1:1:79-31:12:86 - 57 patients (median age 0.75 yr) met British Reye's Syndrome Surveillance Scheme (BRSSS) criteria. Of 50 survivors, 40 were studied retrospectively (1987-89). No case has yet been proven to have an IEM. Two of the original 57 may have an IEM, in one possibly a mitochondrial long chain fatty acid beta-oxidation defect (LCD). 1:1:87-31:12:88 - Among 15 patients who did not meet BRSSS criteria, 2 have a proven IEM - 1 medium chain acyl CoA dehydrogenase (MCAD) deficiency, and 1 ethylmalonic-adipic aciduria; 1 other likely had an LCD. 1:1:89-30:11:91 - Among 19 patients with a similar Reye-like illness, 6 have a proven IEM - 3 MCAD deficiency, 1 long chain 3 hydroxy acyl CoA dehydrogenase deficiency, 1 glutaric aciduria-type I, 1 vit. B₁₂ responsive methylmalonic aciduria and one child with a presumed ketolytic defect.

In conclusion - No RS patient has yet been shown to have an IEM. Since 1988 these are being increasingly recognised in patients presenting with a Reye-like encephalopathy as a result of improved diagnostic technology using GC-MS.

A NEONATAL HEARING SCREENER

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Neonatal hearing screening has not been possible because of the lack of a short, cheap, credible and robust test. Many techniques have been devised to test neonatal hearing, but none has proved convenient and efficient for mass screening.

The Algo-1 Plus Infant Hearing Screener (Natus Medical Inc., Foster City, California) represents a new advance. The screener emits 35 DB clicks, which pass via two acoustic tubes bar couplers enclosing each pinna. Three surface electrodes detect the Infant's Auditory Brainstem Response which is compared to the internal ABR algorithm.

Since December 1990, we have screened 197 neonates in our Intensive Care Unit. Testing, including electrode and coupler application and screener operation, takes an average of 30 minutes per infant. One hundred and ten infants (55.8%) were high risk for hearing deficits and nine (8.2%) of these failed the screening test. Four infants (4.6%) from the low risk group also failed.

In summary, this new screener is a promising system for testing newborn infants' hearing and represents an advance in this area.

A REVIEW OF PATIENT DUCT LIGATION OF THE PREMATURE INFANT IN INTENSIVE CARE

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From Jan. 1, 1984, we have pursued a policy of patent duct ligation in the premature infant in intensive care using the Ohio Neonatal Nursing Unit, because of the occurrence of dangerous hypothermia when operation is performed in the standard operation room. Twenty-six infants were operated upon; all were transferred from maternity units country wide to the ITU within 24 hours of the appointed surgical time. Twenty-three patients were ventilator dependent. The diagnosis was confirmed on admission by a paediatric cardiologist and 2D echocardiography. Surgical ligation was performed through a standard lateral thoracotomy; the infant remaining in his Ohio Neonatal Nursing Unit. Average gestation age at birth was 29 weeks, (24-33 wks). Mean age at surgery was 25 days. Operative weight ranged from 650-2,400 gs (mean 1400 gs). The duct was ligated using a simple suture ligation technique with a ligaclip applied to the pulmonary side of the duct. Chest drainage was not routinely used. Complete temperature data was available on 22 patients (85%). The mean change in core temperature was noted to be in elevation of $0.16^{\circ}\text{C} \pm 1.1$. In 14 cases, the temperature fell but only in two was this greater than 1°C . No operative or peri-operative mortality occurred. Post-operatively patients were returned to the maternity unit when stable. 70% were transferred within 3 days. Twelve (46%) were treated as day cases. No wound sepsis occurred. Patient duct ligation can be performed safely and effectively in the Ohio Neonatal Nursing Unit reducing the incidence of hypothermia significantly.

AMYOTROPHIC LATERAL SCLEROSIS AND THE ISLAND OF GUAM - AETIOLOGICAL SIGNIFICANCE FOR CALPAIN 1?

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Environmental calcium deficiency with aluminium excess is virtually the only common factor shared by Western Pacific foci with a high incidence of amyotrophic lateral sclerosis (ALS). An experimental review was carried out to investigate this phenomenon.

It was found that a recently discovered regulatory calcium dependent protease - Calpain 1 (CL 1) - was localized predominantly to the neural regions characteristically affected in ALS. CL 1 inhibition by calcium deprivation induces characteristic neuronal accumulations of 10nm neurofilament (NF), the key feature described by Hirano in his classic neuropathological study of ALS². Aluminium toxicity also forms protease resistant NFs, promoting accumulation.

Thus calcium deficiency with aluminium excess (as found in water supplies to Western Pacific ALS foci) may induce ALS changes by causing CL 1 dysfunction and NF accumulation. Migration to Guam increases ALS rates but these have receded with improved water supplies. Primates on low calcium/high aluminium diets develop ALS in Western Pacific foci.

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PUBLIC HEALTH MEDICINE/EPIDEMIOLOGY IS A THREE DRUG REGIMEN THE BEST TREATMENT FOR TUBERCULOSIS?

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We present the data on 218 consecutive patients with TB treated with Rifater (combination RHZ) and who have been followed for up to 2 years post completion of treatment. Comparison with previous series (IMJ, 1989; 82: 11-13) shows: that patients had fewer visible cavities on X-ray ($p=0.0004$); more patients negative direct/positive culture ($p=0.02$); no difference in terms of radiological extent of disease, pleural effusion, extrapulmonary TB, drug toxicity, mortality, other reasons for withdrawal from therapy. More patients are consistently culture negative when treated with Rifater at one month and two months compared to the other regimens - RHEZ x 6 months, RHE x 9 months.

Relapse rate: To date of the 98 patients who have completed treatment 39 have one year or more post treatment follow-up. Two patients have relapsed with fully sensitive TB. Both patients, one HIV positive, admit non-compliance with treatment.

Conclusion: The 3 drug regimen of Rifampicin, Isoniazid, Pyrazinamide (Rifater) produces significantly faster consistent sputum culture conversion than other regimens. These results support a policy of ongoing treatment with Rifampicin, Isoniazid, Pyrazinamide without Ethambutol or Streptomycin in the management of TB.

EPIDEMIOLOGY CHARACTERISTICS OF NIDDM IN IRELAND - A STUDY OF 501 NEWLY DIAGNOSED CASES

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This study presents the first profile of NIDDM in Ireland. The objective was to focus attention upon NIDDM as a possible health problem in Ireland. Five hundred and one cases (233 male, 268 female) presented to our clinic over five years (Jan. 1 1980 - Dec. 31 1984). Incidence in females increased progressively with age but in males peaked at 50-59 years and declined significantly thereafter. 72% males vs 47% females were younger than 60 years. These differences do not reflect Irish population charac-

teristics. 70% had classical onset. Seasonality was not observed. 30% had a diabetic first degree relative. 70% were overweight or obese. Females had significantly higher BMI than males (28.9 ± 6.9 vs 27.6 ± 4.7 , $p<0.02$). Obesity was twice as common as in Irish non-diabetics. 62% were treated with diet alone. Insulin treatment (14%) reflected younger age ($p<0.001$) and lower BMI ($p=0.024$). 32% were on antihypertensives. Treated hypertension was associated with ageing (61.8 ± 11.8 vs 54.7 ± 12.8 yrs, $p<0.001$) higher BMI (30.2 ± 6.4 vs 27.4 ± 5.6 , $p<0.001$) and macrovascular disease (RR 2.14). 7.2% had retinopathy and 23% macrovascular disease and/or peripheral neuropathy. Multiple regression models revealed that age was the most significant predictor variable for complications ($p<0.001$). NIDDM in Ireland affects middle-aged males and elderly females. Aetiology may differ with gender and age. Obesity, hypertension and heredity may be risk factors. Further population-based studies are indicated to define risk factors and institute intervention policies.

MORBIDITY AND MORTALITY ASSOCIATED WITH DIABETES MELLITUS (DM) IN IRELAND - A STUDY OF 584 CASES AT 20-25 YEARS DM

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The objective of this study was to investigate and report morbidity and mortality in Irish diabetics with long duration DM. Five hundred and eighty-four cases (254 males, 330 females) comprise a complete cohort diagnosed diabetic between 1960-1964 (inclus.). At 20-25 years DM 183 attended regularly, 156 had defaulted and 245 were deceased. 76% females, 69% males aged 30-50 years at diagnosis survived 20 diabetes years compared with 91.4% IDDM cases ($n=147$). Clinic attenders were examined for complications in 1985. Nephropathy (DN) was uncommon, even in IDDM (13% including deceased), and was associated with male gender (22.5% vs 6.2% females). 70% cases had some retinopathy (DR). 20% had proliferative DR. Significant DR related to higher systolic blood pressure in IDDM cases without DN (134.5 ± 14.8 vs 125.0 ± 13.8 mmHg, $p<0.001$). 40% had neuropathy and prevalence of neuropathy increased with age. Macrovascular disease (MVD) in survivors was associated with male gender (24.3% vs 11.9% females). MVD accounted for 66% deaths. 56% males vs 41% females died from cardiovascular disease. Diabetes related causes accounted for 40% IDDM deaths. This study is the first audit of diabetes morbidity and mortality in Ireland, but reflects experience at a specialist centre. It reports results which can be utilised to define targets towards improving health and the life expectancy of Irish diabetics. Diabetes associated MVD is identified as a problem which requires urgent national attention.

REGIONAL DIETARY IODINE INTAKE IN IRELAND

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As no contemporary data was available on iodine status in Ireland, this study was established with a view to providing regional information on dietary iodine intake. Casual urine samples were obtained in a representative group from five different counties

in Ireland, namely Dublin, Cork, Galway, Meath and Tipperary. Iodine levels were measured in urine specimens using the alkaline ashing technique. Mean urinary iodine excretion values \pm SE varied from a high of $125.4 \pm 11.4 \mu\text{g}$ in Tipperary to a low of $73.4 \pm 4.3 \mu\text{g}$ in Galway. Mean values for Cork, Dublin and Meath were $88.2 \pm 5.9 \mu\text{g}$, $97.2 \pm 1.8 \mu\text{g}$ and $90.6 \pm 6.3 \mu\text{g}$ respectively. At low levels of iodine excretion, i.e. less than or equal to $50 \mu\text{g}$, approximately one fifth of subjects fell into this category in all counties. At the other end of the scale, i.e. values greater than or equal to $150 \mu\text{g}$ (minimum level recommended by the WHO) the percentage of subjects in this category showed a wide variation between groups, with percentages varying from 4.1% to 25.3%. The relatively high percentage of elevated values in Tipperary (25.3%) presumably reflects an increase in dietary iodine intake due to the local practice of using iodized salt. The results, while excluding severe iodine deficiency in the study population obscure the fact that 21.6% had iodine excretion values less than or equal to $50 \mu\text{g}$, consistent with iodine deficiency, reflecting the lack of iodine supplementation. The absence of significant regional variation in the study population can be attributed to the homogeneity of the Irish diet.

A RETROSPECTIVE STUDY OF CHRONIC FATIGUE SYNDROME

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To establish some epidemiological features of chronic fatigue syndrome, questionnaires were sent to patients fulfilling the diagnostic criteria. Two hundred and ninety-one (74%) were returned detailing patient characteristics, course of illness and current health status. The mean age at onset was 33 years (range 5-76 years) with an overall female : male ratio of 2:1. The sex ratio varied with age; in patients under 20 years old the ratio was 1:1 compared with 2.6:1 and 1.7:1 in the 20-39 and over 40 years age groups respectively ($p=0.019$). Patients had been ill for on average 5.22 years (range 6 months - 26 years) and although tending to have frequent relapses most felt that they were improving. Fifty-four (18.6%) patients reported they had recovered, with younger patients (<20 years) having a significantly higher recovery rate of 40.5% ($p=0.001$). The average duration of illness was 2.9 years. We believe this to be the first population study of patients with chronic fatigue syndrome attending a regional referral centre using strict diagnostic criteria and helps establish the pattern of illness and prospects for recovery.

A GEOGRAPHICAL DISTRIBUTION OF MORTALITY AND DEPRIVATION

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Because of paucity of data on the geographical distribution of mortality and deprivation in the Republic of Ireland, SMR's for each county for the years 1982-1986 were calculated. Two measures of mortality were used, all cause mortality (ACM) and avoidable mortality (AM). Two indexes of deprivation were also calculated for each county, Townsend's and a new Irish index. Counties that had SMR's significantly below the national standard of 100 were Meath (ACM - 90, AM - 91), Donegal (ACM - 90, AM - 87) and Galway (ACM - 92, AM - 88). Counties with sig-

nificantly high SMR's were Louth (ACM - 112, AM - 121), Limerick (ACM - 113, AM - 113) and Westmeath (ACM - 113, AM - 112). Counties with the greatest deprivation were Donegal, Louth, Offaly and Dublin and the least deprived counties were Roscommon, Meath, Cavan and Leitrim. County SMR's were correlated with both deprivation indexes and no significant correlation was found to explain the apparent differences in mortality. This is in contrast to that found elsewhere.

CAMPYLOBACTER SURVEILLANCE IN DUBLIN

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A cooperative effort between Microbiologists and Public Health doctors has resulted in a new population based surveillance system, on certain infectious diseases, called the laboratory surveillance system (L.S.S.). It is the purpose of this paper to outline the first results of population based surveillance of campylobacter in Dublin in 1991.

Nine laboratories in Dublin, including all major enteric laboratories reported to L.S.S. in 1991. Campylobacter was routinely looked for in all the labs. Reports of those resident in Dublin were included in the analysis.

Eighty six isolates of campylobacter were reported in 1991 giving a rate of 8.4 per 100,000. A bimodal age trend, male excess and an increase in the summer months was noted. Campylobacter was reported less often than Rota virus, Salmonella or Shigella. The following factors were noted:- the presence of a second pathogen (5), foreign travel (3) and immunosuppression (3).

Campylobacter infection appears a small problem in Dublin compared with other enteric pathogens and experience in other countries. Yet the epidemiological pattern is similar to that of other developed countries. Ongoing surveillance, preferably throughout Ireland, is required to establish the exact nature and extent of this public health problem.

A HEALTH STATUS PROFILE OF NORTH-WEST DISTRICT OF CORK CITY

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There is a general perception that the North-West District of Cork City (pop. 33,325) is disadvantaged. A stratified random sample of 581 of the 8580 households in the district was interviewed to determine its health status. A quarter of respondents rated their own health as fair/poor. A very high level of contact between respondents and the Health Services was noted. 87% visited their G.P. and 25% used hospital emergency facilities at least once in the previous year. The majority (83%) of respondents expect to receive a prescription from a G.P. visit. Two-thirds of respondents take prescribed and 50% take non-prescribed medication routinely. 46% of respondents were smokers and of these 60% smoked more than 10 a day. The rate of combined drinking and smoking is almost double (43%) among the under 26 group compared with over 66 group.

Less than 5% used alternative forms of medicine. The most common perceived problems recorded by the respondents were "back trouble" (27%), "migraine" (26%), "arthritis" (23%), "hypertension" (17%) and "digestive disorders" (15%).

A Health for all strategy¹ for this area was devised using targets for action based on the study results.

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AN OUTBREAK OF MENINGOCOCCAL DISEASE IN CORK, 1991

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In 1991 38 cases of meningococcal disease were notified in the Cork Community Care Area. This compared with an average of 7 notifications per year for the previous 3 years. A review of all 1991 notifications was carried out in this area (population 289,501).

Twenty five (66%) of the 38 notifications were clinical diagnoses only. Thirteen (34%) were bacteriologically proven, giving an incidence of proven disease of 4.49 per 100,000 population. The serogrouping of isolates showed the following distribution: group B 7 (54%), group C 5 (38%), ungrouped 1 (8%). The peak incidence was in April. Two deaths occurred. The age range was 3 months to 36 years, with the greatest number of cases in the 0-4 and 15-19 year age group.

There has been a steady increase in meningococcal disease in England and Wales since 1984 and in 1990 the regional incidence varied from 1.5 to 4.5 per 100,000 population¹. The increase in Cork in 1991 to a level of 4.49/100,000 is similar to the highest regional incidence in England and Wales. It is not possible to predict if this high incidence will continue.

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IN CHILDHOOD ASTHMA DOES SMALL AIRWAYS DYSFUNCTION (SAD) RESPOND TO THERAPY?

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Using the maximum expiratory flow volume curve (MEFVC) and 3 gas mixtures (oxygen:helium & oxygen: sulfurhexafluoride & oxygen) we detected evidence of small airways dysfunction (SAD) in childhood asthma. The most sensitive test of SAD is V 50% light gas/heavy gas. We set out to determine if SAD was reversible

Results: 40 children with childhood asthma and SAD were studied. Each child did not take part in each limb of the study.

Drug	No. studied	No. improved
Salbutamol	10	2
Ipratropium	9	3
Theophylline	10	1
Intal	10	5
Inhaled steroids	10	2
Oral steroids	10	3
Ketotifen	14	5

Some children responded to more than one therapeutic agent. Conclusions: Liability of SAD varies from children who respond to several agents to those who respond poorly or not at all.

Response is not predictable. SAD may be a fixed irreversible phenomenon. All children were on Salbutamol by inhalation prior to entry into the study so the possibility exists that any reversibility may have already occurred.

SOCIAL CLASS DIFFERENCES IN CHRONIC DISEASE MORBIDITY IN DUBLIN

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The aim of this study was to determine if there was a social class gradient in the prevalence of chronic medical conditions in middle aged persons in Dublin.

The one year period prevalence rate of 12 chronic conditions: coronary heart disease, stroke, chronic bronchitis, cancer, and treated cases of hypertension, diabetes, asthma, dyspepsia, rheumatic disorders, depression, anxiety disorders, and psychoses, was recorded prospectively in 3,111 persons attending 3 large general practices. A community based study of 1,024 persons was conducted to assess several potential biases. 95% confidence intervals were calculated to compare age/sex standardised morbidity rates between social classes. Persons from social classes 3/4 and 5/6 had a 21% and 70% excess morbidity, respectively. Persons from social classes 5/6 had significant excess of all conditions except asthma and cancer.

Social class differences in morbidity in Dublin mirror published social class mortality differentials in Britain.

MEDICAL AUDIT IN A REGIONAL TEACHING HOSPITAL

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In March 1990 a regular monthly medical audit was commenced at University College Hospital, Galway. We evaluated the experience of one year's audit of medical inpatients. Ten case notes with a specific discharge diagnosis were reviewed according to a defined protocol. All seven physicians were included. The protocol consisted of a detailed questionnaire with yes or no answers covering admission, documentation, investigation and treatment. We evaluated the impact of medical audit by comparing the initial three months with the last three months of the year. Overall attendance was poor for both consultants and N.C.H.D.S. Significant improvement was noted in a limited number of areas (i.e. documentation). Deficiencies in management and recording of patient data were noted and recommendations to improve these have been agreed. With a part time audit assistant we are expanding the audit and expect it to have major impact on hospital care in the future.

ANAESTHESIOLOGY/CRITICAL CARE

PENTOXIFYLLINE AND SURVIVAL FOLLOWING HAEMORRHAGIC SHOCK

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Pentoxifylline (PTF), has been shown to improve survival from

haemorrhagic shock in rats¹. We studied the effect of PTF in a canine model of haemorrhagic shock. Shock was induced in 10 anaesthetised dogs. The animals were bled to a mean arterial pressure of 30 mmHg. This pressure was maintained for 4 hours or until 20% of the shed blood was retransfused (Wigger's model). The animals were allocated to one of 2 groups. The treatment group received PTF 25 mg/kg, (n=5), 30 min. after induction of shock. The control group (n=5) were given normal saline. Arterial pressure, heart rate, and cardiac output were measured at 30 min. intervals. The animals were observed for 24 hours.

Haemodynamic parameters were similar in both groups before and during the shock period. All the PTF animals survived for 24 hours. One of the controls died during shock, the others survived for 1½, 2¼, 7, and 24 hours respectively. PTF significantly improved survival from haemorrhagic shock (p<0.05, log rank test). The mechanism of action is unclear but may involve improved microcirculatory flow, decreased adhesiveness of activated PMN's, and TNF inhibition.

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THE INFLUENCE OF INTRAVENOUS COMPOUND SODIUM LACTATE ON SERUM LACTATE LEVELS DURING MINOR SURGERY

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Blood lactate levels reflect the adequacy of cellular oxygenation. Elevated blood lactate has been demonstrated in the peri-operative period in major surgical patients^{1,2}. The aim of this study was to ascertain whether a lactaemia occurs during minor surgery and to determine whether exogenous lactate administration, in the form of compound sodium lactate, contributes to a rise in blood lactate.

Patients and methods: Eighteen patients (ASA 1 & 2) presenting for minor surgery were randomly allocated to receive normal saline, (NS) (N=8), 20 ml/kg or compound sodium lactate (RL) (N=10) 20 ml/kg intravenously over 36 minutes. Serum lactate was measured before commencement of infusion and serially over 60 minutes (Fig. 1). Statistics: Student's t-test.

Results: Figure 1 demonstrates lactate levels. There was no significant rise in blood lactate in either the RL or the control group and there was no significant difference between the two groups.

Conclusion: The data demonstrate that peri-operative lactate administration in the form of compound sodium lactate does not elevate blood lactate levels. Further it suggests that tissue oxygen deficit is not a feature of minor surgery

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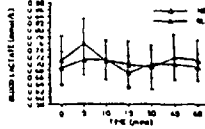


Fig. 1

INTRA-ARTICULAR MORPHINE FOR PAIN RELIEF AFTER ARTHROSCOPIC KNEE SURGERY

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A randomised double blind study was conducted in patients undergoing elective knee arthroscopy, to assess the effect of intra-articular morphine on post-operative pain relief. The plasma profiles for morphine and its metabolites were assayed to determine the level of systemic uptake of morphine to rule out systemic absorption as the mechanism of analgesia. Patients in the study group (n=10) received 5 mg morphine in 25 mls dilution intra-articularly, while those in the control group (n=10) received 25 mls saline.

Patients in the study group showed significantly lower pain scores than those in the control group. These pain scores complemented the lower requirements of systemic analgesics in the study group. The plasma morphine levels exhibited were markedly lower than generally accepted as necessary for a systemic analgesic effect. The study provides evidence to suggest that the analgesia obtained is mediated via a local action within the knee joint.

TRANSFUSION THERAPY IN ELECTIVE TOTAL HIP ARTHROSCOPY

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A retrospective study of transfusion practice in 150 consecutive elective primary total hip arthroplasties was undertaken, to examine blood usage and to determine the potential for reduction in its use.

Predetermined criteria were used to measure unnecessary transfusions. Transfusion was considered unnecessary if the discharge haematocrit exceeded 36%, or if patients who lost less than 30% of their estimated blood volume, were transfused. Using these criteria, overtransfusion occurred in 42-45% patients.

The intra-operative blood transfused correlated well with intra-operative blood lost. All other variables showed no significant correlation with both intra-operative and post-operative blood transfused. Females lost less and were transfused significantly more than males.

The study corroborates previous reports of blood overuse. These results suggest that adopting standard of practice to measure and to monitor transfusion practice (quality assurance programmes) would be a worthwhile objective.

EFFECTS OF LOW DOSE DOPAMINE AND DOPEXAMINE ON RENAL FUNCTION DURING C/P BYPASS

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Dopamine protects against renal dysfunction in major surgery. Dopexamine, a dopamine analogue, has 60-fold beta 2 activity and may bestow enhanced renal protection¹. This study compared renal effects of prophylactic dopamine and dopexamine infusions

during cardiopulmonary bypass (CPB), a fixed cardiac output state. Patients (n=19) for coronary artery bypass surgery were randomly assigned to one of three groups, receiving assigned N-saline, dopamine or dopexamine (2 ug/kg/min) after induction. Measured during CPB were MAP, CVP, temperature ABG, serum and urinary catecholamines, urinary excretion of sodium, creatinine clearance and urine output. Statistical analysis was by Student t-test.

Creatinine clearance was greater ($p<0.05$) in the dopexamine group than in the dopamine or control groups. Sodium excretion and urine flow were similar in the dopamine and dopexamine groups.

Dopexamine had a superior effect on renal function (i.e. increased creatinine clearance), probably beta 2 receptor mediated.

Reference

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"METABOLIC ALKALOSIS AND RESPIRATORY DEPRESSION" - ITS TREATMENT WITH ACETAZOLAMIDE

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Metabolic alkalosis has an associated morbidity and mortality (by A.P.A.C.H.E. Scale) in I.T.U. patients.

Two patients presented with severe C.C.F. (N.Y.H.A.IV) because of mitral disease for valve replacement. Both patients demonstrated severe pulmonary artery hypertension (PAP 70/40, 60/35) at catheterisation. Attempts to wean ventilation resulted in several episodes of L.V.F. and dyspnoea in both patients. Both were concurrently alkalotic at the time of attempted weaning. PH (7.46-7.54). A compensatory increase in PCO_2 (7.9kPa) occurred at this time.

Acetazolamide, a carbonic anhydrase inhibitor was used to treat the metabolic alkalosis, reduce the base excess and normalise PCO_2 . We postulate that elevated PCO_2 values in these patients aggravated pulmonary hypertension causing interventricular shift, reducing cardiac output and compromising weaning from ventilation. In both cases treatment with acetazolamide and reduction in PCO_2 facilitated ventricular weaning and we recommend it for treatment of metabolic alkalosis in this group of patients.

CONTRIBUTION OF RAISED INTRA-ABDOMINAL PRESSURE (I.A.P.) TO OLIGURIC RENAL FAILURE

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Two post-operative patients developed oliguric renal failure which did not respond to standard therapy such as optimization of haemodynamic variables or low dose dopamine. Both patients had undergone laparoscopy for emergency bowel surgery and required further laparotomies for deteriorating conditions. Bladder pressures were used as a measure of I.A.P. and findings pre and post laparotomy are shown in Table I.

Patient	IAP Pre Decompression	IAP Post Decompression	Duration of Oliguria before Decompression
A	41	20	4 hrs
B	50	12	12 hrs

The renal function of patient A who had 3 litres of haematoma evacuated recovered completely. Patient B who had 3 litres bowel secretions evacuated had an initial improvement in renal function which deteriorated. These cases highlight: (1) the contribution of raised I.A.P. to oliguric renal failure. (2) That this component is not responsive to manipulation of perfusion pressure because of elevated renal vascular resistance. (3) The importance of early detection of raised I.A.P. (4) That this can be done simply and non-invasively using a Foley Catheter. We suggest therefore that patients with impairment of renal function should have measurements of I.A.P. as part of routine monitoring. Rising I.A.P. should be used as a criterium for re-exploration.

HIGH FREQUENCY JET VENTILATION VIA MINITRACHEOSTOMY: AN AID TO WEANING

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Introduction: Minitracheostomy has been established for the management of sputum retention. High Frequency Jet Ventilation (HFJV) compared to conventional ventilation has been shown to result in similar arterial oxygenation, adequate alveolar ventilation, unchanged or lower mean airway pressure without high peak inspiratory pressure¹ and unchanged haemodynamic function².

Patients and methods: In a general intensive care unit seven patients with marginal respiratory reserve who had minitracheostomies were weaned using HFJV. Ventilatory management initially consisted of a respiratory rate of 50-100 bpm, I:E ratio; 1:2 driving pressure 1-2 bar. HFJV was continued intermittently after extubation and spontaneous respiration was allowed as long as pH remained 7.35-7.45.

Results: Six patients were weaned and extubated. Arterial oxygenation and alveolar ventilation were found to be adequate in all patients.

Conclusion: In patients whose respiratory reserve is poor HFJV via minitracheostomy avoids the need for re-intubation if further ventilatory support is required. Advantages include: adequate gas exchange, continued respiratory effort, and facilitated tracheo-bronchial toilet without haemodynamic instability.

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ANAESTHESIOLOGY/CRITICAL CARE/ CARDIOLOGY

LACTIC ACIDOSIS IN THE CRITICALLY ILL

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The aim of this prospective randomised observer blind study was having determined the degree and duration of lactic acidosis

that occurs; to assess the effect of augmenting haemodynamic indices on oxygen delivery (DO₂) and oxygen consumption (VO₂) in the critically ill. Twenty four patients having elective CABG with ejection fraction >50% were randomly assigned to two groups. After induction of anaesthesia, baseline lactate, cardiac index (CI), systemic vascular resistance (SVR) and DO₂/VO₂ were measured. The treatment group received an infusion of Dopexamine at 2 ug/kg/min and the controls received saline. Recordings continued at preset intervals for thirty hours. Lactate rose significantly in both groups (P<0.05) and remained elevated for twenty four hours. However in the group receiving Dopexamine, CI and DO₂/VO₂ were significantly greater (P<0.05) and SVR was significantly lower than in controls (P<0.05) and lactate levels fell more rapidly in this group. This study demonstrates that the significantly augmented VO₂, coupled with the more rapid clearance of lactate were related to the inotropically augmented DO₂. This suggests that prophylactic augmentation of DO₂ by pharmacological manipulation would be a rational therapeutic option in the critically ill patient.

CARDIOLOGY

LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IDENTIFIED BY DOPPLER ECHOCARDIOGRAPHY IN ASYMPTOMATIC ANKYLOSING SPONDYLITIS

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Cardiac involvement in the form of conduction abnormalities or aortic regurgitation occurs clinically in 5-10% of patients (pts) with ankylosing spondylitis (AS). This study assesses the prevalence of subclinical cardiac abnormalities in pts with AS and attempts to correlate these abnormalities with clinical features.

All pts underwent full clinical examination; ECG and 24 hour Holter monitoring; and 2D, M-mode and Doppler echocardiography. An age and sex-matched control group was also studied.

Fifty-five pts (42 males and 13 females; mean age 43.5±10.7 years) were assessed. Mean duration of disease was 18.2±9.0 years (range 1-42 years). Seventeen pts had evidence of non-cardiac extra-articular manifestations. Cardiac examination was normal in all pts.

During echocardiography abnormal left ventricular diastolic function was detected in 12 pts (22%). Prolonged isovolumic relaxation time and reversal of the peak early and late transmitral diastolic flow velocities (E/A ratio) was noted in 10 pts. In 2 pts there was an increased E/A ratio. One case of aortic root dilatation and 1 case of subaortic valve echodensity was seen. Mild aortic regurgitation and mitral regurgitation was seen in 1 and 5 pts respectively. No abnormalities of left atrial size, left ventricular systolic or diastolic dimensions or wall thicknesses were noted. There was a significant correlation between the presence of ventricular diastolic dysfunction and indices of severity of AS (P<0.05) and disease duration >20 years (P<0.01).

Left ventricular diastolic dysfunction occurs frequently in AS pts in the absence of clinical cardiac involvement. The presence of diastolic dysfunction occurs more frequently in pts with longer disease duration and more restricted spinal movements. Further follow-up will show whether these abnormalities contribute to the long-term morbidity of this condition.

QUANTITATION OF AORTIC STENOSIS: COMPARISON OF TRANSOESOPHAGEAL ECHOCARDIOGRAPHY WITH CARDIAC CATHETERISATION

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The assessment of aortic valve disease by standard transthoracic echocardiography is hindered by technical difficulties resulting in inadequate views or inaccurate doppler signals in a significant number of patients. Transoesophageal echocardiography (TOE) allows enhanced echocardiographic views of the aortic valve in most patients. This study assesses the value of TOE in estimating aortic valve area in patients with aortic stenosis.

Maximal aortic valve area was calculated by planimetry from the short axis view using TOE. Cardiac catheterisation was carried out during the same hospital admission and valve area again calculated using the Gorlin formula.

Sixteen patients (11 males and 5 females; mean age 65±8.4 years) with clinical aortic stenosis were studied. An adequate cross-sectional view of the aortic valve was obtained in 15 patients. Mean (±SD) valve area by TOE was 0.81±0.57 cm² (range 0.30-2.11 cm²) and by the Gorlin formula 0.80±0.48 cm² (range 0.44-1.7 cm²). No significant difference was found between each method of calculation at the 95% confidence level (P=0.48, NS).

We conclude that direct measurement of the aortic valve area can be reliably made by TOE in the majority of patients with aortic stenosis. Results are comparable to those achieved at cardiac catheterisation.

MEASUREMENT OF ANTIBODIES TO STREPTOKINASE BY ENZYME LINKED IMMUNOSORBENT ASSAY (ELISA)

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Intravenous streptokinase is widely used as a thrombolytic therapy for myocardial infarction and has been shown to reduce mortality. Many patients show clinical evidence of a reaction to streptokinase and a neutralising antibody to streptokinase is believed to exist. An Elisa assay has been developed to quantitate the level of antibody. Serum samples were taken from subjects between day 0 and day 15 after administration of streptokinase. Results are expressed as % absorbance of a standard serum known to have a high titre of streptokinase antibodies. The CV around the mid point of the titration curve is 7.1% within day and 14.1% between days. Antibody levels rose from around day 7 (8-40%) to reach levels in the range 100-300% on days 14 or 15 post streptokinase treatment.

If the level of neutralising antibody is known prior to therapy it might influence the dose of streptokinase given or it might lead to an alternative therapy being used.

LEUCOCYTE CYASTATHIONINE B-SYNTHASE ACTIVITY - POTENTIAL AS A SCREENING METHOD FOR HYPERHOMOCYSTEINAEMIA

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Hyperhomocysteinaemia has been implicated in human vascular disease and is currently screened for by a complex methion-

ine loading test. This study set out to measure cystathionine β -synthase (CS) activity in human leucocytes to evaluate its potential as a screening procedure for this condition. Leucocytes, isolated from 20 ml of blood, were cultured in the presence of the mitogen, phytohaemagglutinin for 72 hr prior to homogenisation and incubation with buffered homocysteine and [14 C]-serine. The conversion (%) of [14 C]-serine to [14 C]-cystathionine, following separation by thin-layer chromatography, was used as an index of enzyme activity. In a range of healthy laboratory volunteers (n=10) the mean CS activity (% conversion of [14 C]-serine/mg leucocyte protein) was 12.5%. For 3 children, clinically diagnosed as homozygous homocysteinurics, no activity was detected. In the mother of one of these children, by implication heterozygous for the condition, the CS activity was 4.7% and two adult hyperhomocysteinaemic patients had a mean activity of 7.5%. These data indicate some potential for this assay in screening individuals with homocysteinaemia for a more precise and convenient characterisation of the condition.

SERUM LIPID PEROXIDATION PRODUCTS AND ANTIOXIDANTS IN HOMOCYSTEINAEMIA AND CORONARY HEART DISEASE (CHD)

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In homocysteinaemia, raised serum homocysteine levels may play a role in superoxide production, resulting in increased free radical activity and atherosclerosis. The aim of the present study was to investigate free radical activity (by measuring serum Malondialdehyde (MDA), by the thiobarbituric acid assay), and also antioxidant status (by measuring serum vitamin E and A by HPLC) in CHD patients with homocysteinaemia (n 16, mean age (SD) 44 (4.6) years), CHD patients without homocysteinaemia (n 20, mean age (SD) 47 (4.9) years) and in control subjects without overt disease (n 19, mean age (SD) 45 (6.1) years). There was no difference in antioxidant status between the three groups, however there was some evidence for increased lipid peroxidation in CHD patients without homocysteinaemia, mean serum MDA (SD) 1.7 (0.6) nmol/ml (P<0.05), compared with homocysteinaemics 1.3 (0.38) and controls 1.3 (0.31) nmol/l. These results do not therefore support the hypothesis that free radical activity is implicated in the pathogenesis of CHD in homocysteinaemia, though it may be of importance in CHD of different aetiologies.

THE EFFECT OF HYPOTHERMIA ON OXYGEN FLUX AND LACTATE PRODUCTION

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Cardiopulmonary bypass (CPB) allows us examine the effect of hypothermia in humans. In a controlled prospective randomised study, patients were divided into three groups of 24 patients each and the CPB in each group was managed at a different temperature. Group A: cooled to 25 degrees, Group B to 28 degrees and Group C to 37 degrees. Serum lactate levels were measured and the parameters of oxygen delivery (DO₂), and oxygen consumption (VO₂) were calculated at ten minute intervals during CPB.

The results show that VO₂ was significantly lower in the

hypothermic groups and that while it was possible to significantly increase DO₂ relative to baseline during hypothermic and normothermic CPB, this was not accompanied by a rise in VO₂ at hypothermia. There was no significant difference in lactate production between the groups. This supports the concept of a biphasic relationship between DO₂ and VO₂ and suggests that the "critical DO₂", that is the level of DO₂ at which the VO₂ reaches a maximum, is lower during hypothermia. This physiological relationship would be of importance in the management of oxygen debt in the critically ill.

ATRIAL MYXOMA: FOURTEEN YEAR EXPERIENCE IN ONE UNIT.

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Urgent cardiac surgery is usually recommended for atrial myxoma, although evidence from Ireland and UK to support this approach is lacking. We reviewed all patients admitted to the National Cardiac Surgery Unit with atrial myxoma to assess pre-operative diagnosis and management, surgical technique, and outcome. Twenty three patients were admitted to the Unit since 1977. Pre-operative symptoms were: congestive cardiac failure (10 patients), embolism (8 patients), constitutional (3 patients), tachyarrhythmia (1 patient) and asymptomatic (1 patient). The diagnosis was confirmed by D₂ echocardiography alone in eleven patients and by a combination of echo and angiography in twelve patients. Magnetic resonance imaging was used in one patient. One patient collapsed on induction of anaesthesia. At operation the site of the tumour was left atrial in 22 patients, with one patient having an extensive bi-atrial tumour. In all cases the tumour was examined histologically. All patients made a good post-operative recovery, although one patient developed a DVT. One patient died five months post-op with a CVA. Serial echocardiography has revealed one recurrence to date (8 years post-op); the original tumour was an extensive bi-atrial tumour in a 24 year old girl. Re-operation was successful. Although benign, atrial myxomas require both urgent surgery due to their potentially serious sequelae, and diligent long term follow-up to detect recurrence.

NON-INVASIVE AV SEQUENTIAL PACING USING A NEW HEXAPOLAR GASTRO-OESOPHAGEAL ELECTRODE IN PATIENTS WITH BRADYARRHYTHMIAS

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Transcutaneous non-invasive cardiac stimulation has inherent disadvantages: low success, high current requirements, lack of atrioventricular (AV) sequential pacing capability, and poor patient tolerance. We have developed a new hexapolar gastro-oesophageal (GO) electrode which allows separate atrial, ventricular and AV sequential pacing. The electrode is passed into the stomach under light sedation and positioned by withdrawing the steerable tip until it meets the resistance of the GO junction. Ventricular pacing is performed using a cathodic point source mounted distally on the electrode tip and a high impedance chest pad. A filtered bipolar oesophageal electrogram is obtained by scanning the lower oesophagus using successive adjacent combinations of five ring

electrodes mounted proximally on the GO electrode. Once located, the pair of ring electrodes generating the maximal atrial deflection is used for bipolar atrial stimulation. A new generator permits separate atrial, ventricular and AV sequential pacing with variable currents (range 0-50mA) pulse duration (atrial 3-21msec, ventricular 10-40msec) pacing rates (40-160/min) and AV delays (50-250msec). Using this technique stable atrial, ventricular and AV sequential pacing were easily established in six patients (4 male, 2 female; average age 74.8, range 66-85) and maintained for upwards on 30 minutes. Average threshold current requirements for atrial and ventricular capture were 17.7mA (range 10-24) and 17.5mA (range 15-22) at pulse duration of 9msec and 40msec, respectively.

THE EFFECTS OF ENOXAMINE, DOPEXAMINE AND DOPAMINE ON RENAL FUNCTION DURING CARDIO-PULMONARY BYPASS

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Cardiopulmonary bypass (CPB) is associated with renal impairment, attenuated by dopexamine¹. The effects of 3 agents on renal function were studied during CPB for elective surgery.

Nineteen consented patients were randomly allocated to receive enoxime (5 mg/kg/min for 10 minutes than 2 ug/kg/min), dopamine 2 ug/kg/min, dopexamine 2 ug/kg/min or normal saline 2 ml/hour for the duration of CPB using a standard anaesthetic and CPB technique with a cardiac index of 2.41l/m²/min.

Exclusion criteria include renal disease, diabetes mellitus and cerebrovascular disease.

Arterial blood gases, urinary sodium excretion and creatinine clearance were measured prior to and at 30 minute intervals during CPB.

Creatinine clearance fell in all groups during CPB by 85% in controls, 56% with dopexamine, 38% with enoxamine, 28% with dopamine.

In this study with constant cardiac index and comparable haemodynamic indices the fall in creatinine clearance was attenuated by all 3 drugs. This is further evidence of a peripherally mediated effect on the kidney, not solely dopaminergic. Their use would appear to be beneficial during CPB.

Reference

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SILENT MYOCARDIAL ISCHAEMIA AND HYPERLIPIDAEMIA

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Inhibitors of HMG COA reductase may impair stress responses due to deficient cortisol synthesis. We investigated this in patients treated with simvastatin, using a maximal treadmill exercise test as the physiological stressor. We studied 33 patients (18 males; age range 20-61 yrs) with hyperlipidaemia. We performed a maximal treadmill exercise test with cardiac monitoring (single lead CM5). Symptomatic angina was an exclusion criteria, but 6/33 patients had evidence of myocardial ischaemia during the exercise test.

Patient	Sex	Age	Chol.	ST Depression
EM	F	54	9.2	1.9 mm
HD	M	51	10.2	3.0 mm
DM	M	50	10.4	5.0 mm
BB	M	41	8.0	6.0 mm
MW	F	54	9.2	2.4 mm
MM	F	45	9.7	3.2 mm

In this small group of patients studied 18% have shown evidence of myocardial ischaemia which is asymptomatic. Two of the six have had further investigation and one is awaiting coronary artery by-pass grafting. This raises the question as to whether all patients with hyperlipidaemia should be offered an exercise stress test.

TUMOUR NECROSIS FACTOR IN THE CIRCULATION

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Tumour necrosis factor (TNF) is an important cytokine which has been extensively investigated since its discovery in 1975. There is little information on the flux of TNF through the circulation *in vivo*. We investigated the dynamics of TNF by measuring levels simultaneously at different sites in the circulation. We studied 5 men with ischaemic heart disease (IHD) undergoing cardiac catheterisation. 2 ml of blood was withdrawn simultaneously from the pulmonary artery (PA), femoral artery (FA) and vein (V), after removal of dead space. Plasma TNF was determined by ELISA using a monoclonal antibody CB0006.

Patient	1	2	3	4	5
TNF (pg/ml)					
PA	27	16	11	7	64
FA	7	15	8	14	110
V	9	7	21	17	79

TNF was detectable in all 5 patients studied and levels differed at all three sites, showing that TNF is not evenly distributed throughout the circulation. This would suggest that there may be pulsatile secretion and variable clearance of TNF in patients with IHD.

CORONARY BYPASS GRAFTING FOR PATIENTS LESS THAN 40 YEARS OF AGE

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The Irish Cardiac Surgical Register has provided a continuous record of all adult cardiac operations performed in the Republic of Ireland since 1983. We present a review comparing the profile of patients presenting for coronary artery bypass grafting (CABG) less than 40 years of age with patients aged 40 years or more. There were 209 patients less than 40 years (group 1) and 6467 patients greater than 40 years (group 2). The mean age of group 1 was 36.5 years and was 56.5 years in group 2. The majority of patients in both groups were male. No difference was found between the groups when examined for sex distribution, anginal status, myocardial infarction, left ventricular function or the number of grafts performed. Group 1 patients had a higher proportion of good distal vessels and a lower proportion of poor distal vessels

when compared with group 2 ($p < 0.0005^*$). Patients in group 1 had a significantly higher incidence of familial disease ($p < 0.05^*$) and were more likely to smoke ($p < 0.005^*$) than patients in group 2. No difference was found between the groups when examined for in-hospital, 30 day, one year and five year mortality. There was no difference between the groups in patients with grade III or IV angina at the one or five year follow-up. A higher proportion of group 1 patients had returned to work at follow-up. In conclusion, younger patients tend to have better preserved distal vessels, are much more likely to smoke and have a positive family history. There is no significant difference between early and late mortality nor between recurrence of angina. (* Chi squared)

CAROTID ENDARTRECTOMY – A HIGH-RISK SUBGROUP?

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In our unit, we favour general anaesthesia and generally avoid shunting during carotid endarterectomy. Audit of our most recent 100 patients revealed that endocrine disease rather than either myocardial ischaemia or hypotension contributed to perioperative morbidity. Four patients (3 female, 2 non-smokers) sustained either disabling stroke (2 female) or partially reversible ischaemic neurologic deficit. All 3 female patient had diabetes mellitus or myxoedema.

Long-term anti-hypertensive therapy resulted in more stable intraoperative blood-pressure, a greater frequency of reduced back-bleed but no increased operative risk.

Absence of a single vertebral vessel occurred frequently, but all patients with total occlusion of the contralateral internal carotid artery had at least a well-developed vertebral vessel and no patient in the series had external carotid artery occlusion.

The concentration of morbidity in female patients with coincidental endocrine disease (especially non-smokers) suggests a high-risk sub-group with an alternative natural history either at arterial level or directly affecting the cerebral cortex. However, confirmation of these findings would require a pooled, detailed multicentred audit.

MOLECULAR MARKERS IN ABDOMINAL AORTIC ANEURYSM

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Abdominal Aortic Aneurysm (AAA) is characterised by progressive aneurysmal degeneration of the abdominal aorta and is a relatively common disease of the elderly. Investigation of clinical and genetic parameters in patients and their families may reveal disease markers which have a predictive value. Patients presenting at Beaumont Hospital Vascular Clinic are investigated by ultrasonography, detailed family histories are taken and bloods are drawn for genetic analysis. Age- and sex-matched control subjects are drawn from orthopaedic outpatients.

An association between the incidence of AAA and genetic polymorphism at several loci on chromosome 16(16q21-24.1) has been observed. The Polymerase Chain Reaction (PCR) was used

to screen a range of polymorphic dinucleotide repeat loci *mfd* 23, 24, 62 & 65, in the region 16q21-q22.4. Allele-frequency data has revealed a novel 91bp allele of *mfd* 23 in the Irish population which is not observed in the US reference population. The observed frequency of this allele in the Irish affected and relative groups shows a statistically significant reduction relative to that in the control group. In addition, a novel 90bp allele at *mfd* also shows reduced frequency in the affecteds as compared with the relatives and controls. These allele frequency changes may have some predictive value in AAA.

NON-Q WAVE MYOCARDIAL INFARCTION: PROGNOSTIC ROLE OF DIPYRIDAMOLE TECHNETIUM MIBI SCAN

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Patients who survive an acute non Q wave myocardial infarction (MI) have a greater potential for late reinfarction. The role of early dipyridamole technetium (Tc) 99m MIBI scintigraphy, when used to identify patients who are at greater risk of developing subsequent ischaemic events was evaluated prospectively. Thirty patients who had an uncomplicated acute non Q wave MI confirmed by CK (MB) elevation were studied. All patients had a resting Tc 99m MIBI scan performed. Following an IV infusion of dipyridamole 0.56 mg/kg a repeat Tc 99m MIBI scan was performed. Coronary angiography was performed on all patients. Angina status was assessed after 8 weeks.

During the dipyridamole infusion 11 patients (36%) developed mild angina and 10 (33%) had ST segment depression.

MIBI scan	No.	Angiogram		Clinical Review			
		<75%	>75%	angina	MI	PTCA	CABG
Infarct only	18	6	12	2	0	1	0
+ Ischaemia	12	3	9	9	1	4	3

We concluded that dipyridamole Tc 99m MIBI scanning identified patients who had both an area of infarction and an area of ischaemia from those who had evidence of infarction only. The infarct/ischaemia group of patients had a higher incidence of post infarction angina and a greater requirement for early revascularisation.

AORTIC ROOT PRESSURE DURING CARDIOPLEGIA ADMINISTRATION: IS IT NECESSARY?

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Aortic root pressure during cardioplegia infusion is usually assessed by palpation. Excessive or inadequate perfusion may be deleterious to the ischaemic myocardium. This study was undertaken to identify what factors influence root pressure during cardioplegia administration.

Intra aortic pressure was measured in fifty consecutive patients (five women) undergoing isolated coronary artery surgery. Cardiac arrest was achieved with one litre of St. Thomas's cardioplegia at 4°C, pressurised to obtain a mean root pressure of 80 mmHg. Aortic regurgitation was assessed manually and coronary disease scored.

Patients were divided into groups according to infusion pressure: Group I > 300 mmHg 6 (12%), Group II 200-300 mmHg 30 (60%) and Group III < 200 mmHg 14 (28%). Coronary anatomy, myocardial size and aortic regurgitation all influenced infusion pressure.

These findings indicate the wide range of perfusion pressures required for the effective administration of cardioplegia. We believe routine intra aortic monitoring will enhance post ischaemic myocardial recovery.

AORTIC HOMOGRAFTS: AN ADDITIONAL BONUS TO CARDIAC TRANSPLANTATION

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The use of homograft (allograft) aortic valves for aortic valve replacement of complete aortic root replacement has expanded with the development of the cardiac transplantation programme in this country, which has provided the source of the fresh homografts from the explanted native heart at the time of transplant. There have been twenty homograft valves inserted. Fifteen valves were harvested from the explanted heart at the time of transplant, the remaining from the unmatched donor hearts. The indications for the use of homografts were age 70 yrs (4 patients), occupation (2), poor anticoagulation risks (3), personal choice (1), impending surgery/risk of endocarditis (4), chronic dehiscence of prosthetic valves (1) and aortic root replacement for endocarditis (5).

There was no increased morbidity associated with their use. No anticoagulation was used post operatively. The risk of endocarditis equals that of a normal valve. All patients have been followed up with regular doppler echocardiography. The haemodynamic performance of the homograft most closely approximates to that of a native valve and we have found it a very acceptable alternative in a selected group of patients.

CARDIOLOGY/RESPIRATORY MEDICINE

PSEUDOMONAS EXOTOXIN A INDUCES PULMONARY ENDOTHELIAL CYTOTOXICITY IN VITRO: MODULATION BY DIBUTYRYL-cAMP

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Bacterial lipopolysaccharide or endotoxin has been proposed as an important mediator of septic shock and the adult respiratory distress syndrome (ARDS). Certain bacteria also elaborate cytotoxic exotoxins, but their contribution to lung injury is less clear. Recently, we demonstrated that *Pseudomonas aeruginosa* exotoxin A (Exo A) produced endothelial and epithelial cell injury *in vitro*, which attenuated by co-incubation with dibutyl cyclic adenosine monophosphate (db-cAMP). In the current studies, injury produced by Exo A was further characterised by quantitating the duration of exposure required to produce injury to bovine pulmonary artery endothelial cells (BPAEC). The effect of post treatment with db-cAMP was also examined. Exotoxin A was added to (BPAEC) and the release of incorporated Cr-51 used to indicate cell injury.

Progressive shortening of the exposure period to Exo A demonstrated that exposure as brief as 5 minutes resulted in cytotoxicity comparable to 18 hours exposure. Post treatment with db-cAMP

attenuated Exo A induced injury when added up to one hour following Exo A; 7% specific Cr-51 release compared to 29% specific Cr-51 release with Exo A alone ($p < 0.05$). We conclude that BPAEC are injured by brief exposure to Exo A and post treatment with db-cAMP is protective against Exo A induced endothelial injury.

RESPIRATORY MEDICINE

PROSPECTIVE HOSPITAL STUDY OF COMMUNITY ACQUIRED LOWER RESPIRATORY TRACT INFECTION - A PRELIMINARY REPORT

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Mortality rate for lower respiratory tract infection (LTRI) in hospitals varies from 5-11% in Ireland but little data is available on morbidity. We report on the aetiology, progress and outcome of 200 consecutive cases of clinically diagnosed community acquired LRTI requiring admission. Immuno-compromised patients were excluded.

The mean age of patients was 64.3 years (range 15-87). Patients were symptomatic or had acute or chronic symptoms for an average of 7 days (1-28) prior to presentation and 45 (22.5%) patients were prescribed antibiotics prior to presentation. Sputum samples and blood cultures were obtained from 120 (60%) and 66 (33%) patients respectively. At least one organism was isolated in 40% of the sputum samples (*Haemophilus influenzae* 29% and *Streptococcus pneumoniae* 21%) and 9% of blood cultures.

The mean duration of stay for all patients was 7.9 days (1-23) and the mean time to clinical improvement was 3.5 days (1-11). 145 patients were treated with 7 days of antibiotics, 18 required more than 7 days of treatment and 23 had their antibiotic treatment altered before discharge. 14 (7%) patients died during the study period.

Our outcome is in agreement with literature in the U.K. The above figures are important for medical audit and in helping physicians plan management of patients with community acquired LRTI.

DOES HOME NEBULISATION THERAPY IMPROVE THE QUALITY OF LIFE OF PATIENTS WITH SEVERE CHRONIC AIRFLOW OBSTRUCTION

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Objective: To determine whether long term home nebulisation therapy has an effect on the quality of life of patients with severe chronic airflow obstruction and in addition affects the number of admissions and duration of hospital stay, the number of general practitioner visits and the number of courses of antibiotics received.

Design: A retrospective study by questionnaire to quantify changes in quality of life parameters before and after long term domiciliary nebulisation^{1,2}.

Setting: Chest Clinic at a District General Hospital.

Patients: 108 patients (64 male, 44 female) with severe chronic airflow obstruction (N.Y.H.A. classification grade III and IV breathlessness) were included in the study.

Main results: There was an improvement in all the parameters of quality of life with most reaching statistical significance.

Conclusion: Long term home nebulisation therapy improved the quality of life of patients as well as reducing the number of general practitioner visits, number of antibiotic courses prescribed, number of hospital admissions and duration of hospital stay. In our study no significant long term problems were encountered with the practical use of nebuliser equipment due to regular surveillance undertaken by the respiratory care team.

References

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**TUBERCULIN CONVERSION IN MEDICAL STUDENTS
AFTER ELECTIVE PERIODS IN THE DEVELOPING
WORLD**

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We have studied the tuberculin status of fourth year medical students of University College, Cork before and after summer elective periods in the developing world (Africa) for the four years 1988-91 inclusive: 61 students (34 females; 27 males) age range 22-25 were investigated. Tuberculin testing prior to departure and on return was done using the Mantoux test 1:1000 solution. Induration ≥ 10 mm at 48-72 hours was read as positive. Forty-two students (69%) were tuberculin negative prior to departure. Chest x-rays were done on all students before going on elective (all normal) and on tuberculin converters on return.

Results show that 14 students (33% of tuberculin negatives) were tuberculin converters. Two conversions occurred in 1988, 6 in 1989, 1 in 1990 and 5 in 1991. Conversion differences from year to year were not statistically significant (Fisher's exact test). All repeat chest x-rays remain normal. All converters remain well at up to 3 years of follow-up.

Although numbers investigated to date are limited the results suggest that tuberculin conversion is a hazard for Irish medical students on developing world elective periods.

CHRONIC BRONCHITIS AND EMPHYSEMA, MORTALITY AND CARDIAC ARRHYTHMIAS

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We examined 108 consecutive admissions with acute exacerbation of COAD to see which clinical features at admission predicted mortality or were associated with cardiac arrhythmias (X^2 analysis).

Mortality: 11 patients died. Mortality was best associated with hypercarbia ($p=0.0005$); elevated blood urea ($p<0.06$); the presence of heart failure ($p=0.14$). Patients who died were also more likely ($p=0.0001$) to receive i.v. Doxapram; less likely ($p=0.007$) to have proven bacterial infection.

Arrhythmias: 23 patients had arrhythmia: multifocal atrial tachycardia (14); atrial fibrillation (7); atrial ectopics (2). Patients with an arrhythmia were more likely to have X-ray evidence of heart failure or pneumonia ($p=0.05$); clinical heart failure ($p=0.0007$) but were not more likely to die. Neither mortality nor the presence of an arrhythmia were related to treatment prior to admission.

Conclusions: Patients admitted with acute exacerbations of COAD are more likely to die if they have elevated carbon dioxide, elevated urea or heart failure. Arrhythmias are common in these patients and multifocal atrial tachycardia is the commonest arrhythmia.

**LUNG FUNCTION FOLLOWING TREATMENT FOR
TUBERCULOSIS**

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Ninety five consecutive patients had lung function assessed after treatment for pulmonary TB. Lung function is expressed as % predicted standardised for age, height, weight and sex. To determine which clinical features best predicted post treatment lung function we used Multiple Regression Analysis (MRA), Linear Regression Analysis and X^2 test.

Results: Low FEV1 \pm low FEF 25-75% (46 patients); high TLC (17 patients); high RV (59 patients) high RV/TLC ratio (71 patients). Low gas transfer (18 patients); low DLCO/VA (30 patients). Likelihood of airflow obstruction was well correlated ($r=0.97$) with radiological extent of disease at diagnosis as was low gas transfer ($r=0.95$). Using MRA FEV1, FVC, FEF 25-75% correlated best with radiological extent of disease at diagnosis and age at completion of treatment. TLC and RV both correlated best with radiological extent of disease at diagnosis and the presence of cavities post treatment.

Conclusion: Lung function after treatment is best correlated with radiological extent of disease at diagnosis. This suggests that the pre-treatment duration of illness may be important in determining subsequent pulmonary function and gives added impetus to rapid diagnosis and treatment of TB. Other clinical parameters are weakly correlated with lung function after treatment.

**SEQUENTIAL MEASUREMENT OF RENAL BLOOD
FLOW IN HYPOXAEMIC RESPIRATORY FAILURE**

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We have used a non invasive technique to sequentially measure renal blood flow in hypoxic respiratory failure. Duplex Doppler ultrasound of renal interlobar arteries was performed on 16 patients with hypoxic respiratory failure ($PaO_2 < 8$ kPa) while hypoxic and again following 20% improvement in arterial blood oxygen tension. (COPD-12, asthma-1, bronchiectasis-1, interstitial lung disease-1). An Acuson 128 computerised real-time sonography system with a 2.0 MHZ imaging transducer was used to scan the renal vessels via the translumbar route with the patient in the sitting position. Pulsatility Index (PI) was calculated as a measure of renovascular resistance. PI is obtained by dividing the difference between the maximum systolic height and the minimum diastolic height of the waveform by the mean height. A fall in PI corresponds to a fall in the distal resistance to flow. All results were paired observations with each patient acting as his or her own control. The data was analysed using Student's t test. A rise in blood oxygen tension of $>20\%$ was accompanied by a significant fall in PI ($P<0.001$).

This study suggests that the correction of hypoxia reduces renovascular resistance.

PROCOLLAGEN PEPTIDE LEVELS IN LUNG DISEASE

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Histological studies have demonstrated an increase in the relative amount of Type I to Type III collagen in the fibrotic lung. Deposition of newly synthesized collagen is accompanied by the release of N- and C- terminal peptides from procollagen precursors. The aim of the present study was to ascertain if the relative levels of Type I and Type III procollagen peptides in BAL or serum might reflect fibrosis in patients with interstitial lung disease (ILD). Procollagen peptide (PCP) levels were analysed in BAL and serum samples from 20 patients with ILD. No patient was on corticosteroid treatment at the time of study. Patients were divided into three categories: C1 = patients with no X-ray evidence of interstitial involvement (n=5); C2 = patients with interstitial infiltrates but no evidence of fibrosis (n=9) and C3 = patients with X-ray evidence of fibrosis (n=6). BAL levels of both Type I and III PCPs increased with increasing lung involvement (Type I vs Category: F ratio = 3.43, p<0.05; Type III vs Category: F ratio = 8.51, p<0.001). The proportion of Type I to Type III PCP in BAL also increased with increasing lung involvement. Serum levels of either peptide alone did not distinguish ILD patients from normal control subjects. However, the contribution of Type III PCP to total serum procollagen peptide levels was increased in C3 patients (p<0.04 vs control group). These results suggest that BAL levels of PCPs reflect the alteration in deposition of Type I and Type III collagens found in the fibrotic lung and that the relative proportion of Type III PCP in serum may reflect increased collagen deposition in the lung.

ANALYSIS OF SARCOID CHEST X-RAYS OVER 5 YEARS

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Four hundred and fifty biopsy-proven patients have been followed regularly, since 1981, at the Sarcoidosis Clinic. Comprehensive clinical data was recorded using spreadsheets and databases held on a personal computer system. The aim of this study was (1) to identify useful analyses of radiological changes/patterns in the management of sarcoid; (2) to assess the effectiveness of our present database techniques in managing CXR follow-up data. Complete 5-yr data with use of a modified Siltzbach and ILO/UC radiological scoring system in addition to complete clinical data is available for 127 patients (68 females, mean age 30 yrs) from an initial total of 311 patients (mean age 31 yrs; 159 males). The main presenting complaints were pulmonary symptoms (18%); acute erythema nodosum (17%); ocular (16%) while 16% were asymptomatic at presentation.

CXR stage	CXR staging over 5 years				Total
	0	1	2	3	
initial	18	76	110	71	296
2 yrs	36	23	61	53	198
5 yrs	20	6	25	50	127

Semi-quantitative measurements of nodal size and parenchymal perfusion showed changes in up to 50% of patients who had unchanged CXR staging. Detailed analysis of CXR and clinical patterns provides more accurate estimations of prognosis over time in sarcoidosis. Our present sarcoid database requires modification to allow more efficient and accurate data maintenance and follow-

up of clinical and CXR-data in the long-term management of sarcoidosis.

RESPIRATORY MEDICINE/INFECTIOUS DISEASES

THE DEVELOPMENT OF A SENSITIVE ELISA FOR MEASUREMENT OF NEUTROPHIL ELASTASE

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Recent studies suggest that the release of small quantities of neutrophil protease may play a role in disease characterised by a low-grade inflammatory response. In this study, a competitive ELISA, designed to detect low levels of neutrophil elastase in biological fluids, was established. The detection limit (2.5 ng/ml) and range (2.5 - 100 ng/ml) of the assay represented an improvement in sensitivity compared to previously reported assay systems. Validation of the assay was achieved by assessment of elastase levels in plasma from normal subjects and cystic fibrosis (CF) patients. Low background absorbances indicated little non-specific interference in the system. Normal plasma levels (2.4 ± 1.0 ug/ml, n=20) were similar to those reported by other investigators¹. As expected, significantly higher levels (5.5 ± 3.9 ug/ml, n=42; p<0.001) were observed in plasma from CF patients. Measurement of elastase in bronchoalveolar lavage (BAL) fluids from a group of patients with interstitial lung disease indicated that 3 of 5 patients with idiopathic pulmonary fibrosis (IPF) had elevated BAL elastase levels compared with only 2 of 30 patients with sarcoidosis and none of 4 patients with extrinsic allergic alveolitis. As IPF is associated with elevated BAL neutrophils, these results lend validity to the proposal that elastase can serve as a sensitive marker for *in vivo* neutrophil degranulation.

Reference

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I.V. DRUG ABUSE, AIDS AND TB: DUBLIN EXPERIENCE

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Ireland has a TB rate of 22:100,000 and we treat 30% of reported cases. In the period 1980-1985 we treated 1641 patients for TB; 2 were known i.v. drug abusers (IVDA); none were positive for human immunodeficiency virus (HIV). Of 1000 TB patients seen since 1986, 18 were HIV related and 6 were IVDA.

n=24	IVDA	HIV+	Homo/Bisexual
6	+	-	-
11	+	+	-
6	-	+	+
1	+	+	+

Twelve HIV positive patients had atypical chest X-rays; 12 HIV positive had extrapulmonary TB; 3 HIV patients had atypical organisms; 21 had fully sensitive M.TB

Conclusion: These data show an increase in TB in IVDA (HIV positive and HIV negative) and remind us that efforts to prevent TB in this group must be intensified.

INFECTIOUS DISEASES

INCIDENCE OF TUBERCULOSIS IN A COHORT OF HIV INFECTED PATIENTS: A TWO YEAR FOLLOW UP STUDY

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The aims of this study were to assess the incidence of tuberculosis in the Irish human immunodeficiency virus (HIV) infected population, and to assess the usefulness of tuberculin skin testing as an indicator of active tuberculosis in this population. Between February and September 1988 thirty-eight HIV positive patients were recruited into the study. A skin test score was derived for each patient using the Multitest system. Patients were reviewed in January 1991, ten had died, three were lost to follow-up, and twenty-five were alive. The mean follow-up period was 22 months (range 6-34). Eleven patients were tuberculin positive on entry into the study; one of these developed tuberculosis. Twenty seven patients were tuberculin negative; three of these developed tuberculosis. Differences in the incidence of mycobacterial infection between tuberculin positive and tuberculin negative individuals are not statistically significant. There was a strong negative correlation between Multitest score and advanced disease ($R = -0.7$ $p < 0.001$). The incidence of tuberculosis in the population which we studied is approximately 5% in tuberculin negative and tuberculin positive individuals; this has grave implications for Irish health resources.

TALE OF TWO CITIES

C. O'Mahony

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Dublin.

The purpose of the study was to determine if the rumours about HIV and AIDS in Dublin were true. Could two cities so similar in population and characteristics as Dublin and Liverpool be so different in the context of HIV disease?

A 2-week locum for a Merseyside Genito-Urinary Medicine (GUM) Consultant in St. James's Hospital in Dublin was the method of investigation.

Over 700 HIV positive patients had attended St. James's GUM department and approximately 550 of these were drug related infections either through intravenous drug use and/or sexual transmission to partner. In comparison, there were 18 HIV positive drug addicts out of a total of 192 infections recorded in Mersey Region. The comparison in services - GUM, substance abuse, outreach and needle exchange was equally disparate.

In conclusion, despite the obvious dedication of the few dealing with so many, the number of infections continues to rise. As the tide of asymptomatic HIV disease progresses inexorably towards full blown AIDS, the city's health services are facing a disaster. Could Dublin in 1992 become the "European City of (HIV) Culture"?

THE USE OF POLYMERASE CHAIN REACTION (PCR) IN THE DETECTION OF HEPATITIS C VIRUS

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In this study the PCR technique was developed to detect a hepatitis C (HCV) genome sequence of approximately 270 base

pairs (bp) primarily in sera with inconclusive test results for antibody to hepatitis C. HCV is a single-stranded RNA flavivirus with a lipid envelope, 50-60 nm, diameter with a genome of just under 10,000 nucleotides. The sequence amplified and detected in this study was from the highly conserved non-structural 5 region. The virus RNA was extracted from serum and precipitated; reverse transcription was performed using the downstream primer NCR2. The copy DNA (cDNA) produced was amplified by the nested technique using outer primers NCR1 and NCR2 and two inner primers, NCR3 and NCR4. The c270 bp product was detected by ethidium bromide gel electrophoresis. 121 sera from 13 clinical categories of patients and risk-groups for hepatitis were analysed. 24 were positive and 92 were negative. An HCV probe for confirmation of these results is presently under development. PCR provided an early and sometimes only indicator of hepatitis C infection, in others it has clarified serology results. It remains the only method to detect hepatitis C virus at present.

QUININE, COTRIMOXAZOLE AND TETRACYCLINE IN MANAGEMENT OF CEREBRAL MALARIA

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The purpose of this study was to assess the benefit of administration of tetracycline along with quinine and cotrimoxazole in the treatment of cerebral malaria.

Two hundred and fifty-four cases of cerebral malaria have been studied. The patients were divided into two groups. Group A (100 patients) was treated with intravenous quinine dihydrochloride 10 mg/kg 8 hourly in 5% dextrose in aqua along with cotrimoxazole (800 mg sulphamethoxazole + 160 mg trimethoprim) twice daily. Group B (154 cases) was given triple therapy including intravenous quinine and co-trimoxazole in the same dose as in group A along with parenteral tetracycline 200 mg 8 hourly. Parenteral quinine and tetracycline were continued till the patients became conscious and were able to retain oral medication. Duration of treatment ranged from 7-10 days.

Fatality in group without tetracycline was 18%, whereas as in the tetracycline group it was 12.33%.

We conclude that co-administration of tetracycline with quinine and cotrimoxazole has a significant effect in lowering fatality of cerebral malaria.

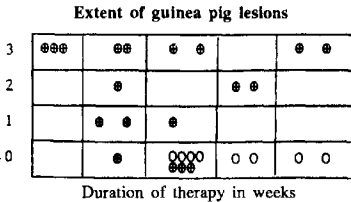
MICROBIOLOGY

THE PATHOGENICITY OF MYCOBACTERIUM TUBERCULOSIS DURING CHEMOTHERAPY

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We used the guinea pig as an experimental model to investigate the pathogenicity of mycobacterium tuberculosis. Sputum samples were injected subcutaneously into guinea pigs and after eight weeks the animals were killed and an autopsy performed. The likelihood of the sputum samples producing tuberculosis in the guinea pig was related to culture positivity rather than to duration of chemotherapy. This study does not support the belief

that a change in pathogenicity occurs during treatment of pulmonary tuberculosis.



The extent of tuberculosis lesions in relation to duration of therapy. ○: specimens of sputum with positive culture. ●: specimens of sputum with negative culture.

SALMONELLA IN CORK

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Salmonella is a common enteric pathogen, worldwide. Throughout the 1980's infection due to *Salmonella enteritidis* has dramatically increased. Eight hundred and sixty *Salmonella* spp. (human cases) were isolated at Cork Regional Hospital from 1986-1991. Over this 5 year period, *S. enteritidis* phage type 4 has emerged as the dominant serotype isolated, accounting for 63% of all *Salmonella* spp. isolated in 1991. The prevalence of this serotype of *Salmonella* differs from the rest of the country. Data will be presented outlining the seasonal epidemiology of this organism from human and food sources.

NEPHROLOGY

THE USE OF ENALAPRIL IN POST RENAL TRANSPLANT ERYTHROCYTOSIS

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Following successful renal transplantation between 6 and 15% of recipients will develop erythrocytosis. The importance of this as a clinical problem is that these patients are at increased risk of thromboembolic events. Traditional therapies for this condition has involved repeated phlebotomy or bilateral native nephrectomy. A number of mechanisms have been proposed for this phenomena, most of which involved abnormally high production of erythropoietin by the native kidneys. Enalapril has been shown in a number of settings to reduce circulating EPO levels and to exacerbate anaemia in dialysis patients.

Nine renal transplant patients with a haematocrit of 0.51 or greater on two consecutive occasions were enrolled in a study in which existing anti-hypertensive medication was substituted with Enalapril 2.5mg. Baseline measurements of haematocrit and serum EPO were made. Patients were followed at two weekly intervals for 6 months.

Mean haematocrit fell from 0.52 to 0.45 after 8 weeks and remained at that level for the subsequent 12 weeks ($p < 0.05$), serum EPO also fell from 61.12u/ml to 18.25u/ml ($p < 0.05$) after 4 weeks.

The mean blood pressure, serum K or serum creatinine did not change during the 6 month period of observation.

It would thus appear that Enalapril is a safe and effective treatment for post renal transplant erythrocytosis

EXPERIENCE WITH 50 PERMANENT PERCUTANEOUS PERITONEAL DIALYSIS CATHETERS

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Difficulties in establishing prolonged peritoneal access limits the role of peritoneal dialysis (PD) in the management of acute renal failure (ARF). Forty-eight patients presenting in ARF had silastic PD catheters (No. = 50) inserted by the Seldinger technique since Oct. '88. Follow-up to Nov. '91 is presented. Patients selected were unfit for general anaesthesia or haemodialysis. Insertion of a PD catheter was a ward procedure. Long term dialysis was established in 85% of cases. Excluding primary failure, mean catheter use was 6.3 months [range 0-20 months]. The major endpoints were death 28% and infection 28%. Comparative analysis with 107 PD catheters inserted by open surgical techniques in patients with established chronic renal failure during the same period revealed a higher incidence [$p < 0.01$] of early dialysis leak (20% vs 9.3%), and obstructed flow [$p > 0.05$] (10 vs 5.6%). Post insertion nausea (10.3%) and incisional hernias. Mortality due to underlying pathology in patients on percutaneous PD accounted for a shorter mean duration of catheter use.

We concluded that percutaneous PD catheters provided a safe, reliable access for peritoneal dialysis and could be applied to the management of renal failure outside specialised units.

PLENARY

UTERINE FIBRINOLYSIS AND DYSFUNCTIONAL UTERINE BLEEDING

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Over 60% of women having hysterectomy for excessive menstrual bleeding have no uterine pathology and are diagnosed as unexplained or dysfunctional uterine bleeding (DUB). Increased local fibrinolysis has been implicated in the aetiology of DUB. This study has compared tissue plasminogen activator (tPA) in uterine biopsies taken at hysterectomy from 48 women with normal menstrual loss (mean MBL 42 ml, range 5 - 77) and 57 women with DUB (mean MBL 194 ml, range 81 - 1,059). Endometrial tPA antigen levels were significantly higher in the pre-menstrual phase of the cycle in women with DUB ($p < 0.02$) and showed a significant correlation with the degree of MBL ($r = 0.78$). The tPA was localised in endothelium of small uterine blood vessels by immunocytochemistry. High levels of tPA antigen were also found in menstrual fluid during the first 48 hours of menstruation in women with DUB. Treatment of 20 women with DUB (mean MBL 160 ml, range 82 - 360) with the fibrinolytic inhibitor, tranexamic acid, reduced blood loss by 56% (mean MBL 74 ml, range 22 - 198). These results show an important relationship between uterine fibrinolytic activity and the degree of menstrual bleeding. Supported by the Health Research Board (Ireland).