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Serum albumin, Down Syndrome and Alzheimer’s Disease
Renal transplantation in the elderly - the Irish experience
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Compression bandaging for venous ulcer disease
Autologous stem cell transplantation in myeloma at St James’
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INTRODUCTION

There is evidence of impaired liver synthetic function in Down Syndrome\(^1\), but the degree to which this declines with age is not clear. Hepatitis B infection is particularly common in the institutionalised learning-disabled population; and there is evidence that individuals with Down Syndrome are more vulnerable to such infection than are those with other forms of learning disability\(^1\). The extent to which low serum albumin in Down Syndrome patients can be ascribed to chronic viral hepatitis is, therefore, not known.

Pathological changes of Alzheimer’s Disease are universal in Down Syndrome patients over the age of 40\(^1\), and almost all develop dementia with time. Low levels of serum albumin have been reported in Down Syndrome, but the confounding effects of viral-induced liver disease have not been clarified. There is reason to suspect that Alzheimer’s Disease, both in the presence and in the absence of Down Syndrome, may be associated with low serum albumin levels: low levels of serum albumin have been reported in Alzheimer’s Disease patients without Down Syndrome\(^1\), and Elovaara\(^1\) found low serum albumin in patients with Down Syndrome and Alzheimer’s Disease compared to age-matched controls.

Clinical differences consequent on low serum albumin concentrations in Down Syndrome are only likely with profoundly low values; lower oncotic pressures and pharmacokinetic changes with the use of highly protein-bound drugs, for example. Even mild hypoalbuminaemia might, however, provide further evidence of cellular dysfunction in this syndrome\(^1\). If severe, it could have pharmacokinetic implications when such patients are exposed to highly protein-bound drugs.

ABSTRACT

**Aims** We investigated whether or not serum albumin concentrations in Down Syndrome were lower than those of a cohort of similarly moderately- to severely-disabled institutionalised patients without Down Syndrome and, if so, whether or not this could be ascribed to the presence of liver disease. We also sought to determine the influence of Down Syndrome, age, liver disease, and Alzheimer’s Disease on the serum albumin concentration.

**Methods** We performed a cross-sectional study on 205 institutionalised patients with Learning Disabilities (47 with Down Syndrome, 158 without), and used multiple regression techniques to determine the relative effects of age, liver disease, and the presence or absence of Down Syndrome on the serum albumin concentration. Among Down Syndrome patients. We also sought to determine the association between serum albumin concentration and the presence of Dementia of Alzheimer’s Type.

**Results** Down Syndrome patients had lower serum albumin levels than non-Down Syndrome patients. Serum albumin concentrations declined with age at a similar rate in both groups, such that the effect on serum albumin of having Down Syndrome was equivalent to an additional 44 years of age. The serum albumin concentration in Down Syndrome patients with Alzheimer’s Disease was greater than that in Down Syndrome patients without Alzheimer’s Disease.

**Conclusions** Down Syndrome is associated with a low serum albumin concentration, independently of the presence of liver disease. The advent of Alzheimer’s Disease in Down Syndrome is not associated with a further fall, and may be associated with a rise, in serum albumin concentrations.
We sought to determine, using a cohort study, whether or not serum albumin levels are lower in Down Syndrome patients than in a cohort of similarly disabled non-Down patients, and whether such low serum albumin can be attributed to liver disease. We also hypothesised that the occurrence of Alzheimer’s Disease in Down Syndrome might affect serum albumin concentrations.

MATERIALS AND METHODS
The subjects were all male residential patients in St. Mary’s Hospital, Drumcar, Co. Louth, and were aged between 15 and 70 years. The experimental group comprised all patients with Down Syndrome, the control group all patients without Down Syndrome in the same hospital who had had tests of liver function performed during the same period (1999-2002). Both groups had moderate-profound mental retardation. There were 47 patients with and 158 without Down Syndrome. 12 of the patients with Down Syndrome had Alzheimer’s Disease and 35 did not. Blood testing was performed as part of the routine assessment of this population with learning disabilities. An additional 22 patients did not have blood tests for a variety of reasons, and were not therefore included in the study. Other causes of hypoalbuminaemia, such as malnutrition, protein-losing enteropathy, and nephrotic syndrome, were excluded clinically and, where appropriate, with appropriate laboratory investigations.

Blood samples were drawn on varying occasions from 1999 to 2002. Measurements included serum albumin and alanine aminotransferase. The diagnosis of dementia was made using modified ICD-10 criteria, supported by two cognitive tests (the Down’s syndrome Mental Status Examination (DSMSE)) and the Test for Severe Impairment (TSI), and two observer-rated questionnaires (the Daily Living Skills Questionnaire (DLSQ) and the Adaptive Behavior Scale – 2nd edition ABS-RC2).

The study was approved by the Hospital Ethics Committee. U.K. Medical Research Council Guidelines on research on the learning disabled and on the use of personal information in medical research were followed.

Data Analysis
Some patients having been tested for albumin level on a number of occasions over a short period of time, an average albumin level for each patient was taken. In the analysis, the influence that each patient’s mean albumin level made to the model was weighted according to the number of tests performed. The more a patient was tested, the more accurate the mean value and the greater its influence on the model describing the data. There is a potential bias in this situation, however, in that albumin results might influence the decision to test. To outrule this bias the number of tests was correlated with the albumin level. There was no evidence of a relationship (correlation co-efficient = -0.107 (p = 0.1267)), so it was possible to using weighting in the analysis.

The effects of age, Down Syndrome, Alzheimer’s Disease, and liver disease on serum albumin levels were tested using multiple linear regression. Age was fitted as a continuous variable, while Down Syndrome, Alzheimer’s Disease, and liver disease were fitted as categorical variables. Age was tested individually with each of the categorical variables with linear and quadratic effects and interactions of linear and quadratic effects with the class variable in question. The F-test was used in the regression sum of squares to test the null hypothesis of no difference between the two levels of each class variable. The coefficient of the age covariate was tested by a t-test, and a table of least-square-means was produced for each class variable to illustrate the differences between levels of class variables. For a particular categorical variable, least-square-means represent the means of each level of this class variable, averaged over the other effects in the model. In the case of an interaction, the table of least-square-means comprises the means of all combinations of the class variables involved in the interaction.

Proc GLM of SAS (which has a facility to fit weighted multiple-linear-regression) was used to fit the models. The linear regression approach has the added advantage that it can handle unbalanced data, that is, situations in which the number of patients within each combination of categorical variables differs.

RESULTS
Liver Disease in Down Syndrome and non-Down Syndrome patients
Sixty-six of 205 patients had liver disease, and there was no difference in the prevalence of liver disease among patients with and without Down Syndrome (Table 1).

Age and albumin concentration
The coefficient of the age covariate was -0.081 (std. dev. 0.0236 p = 0.0007), the effect of Down
Syndrome on serum albumin concentration being similar to that of an extra 44 years of age (Figure 1).

The most parsimonious model fitting the data with all significant terms was: $[\text{albumin}] = \text{age}, \text{Down Syndrome, Alzheimer's Disease}.$ The only interaction that approached significance was Down Syndrome $\times$ liver disease ($p = 0.06$). Though not significant, the ‘liver disease’ term must be included because of the interaction. The coefficient of the age covariate was $-0.076$ (se 0.0236 $p = 0.0015$). Table 2 shows the s. albumin levels in the presence and absence of liver disease.

**Down Syndrome and albumin concentration**
The presence of Down Syndrome had a large effect on reducing the albumin level, regardless of age and the presence of liver disease (Table 2).

**Alzheimer's Disease and serum albumin**
The presence of Alzheimer's Disease increased the serum albumin concentration, and the difference between the two groups (as well as being statistically significant) was relatively large (2.0 g/l) (Table 2).

**DISCUSSION**
Our finding that serum albumin concentrations are lower in Down Syndrome than in similarly disabled non-Down Syndrome patients is in keeping with that of other studies$^{1,2}$, and supports the theory that Down Syndrome is associated with widespread organ and tissue dysfunction$^1$. Our clarification that low serum albumin in Down Syndrome is not due to hepatitis extends the findings of previous studies.

The finding that serum albumin concentrations were significantly higher in Down Syndrome patients with Alzheimer’s Disease than in those without Alzheimer’s Disease is surprising; neither age nor liver disease was a confounder, and in no patient was there clinical evidence of nephrotic syndrome or a protein-losing enteropathy.

A possible explanation is that nutritional supplementation administered to Down Syndrome patients who became increasingly disabled with dementia reversed the fall in serum albumin. Although vitamin and mineral supplements were administered to some patients, however, none received enteral or parenteral protein supplementation, anabolic steroids or any other intervention calculated to increase serum albumin levels (though the effectiveness of such measures continues to be a matter of debate$^{11,18,19}$). Another possibility is that patients with higher serum albumin levels had a greater risk of developing Alzheimer’s Disease, in which case the albumin level is most likely to be a confounder; it is difficult to see, however, how this might relate to established risk factors for Alzheimer’s Disease ($e_4$ allele of apolipoprotein $E$, vascular risk factors, head injury, etc.)
The number of patients with Alzheimer’s Disease (12) was low, but the result is statistically significant nonetheless.

This study did not control for the use of anti-epileptic drugs, which can lower serum albumin concentrations; but epilepsy may not be as common in Down Syndrome as in many other causes of learning disability; our estimate of the effect of Down Syndrome on serum albumin concentrations may therefore be an underestimate.

It may be that there was a significant difference in the prevalence of liver disease between Alzheimer’s Disease and non-Alzheimer’s Disease groups, which we failed to detect. One limitation of the study is the absence of histological or serological evidence for liver disease or viral infection. Although the serum alanine-aminotransferase level is the most important test in the detection of acute and chronic liver disease, its concentration is not related to the severity of acute, and only weakly related to the severity of chronic, hepatic injury. There is, however, no reason why erroneous results should be preferentially distributed either in the Down Syndrome, non-Down Syndrome, Alzheimer’s Disease, or non-Alzheimer’s Disease groups.

Confining our study to male subjects may have reduced its generalisability. It also, however, removed gender as a possible confounder of serum albumin concentration.

Our results are consistent with the theory that Down Syndrome is associated with premature ageing in all cells. Whether specific segments of chromosome 21, when triplicated, are responsible for the clinical condition features of Down Syndrome, or whether the syndrome is the result of non-specific effects of aneuploidy interfering with gene replication, is still not clear.

A comparison study of serum albumin concentrations in Alzheimer’s patients with and without Down Syndrome, and a longitudinal study of serum albumin concentrations in Down Syndrome before and after the onset of Alzheimer’s Disease might each shed further light on the natural history of both conditions. It seems unlikely that serum albumin level is a risk factor for Alzheimer’s Disease in Down Syndrome, and further work is needed to explain the association. We have confirmed that Down Syndrome patients have low serum albumin concentrations and have provided evidence that this is not due to acute or chronic liver disease; we have documented the relation between albumin concentration and age in Down Syndrome and non-Down Syndrome patients; and we have found that, for reasons that are not yet clear, Down Syndrome patients with Alzheimer’s Disease have higher serum albumin concentrations than those without Alzheimer’s Disease.

REFERENCES

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Renal transplantation in the elderly - the Irish experience

ABSTRACT

Background The aim of this paper was to evaluate patient and kidney graft survival rates in renal transplant recipients and compare the outcomes between the different patient age groups.

Methods A retrospective review of all adult renal transplants performed at Beaumont Hospital between the years 1986-2001 was carried out. Patients were defined as ‘elderly’ if they were 65 years of age or older and ‘younger’ if less than 65 years at the time of transplantation. Patient and transplant graft survival rates were analysed for each age group.

Results Data were analysed on 1462 ‘younger’ patients and 105 ‘elderly’ renal transplant recipients. Estimated patient survival at 1, 5 and 10 years were 96%, 87% and 74% in the younger patient group compared to 85%, 59% and 33% in the elderly group. The adjusted graft survival rates (adjusted for death due to other causes and with a functioning graft in situ) for the younger group were 89%, 77% and 64% at one, five and ten years respectively, while for the elderly group, adjusted one, five and ten year survival rates were 89%, 83% and 70% respectively.

Conclusions Although the elderly have a shorter life expectancy than the younger population they do benefit from renal transplantation similar to the younger recipients.

INTRODUCTION

The number of elderly persons in the general population is progressively increasing worldwide and Ireland is no exception to this trend. According to the most recent data from the Republic of Ireland Central Statistics Office (CSO), there were 436,001 persons aged 65 or greater in Ireland in 2002 (total population of 3,917,203). Data published early this year (2005) from the CSO predict that the elderly population (aged >65 years) will double in Ireland between the years 1996 and 2031, increasing from the current rate of approximately 414,000 to around 850,000. The average life expectancy in the Republic of Ireland has increased from 57.9 years for someone born in 1926 to 76 years for someone born in 2002 (78.7 years for females and 73 years for males). For someone aged 65, life expectancy for males has increased from 12.8 years in 1926 to 15.4 years in 2002. In females the figures are even more significant with average life expectancy at 65 having increased from 13.4 years in 1926 to 18.7 years in 2002.

Taking this in conjunction with the fact that end stage renal disease (ESRD) increases with advancing age, the need for renal replacement therapy in the elderly has expanded dramatically. The number of dialysis patients older than 65 years has more than doubled within the past 10 years in the United States. In Europe, patients older than 60 years now account for more than 50% of the population requiring renal replacement therapy. In Italy and in France, 35% of dialysis patients are now over 70 years. Haemodialysis is the most commonly used modality in these patients but transplantation is now increasingly considered as a management option in this growing elderly population. Although many elderly patients on dialysis are frail, a consistent number are in good physical health and do not have associated major co-morbid conditions that would be a contraindication to renal transplantation.

In this retrospective study, we report a single-centre long-term follow-up of kidney transplantation in patients aged 65 years and older. The purpose of this study was to evaluate patient and graft survival in renal transplants cases performed at Beaumont Hospital between the years of 1986 and 2001 and identify factors, which influenced this.
MATERIALS/METHODS

We conducted a retrospective review of all adult kidney transplant recipients who attended Beaumont Hospital during the study period from January 1986 through to December 2001 (or at Jervis Street Hospital prior to its relocation to the current site at Beaumont). Beaumont Hospital is the only centre performing renal transplantation in the Republic of Ireland. The Irish Renal Transplant Registry receives annual follow-up data on all renal transplant patients. A dedicated Renal Transplant Database has been in operation since the year 2000 and information attained since this time is collected and stored prospectively. Data attained prior to 2000 were attained retrospectively. As part of a cardiological assessment prior to renal transplantation all patients require a minimum of electrocardiogram, chest x-ray and cardiac exercise stress test. The decision to perform coronary angiography is guided by these investigations, although all diabetics and other high-risk candidates undergo routine coronary angiography. Any significant correctable cardiac lesions must be treated prior to placing a potential candidate on the transplant waiting list. Patients are then admitted to the transplant pool once work-up is complete and the patient has been deemed medically fit for the procedure. Criteria used for the selection of suitable recipients were the number of HLA mismatches and length of time waiting on the transplant pool. Consideration is also given to the ‘age-matching’ of donor kidneys to the renal transplant recipient. The vast majority of transplants performed at our centre are cadaveric grafts.

We have never had any specified age limit criteria for offering renal transplantation in our institution. The decision on a patient’s suitability is made on an individualised basis between the Nephrologist, Transplant Surgeon, each individual patient and their families. Standard immunosuppression of all renal transplants from 1986 to 1994 consisted of Cyclosporin A, Azathioprine and Corticosteroids. During 1992 FK506 (Tacrolimus) was introduced for the treatment of high immunological risk patients and in 1996 Mycophenolate Mofetil was introduced. In general all patients at our institution receive a triple therapy immunosuppression regime consisting of Cyclosporin (or Tacrolimus), azathioprine (or mycophenolate mofetil) and oral corticosteroids.

Kaplan Meier methods were used to determine survival estimates and Log rank tests compared survivor functions between the two groups. Non-parametric (Wilcoxon) and Pearson chi squared tests were used for comparing demographic variables between the different groups. Results were deemed significant for p values <0.05. Stata (Version 8, Texas) was used in all of the statistical analysis.

RESULTS

During the 16-year period from 1986 to 2001 a total of 1762 kidney transplant operations representing 1582 adult recipients were performed at Beaumont Hospital. All but nine of these transplants were cadaveric grafts. Data were available for 1567 patients (99%). We grouped our patients into those under 65 years of age (1462 patients – the ‘younger’ patient group) and those 65 years old or greater (105 patients – the ‘elderly’ group). The 15 patients on whom data was not available were all in the under 65 years group. The median age of a transplant recipient in the younger group was 41 years as compared with 67.5 years in the elderly patient group. Data from the Irish Renal Transplant Registry show the median age of transplant recipients in the 1960’s was 36 years. In 2002 this was 46 years. In the past decade this elderly population has grown to make up 8% of the total transplant service.

The ratio of male to female transplant recipients was significantly different between the two groups with 1.8 male to 1 female recipients in the younger group compared to 3 males for every female in the elderly group. Donor age was also significantly different for the two age groups (Table 1). The cause of the ESRD was documented as determined by the attending physician. The glomerulonephritides and genetic diseases (e.g. Adult Polycystic Kidney Disease, Alport’s) were more common in the younger population while hypertension and renovascular disease were more prevalent in the elderly (Table 2).

Patient survival

The one-, five- and ten-year patient survival rate for the younger group was 96%, 87% and 74% versus 87%, 60% and 34% in the older group. Overall survival rates between the two groups were significantly different (p<0.001). Median patient survival following transplantation in the younger group was estimated at 22.0 years compared to 7.2 years in the elderly group. Of the older patient group (105 patients), 37 patients were followed-up beyond five years and 13 were followed beyond 10 years. Unfortunately we do not have adequate data available to compare these elderly patients who did receive a transplant with
those who were also placed on the renal transplant waiting list but did not get a kidney. We can however compare them with those patients who were on the chronic dialysis programme at Beaumont Hospital during a similar time period. A recent single centre study from Beaumont Hospital (from 1989 – 2003) showed the median patient survival for those patients commencing dialysis aged > 65 years was 2.25 years but this group included some very frail and elderly patients. Further analysis on the patients starting on chronic dialysis aged 65 – 75 years showed a median patient survival rate of 2.57 years (unpublished data).

During our study period 42 of our 105 elderly transplant patients died. Death occurred suddenly, while outside the hospital setting in 9 of these patients. Of these 42 patients who died, cause of death was due to cardiovascular (including peripheral and cerebrovascular) complications in 27 patients (64%) and sepsis in 10 (22%), which was predominantly respiratory. One patient died from a primary malignancy. During our study period a total of 134 deaths were recorded in the less than 65 years old age group. The commonest cause of death in this age group was cardiovascular in 66 (49%), malignancy in 33 cases (25%) and sepsis in 22 (16%).

**Graft survival**
The one-, five- and ten-year graft survival rate for the younger group was 86%, 68% and 46% versus 80%, 51% and 24% in the older group. Again these figures show significant differences between the two groups (p<0.001). The median graft survival following transplantation in the younger group was 9.4 years compared to 5.3 years in the elderly group. However, when graft outcome was censored for death with a functioning graft it showed that most of the elderly patients died with a functioning renal transplant in situ and died in fact from other causes. The adjusted graft survival rates for the younger group were 89%, 77% and 64% at one, five and ten years respectively, while for the elderly group, one-, five- and ten-year survival rates were 89%, 83% and 70% respectively. The difference in survival estimates was not significant at the 5% level, (p=0.4448) and a graph illustrates similar outcomes between the two groups (Figure 2).

**DISCUSSION**
Our results clearly demonstrate that renal transplantation is a feasible option and should be considered in the elderly ESRD patient. The median graft survival time in elderly patients was 5.3 years thereby offering more than half of this patient group at least five years of dialysis-independent life. Furthermore when our figures were adjusted for death with a functioning graft we found that graft survival rates were similar between the two age groups. Although the elderly patients do have a shorter life expectancy, they do benefit from renal transplantation similar to younger renal transplant recipients.

Prior to the introduction of calcineurin inhibitors (1983 in Ireland), renal transplantation was not
advocated as a treatment of end stage renal failure for patients older than 60 years because of poor patient and graft survival rates. Studies performed in this era showed no significant difference in survival between elderly patients on regular dialysis and patients who underwent renal transplantation. Recently, the US Renal Data System demonstrated that in patients over 65 years, renal transplantation reduced the risk of death more than threefold when compared with dialysis. This is supported by a Canadian study by Schaubel et al that found the 5-year survival for patients aged greater than 60 years was 80% for transplanted patients and 50% for those that remained on dialysis. However, it is incorrect to directly compare those elderly patients who receive a kidney transplant to those who remain on chronic dialysis. It must be considered that the patients that are put forward for transplantation are generally in better health, deemed more ‘medically fit’ and have less co-morbid illnesses than those patients who continue on dialysis.

Bonal et al, in a Spanish study demonstrated that the initial 1-year survival was actually better for dialysis patients, however, after five years the survival was 86% for transplant patients versus 77% for dialysis patients. A large Italian study by Segoloni et al found the 5-year survival for patients > 55 years was 85% in transplanted patients versus 72% for patients on dialysis. Other researchers have found that graft survival rates are not significantly different in the older age group. Analysis of UNOS data showed that the 5-year graft survival was similar in transplant recipients aged above 60 years and in those aged 0-60 years. However, graft survival rates then declined in the elderly patients after the 5th year because of their higher rate of patient death. The functional-graft survival was actually slightly better for patients > 60 years, because of the lower number of grafts lost due to rejection in this group. Comparing this study to our own experience we also demonstrated that adjusted graft survival rates were broadly similar between the two groups and that the graft loss in the elderly group was due to patient death from other causes. The difference in graft survival rates between the two reports may in part be explained by the fact that the age definition of the ‘elderly group’ was also different as they defined the elderly patient group as greater than 60 years (compared to 65 years in our study).

Due to the improving results of transplantation, the impact of the recipient’s age has become less relevant and therefore, age per se no longer constitutes a contraaindication to renal transplantation. The Irish results reflect what is happening worldwide and we too are seeing an increasing number of patients over 65 years considered for transplantation. Of all kidney transplants performed at our institution between 1986 and 2001, 5.2% were in recipients at least 65 years old at the time of transplant. There has been a gradual rise in the number of elderly patients receiving renal transplants over the study period.
2001 the elderly accounted for 9.2% of the total renal transplant workload at our institution. The issue of offering a kidney to an elderly patient remains controversial when we consider the number of younger people who remain on the renal transplant waiting lists. However, as consideration is also given to ‘age-matching’ in the allocation of potential donors and recipients it is generally the situation that a younger donor kidney is likely to be offered to a younger recipient and older donor kidneys to an elderly candidate. In this study the mean donor age was significantly different between the two patient groups, 35 years in the younger patient group versus 45 years in the elderly patient group (Table 1).

Recently published work by Briggs et al in Scotland has shown that the survival of patients who have undergone renal transplantation has improved considerably over the past two decades. This is due mainly to better immunosuppressive regimes but also to a combination of better surgical techniques, safer anaesthetic practices, and lesser infective deaths. Cardiovascular disease, infectious conditions and malignancy now account for most of the deaths in the elderly population.

Data from our institution show unequivocally that for those patients in whom surgical contraindications are absent, renal transplantation is a feasible option for the older ESRD patient. In our experience those patients who are deemed fit for transplant and do actually receive a kidney do better than their age-matched counterparts who remain on dialysis. We propose an integrated approach to the management of renal failure in elderly patients and concur with previous studies that age 65 years and greater should not bias the clinician away from the benefits of renal transplantation.

REFERENCES


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INTRODUCTION
Injecting drug users (IDUs) are at high risk of acquiring hepatitis C (HCV), hepatitis B (HBV), and human immunodeficiency virus (HIV) infections. Harm reduction interventions have been advocated in order to prevent the spread of bloodborne virus infections. Since 1992, the Irish Government has pursued a policy of harm reduction by providing methadone maintenance, needle exchange programmes and education through outreach programmes.

Despite the increasing availability of harm reduction interventions, recent studies have estimated that between 52% and 80% of opiate users in Dublin are infected with HCV, with the incidence of HCV in this population estimated to be higher than previously reported. In addition, between 19% and 28% of opiate users are positive for anti hepatitis B core antibody (anti-HBc), while between 1% and 17% are infected with HIV.

The World Health Organisation recommends universal childhood immunisation against HBV. The recently published immunisation guidelines for Ireland recommend that HBV vaccine be given to those at risk of infection, as three doses at intervals of zero, one and six months and in cases at high risk of infection, at intervals of zero, one and three months with a booster dose at 12 months.

While it has been suggested that specialist addiction treatment centres are an effective setting in which to deliver targeted immunisation programmes for opiate users, a recent study in Dublin found only one-third of clients attending such centres had...
evidence of immunity to HBV or evidence of having started an immunisation programme. Following the low uptake of HBV immunisation highlighted in this report, recommendations were devised regarding a vaccination protocol and were subsequently implemented within the addiction services. Low rates of HBV immunisation uptake have also been reported elsewhere.

It has been suggested that harm reduction interventions, in particular methadone maintenance, may not be effective in preventing the transmission of bloodborne viruses. A recent study in Dublin reported continued high risk activity among drug users despite an increase in availability of harm reduction interventions.

As a result, continued monitoring of care provided to drug users at risk of blood borne virus infections and epidemiological surveillance of blood borne virus infections among this population is important. The aims of this study, therefore, are to:

- document screening for bloodborne virus infections;
- determine the prevalence and incidence of these infections;
- describe current care processes regarding HBV immunisation.

**METHODS**

**Setting**
The Eastern Regional Health Authority (ERHA) area (with a catchment population of over 1.3 million people) is Ireland’s largest health region. It is estimated that at least 13,000 people in the ERHA area are current or former opiate users. In 1998, over 5,000 people (85% of the national total) were receiving methadone treatment in the region.

Methadone treatment services in the area are provided by: specialist addiction treatment centres, community based projects (satellite clinics) and General Practitioners (GPs).

Three local area health boards (Northern, South Western and East Coast area health boards) are responsible for the planning and delivery of health and social services in the ERHA. The area covered by the South Western Area Health Board (SWAHB) includes south-west County Dublin, County Kildare and the western part of County Wicklow. Of the six postal districts in the ERHA region with the highest prevalence of illicit opiate use, three are located in the SWAHB area.

A total of 21 clinics provide methadone treatment in the SWAHB area. These clinics range from large centres staffed by a fulltime multidisciplinary team to smaller satellite clinics based in community centres or in local health centres. The larger clinics dispense methadone while the smaller clinics provide methadone prescriptions, which are filled in community pharmacies.

**Subjects**
A total of 1,459 current or former heroin users were attending specialist addiction treatment centres in the South Western Area Health Board in December 2001. A one-in-four consecutive sample was selected from a listing of clients attending treatment (held by the Department of Health and Children on a Central Treatment List) at the time.

**Data collection**
A member of the research team reviewed the medical records of the sample population. Anonymised data regarding demography, drug using history, blood borne virus status and blood borne virus related care was recorded. Data regarding bloodborne viruses was taken from laboratory results or documentation from outside agencies that were present in individual client records.

Following the sampling process six clients were excluded from the study owing to the absence of information regarding bloodborne viral status and related care in their medical records.

The survey was carried out over a six-week period between December 2001 and January 2002.

**Data analysis**
Data were analysed using Statistical Packages for the Social Sciences (SPSS) version 10.0. Analytical techniques included Pearson’s chi squared test to determine the significance of associations between categorical variables (HCV or HIV serostatus and age). Student’s t-test was used to compare means between groups.

The incidence of infections was measured using the persons year method, and is expressed as the number of seroconversions per hundred person years (HPY) at risk, with 95% confidence intervals (CI). The date of the first negative test represented the starting point for all patients when calculating their person years at risk. The endpoint was the date of the last negative test for those who remained seronegative.
The estimated date of seroconversion was used as the endpoint for those who seroconverted and this was calculated by finding the midpoint between their negative and positive tests.

**Viral markers**

Testing for hepatitis C antibodies (anti-HCV) prior to 1993 in the Dublin area was with a second generation enzyme linked immunoadsorbent assays (EIA) and with a third generation EIA thereafter with positive assays confirmed by radioimmunoblot (RIBA) assay. Initial screening for HIV antibodies (anti-HIV) involves two EIAs, with positive assays confirmed by Western Blot assay. The screening test for both HBV surface antigen (HBsAg) and core antibody (anti-HBc) is an EIA.

**RESULTS**

**Population characteristics**

Of the 358 clients surveyed, 214 (60%) were male, the median age was 26 years (range 16-51) and the median length of time attending methadone treatment services was 24 months (range 1-221 months).

**Screening for bloodborne viruses**

A total of 316 (88%) had evidence of testing for HCV, 244 (68%) had evidence of testing for hepatitis B core antibody, 299 (84%) had evidence of testing for hepatitis B surface antigen and 307 (86%) had evidence of testing for HIV. The majority of clients had not been tested within the previous 12 months.

Of those who had been tested for exposure to bloodborne viruses, 207 (66%) tested positive for the presence of anti-HCV antibody, 42 (17%) tested positive for the presence of HBV core antibody, six (2%) tested positive for the presence of HBV surface antigen and 33 (11%) tested positive for the presence of anti-HIV antibody.

Clients aged 25 years or over were significantly more likely to test positive for the presence of anti-HCV antibody (75% compared to 47%, p<0.001), but not for anti-HBc antibody (19% compared to 13%, p=0.211), HBsAg (3% compared to 1%, p=0.309) or HIV (11% compared to 9%, p=0.468).

One hundred and twenty tested negative for the presence of anti-HCV antibody on initial testing. Of these, 27 (23%) had at least one follow-up test, with 11 testing positive for the presence of anti-HBC antibody at follow-up, giving an incidence of 9.0 (95% CI=1.9-26.3) per hundred person years at risk.

Two hundred and five tested negative for anti-HBc antibody on initial testing. Of these, 59 (21%) had at least one follow-up test, with four testing positive for the presence of anti-HIV antibody, giving an incidence of 3.4 (95% CI=0.9-8.7) per hundred person years at risk.

The median intervals from testing negative to testing positive for anti-HCV antibody, anti-HBV core antibody and anti-HIV antibody were: 40 months (range 16-44), 34 months (range 19-44) and 26 months (range 16-44) respectively.

The length of time a client was in treatment was associated with having a second test for anti-HCV antibody (p=<0.001), anti-HBc antibody (p=<0.001) and anti-HIV antibody (p=<0.001). Age was not significantly associated with having a repeat test for any of the three bloodborne viruses.

**HBV immunisation**

While 81% of clients in whom HBV immunisation was indicated had received at least one vaccine, with 69% of these completing the recommended schedule, 15% had never received a vaccine while in treatment and 4% had a documented refusal (see Figure 1). The median interval from entering treatment to receiving a first vaccine against HBV was 6 months (range 1-24 months). For those clients who entered treatment within the last 24 months, this interval was significantly shorter (three compared to 15 months, p<0.001).

Of the 177 clients who had received a completed course of HBV immunisation, 134 (76%) were tested for anti-HBs antibody (see Figure 3 for the distribution of anti-HBs titres). Twenty (15%) of these were found to have an anti-HBs antibody level of less than 10miu/ml, of whom 15 had been revaccinated (see Figure 2).

**DISCUSSION**

**Methodological considerations**

It is with some caution that these findings can be extrapolated to all drug users in treatment in Ireland.
This study presents data on a cross-section of clients receiving methadone treatment in one of Dublin’s three health board areas in late 2001 and early 2002. The sample is older (36% compared to 58% aged under 25) and contains a smaller proportion of males (60% compared to 70%) than the most recently published data on the total population attending addiction treatment services in Ireland. In addition, as data were extracted from clinical records, it is possible our findings may not accurately report the true process of care delivered.

**Screening**

The proportion of patients without documented evidence of testing was 12% for HCV, 32% for anti-HBc, 16% for HBsAg and 14% for HIV. It is difficult therefore to accurately determine prevalence of bloodborne virus infections in the study sample. Of greater importance, however, is the fact that the health status of those who have not been tested is unknown.

A review of bloodborne virus care among clients attending addiction treatment centres in the same area was conducted using a similar methodology in 1997. As only 60% of clients had been screened for at least one bloodborne virus infection, a standardised written protocol for bloodborne virus screening was subsequently introduced to the service. Our findings indicate that uptake of screening for bloodborne viruses has increased since the introduction of this protocol.

Problems in ensuring complete uptake of testing for these viruses has been reported among drug users in other settings. To date, few data exist on reasons why such difficulty is experienced in ensuring adequate screening for bloodborne viruses among this population. Previous work in the Dublin area has highlighted a deficiency in knowledge regarding HCV among drug users, particularly where primary prevention is concerned. As well as incorporating primary prevention into education programmes aimed at drug users, it is possible healthcare professionals working with drug users also need to discuss the importance of secondary prevention, specifically the importance of screening for previous exposure to any of these viruses.

**Prevalence**

It is encouraging to find the prevalence of anti-HCV antibody (66%), anti-HBc antibody (17%), HBsAg (2%) and anti-HIV (11%) antibody to be lower than observed in a similar study in the same area four years ago. It is possible these findings may be in part explained by the recent increase in availability of harm reduction facilities in the Dublin area. Age or length of injecting career are associated with testing positive for HCV, HBV or HIV. While the finding that younger drug users have a significantly lower prevalence of HCV infection is reassuring, the similar prevalence of HIV infection among those aged under 25 is a source of some concern. Another recent study examining the epidemiology of HIV infection among IDUs in the Dublin area reported an increase in the number of new cases of HIV among young IDUs.

The observed bloodborne virus prevalence is however, higher than reported in a large cross-sectional survey of new clients presenting to a specialist addiction clinic in Dublin between 1992 and 1997. This difference is likely to be explained by the fact that our sample had been in treatment for longer and was older (36% compared to 73% aged under 25).

The prevalence and incidence rates of the bloodborne viruses reported in this study may be an under-representation of the rates among IDUs as the study sample included both parental and non-parental heroin users.

**Incidence**

The observed incidence of HCV infection (24.5 per hundred person years) provides further evidence that injecting drug users attending treatment have a high incidence of HCV infection. The observed incidence of HCV among the sample reported in this paper is considerably lower than that reported recently among a cohort attending an addiction treatment centre in Dublin (66 per hundred person years). This finding may be explained by the older age and longer contact with treatment services of the cohort reported in the sample described in this paper, and indeed may indicate the benefit of methadone maintenance treatment.

However, the observed incidence of HIV infection (3.4 per hundred person years) is considerably higher than a number of recently reported incidence figures among injecting drug users in environments in which harm reduction strategies would be similar to those employed in Dublin. These are worrying finding for service planners in our area, as it perhaps
indicates that current harm reduction strategies and localised testing protocols, may not be effective in controlling the spread of HIV infection among this population, as has been previously suggested.\textsuperscript{19} The majority of clients tested for bloodborne virus infections in this sample had not been tested in the past year. Furthermore, a small proportion of those who tested negative for bloodborne viruses on initial testing had subsequent screening performed. The high incidence of HIV and HCV, allied to the continued high risk activity that has been reported among drug users in Dublin despite increased availability of harm reduction interventions,\textsuperscript{17} highlights a clear need for a standardised protocol for follow-up testing of drug users.

We propose the introduction of a standardised risk assessment model that would be performed twelve months following a negative test. This will enable clients to be assessed for risk factors associated with the acquisition of the bloodborne viruses and for those who have put themselves at risk to be subsequently retested.

**HBV immunisation**

Immunisation against HBV is recommended for all injecting drug users. However there are a number of difficulties inherent in the process of conferring adequate immunity to HBV among drug users. Uptake of targeted or opportunistic immunisation programmes is often poor.\textsuperscript{14} In addition, drug users are less likely to mount a protective antibody response to completed immunisation programmes.\textsuperscript{30 31}

Among the sample studied here, 81\% had commenced a course of vaccinations against HBV. While the uptake is not as high as recently reported in addiction treatment centres in Italy,\textsuperscript{31} it compares quite favourably with uptake rates reported in earlier studies from Dublin.\textsuperscript{7} This may be due the recent introduction of guidelines for HBV immunisation in addiction treatment services in the area,\textsuperscript{32} or the regular sustained contact clients have with a multidisciplinary team of healthcare professionals in addiction treatment services in the area.

Fifteen per cent of the sample who had completed a course of vaccinations and had been tested for anti-HBs were found to have an antibody titre of less than 10 miu/ml, thereby supporting the evidence that injecting drug users are less likely to mount an adequate immune response to currently available HBV vaccines.\textsuperscript{30 31} Checking for immunity to HBV and if necessary, revaccinating, should be considered an essential part of any HBV immunisation guidelines, therefore.
CONCLUSIONS

This study reports encouraging findings regarding uptake of testing for bloodborne viruses and an improvement in uptake of immunisation against HBV. The introduction of immunisation and screening protocols appear to have facilitated these improvements.

The findings regarding HIV incidence and HIV prevalence among younger drug users are a source of some concern. Levels of repeat testing for bloodborne viruses are also concerning. There was no evidence of a consistent policy regarding repeat testing following an initial negative test and the introduction of such a policy within addiction services is required.

Given the prevalence and incidence figures of HCV, HBV and HIV in Dublin we can conclude that the rate of risk behaviour among IDUs remains high. While existing harm reduction measures have had an important role in the response to the medical and social problems resulting from illicit drug use, it appears their availability may need to be expanded. Specifically the interception of young users, new onset users and those progressing to injecting is necessary if the spread of HCV, HBV and HIV is to be slowed or halted. In addition, a stronger emphasis needs to be placed on educating drug users to enable the behavioural changes that are necessary to halt transmission of the bloodborne viruses.

It has been suggested that “a rejuvenated and multidisciplinary approach emphasising both sexual and needle sharing risk practices” could be important in preventing HIV transmission. It has also been suggested that a more sophisticated and individualised approach to harm reduction may be necessary. Based on the findings presented in this paper, policy-makers may need to consider a reassessment of current strategies with a view to further expansion and the adoption of alternative educational strategies.

ACKNOWLEDGEMENTS

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We also wish to acknowledge the role of the Virus Reference Laboratory in bloodborne virus testing.

Figure 3. — DISTRIBUTION OF ANTI-HBS TITRES

FUNDING

This study was commissioned by the Addiction Services of the South Western Area Health Board.

CONFLICT OF INTEREST

None.

REFERENCES


Correspondence to: Loretto Grogan, research Nurse, Addiction Services, Bridge House, Cherry Orchard Hospital, Dublin 10, Ireland Tel: 01 6206400 Mobile:086 8454289 Email: lorettogrogan@yahoo.com
Health-related quality of life during four-layer compression bandaging for venous ulcer disease: a randomised controlled trial

ABSTRACT

Background Venous leg ulceration is a chronic debilitating condition which negatively impacts on patients’ quality of life. Despite the application of gold standard treatment a number of patients suffer from ‘slow to heal’ ulcers, which can require treatment for years.

Aims The aim of this study was to compare the effects of four-layer compression bandaging (4LB) for treating venous leg ulcers with other available treatments on health-related quality of life during treatment.

Methods In this pragmatic trial, 200 patients with venous leg ulceration were randomised either to 4LB (intervention group; n=100) or to continue their usual system of care (control group; n=100). Analysis was by intention to treat; quality of life measurements were taken at randomisation and after six weeks of treatment.

Results 4LB provided greater quality of life benefits than the control group particularly in the area of physical activity and social functioning.

Conclusion Due to the long-term nature of treatment for many of these patients, the effects on quality of life should be considered when prescribing treatment. This study has shown that 4LB significantly improves the quality of life of patients during treatment for venous leg ulceration.

INTRODUCTION

Leg ulcers are a common and debilitating problem with a prevalence in Ireland of 0.12% overall, increasing to 1.03% in patients over 70 years of age. Eighty-one per cent of leg ulcers are venous in origin, resulting from venous hypertension. The application of graduated compression bandaging is the most widely recognised treatment for venous leg ulcers. Compression bandaging reverses venous hypertension promoting venous return, allowing the ulcer to heal, and 50-70% of ulcers heal at 12 weeks with this treatment. Venous leg ulceration is a chronic condition which can result in pain, limit mobility, alter body image and lower self-esteem, all of which negatively impact on patients quality of life. Therefore, when choosing treatment for a patient with venous ulceration it is imperative that treatment not only accelerates healing but also improves quality of life.

Many studies have examined the effectiveness of various treatments on ulcer healing but few randomised controlled trials include data on quality of life, which assess the impact chronic leg ulcers have on patients’ day-to-day lives. This study aimed to compare four-layered compression bandaging to other treatments available in a community setting for treating venous leg ulcers and establish what impact this treatment had on patients’ health-related quality of life.

PATIENTS AND METHODS

Public Health Nurses (PHN), Practice Nurses, and General Practitioners (GP) referred patients from the community with a suspected venous ulcer. These patients received written information about the study and were invited to attend for assessment. Assessment was carried out at the Mid-Western Regional Hospital, at local health centres, or at patients’ homes. Patients were included in the trial if they had a venous leg ulcer and were not being treated with 4LB. A venous ulcer was defined when there was clinical evidence of venous disease, the resting ankle brachial pressure index was ≥0.9, and no other cause was identified. Patients meeting the inclusion criteria were invited to enrol in the trial and...
written consent obtained. The trial was approved by the Research Ethics Committee at the Mid-Western Regional Hospital.

In this prospective randomised controlled trial, patients were randomised to 4LB (intervention group) or to continue with their usual care (control group). Before the study began, a random ‘intervention’/‘control’ list was generated for 200 patients by computer, and the results entered sequentially into sealed numbered envelopes. These envelopes were assigned to consecutive patients once consent was obtained. Information recorded at the recruitment phase included the age and sex of the patient, the duration of the ulcer, and any history of deep vein thrombosis (DVT), diabetes or rheumatoid arthritis. The ulcerated area was also measured and photographed.

Quality of life assessment was carried out at recruitment, with each patient completing quality of life assessment questionnaires. The disease specific quality of life instrument for chronic lower limb venous insufficiency (CIVIQ) was used, as well as the SF-36 generic questionnaire. The CIVIQ is a 20 item questionnaire designed specifically to measure health in patients with chronic venous disease. The 20 questions are divided into four domains; psychosocial, physical functioning, social functioning and pain. Lower scores from this questionnaire reflect better quality of life.

The SF-36, a generic questionnaire, consists of 36 questions measuring health across eight domains; physical functioning, role limitation due to physical health, bodily pain, general health, vitality, social functioning, role limitation due to emotional problems and mental health. Responses to questions within a domain are combined together to give a score from 0-100, the higher the score the better health indicated.

The aim of quality of life assessment was to detect differences between the health status of patients in the two groups during treatment. No assessment was made at the end of the study period. The patients were assessed by interview at recruitment to establish baseline scores, and again after six weeks of assigned treatment, if the ulcer remained unhealed (Tables 1 and 2). Six weeks was chosen as the mid-point between recruitment and probable ulcer healing.

Study outcomes were differences in patients’ health-related quality of life status at six weeks, time to healing and the direct cost to the health board per leg healed. The results from this study related to time to healing and cost analysis are published elsewhere.

During the study all patients had their leg ulcers dressed by their usual community nurse. This provided for continuity of care. Prior to this study all public health nurses in this region attended formal workshops and received individual training in the application of 4LB. A standard 4LB was used, comprising a sterile wound contact dressing, a natural padding bandage, a light conformable bandage, a light compression bandage and a flexible cohesive bandage. This combined system provided sustained external compression of 40mmHg at the ankle. The control group received a variety of treatments chosen by the public health nurse and the GP. Treatment in the control group included an assortment of topical dressings, such as hydrocolloids, alginates, paraffin and iodine dressings. Various absorbency dressings, low-pressure bandages and elasticated support were also used. One patient had laser therapy. Five patients in the control group had compression applied at some stage during their 3-month study interval. Twelve patients in the 4LB group were non-compliant, the main reason being intolerance to the high compression bandage. High absorbency dressings (n=11) and desloughing agents (n=8) were used at the discretion of the nurse in some patients in conjunction with 4LB.

Statistical analysis

Appropriate parametric and nonparametric summary statistics were calculated. The two-tailed Student t-test and the Mann Whitney U test were used, respectively to analyse differences in means and medians. A level of significance of 5% was used for all statistical tests. The sample size of 200 was calculated to detect differences between the two groups in time to healing as this was the primary study outcome, this sample size was also considered appropriate to detect differences in quality of life.

RESULTS

Our aim was to determine quality of life for patients while undergoing treatment. Baseline health scores pre-treatment, compared well in both groups (Tables 1 and 2). Quality of life questionnaires were completed for 92.9% (79/85) and 95.8% (91/95) of patients remaining unhealed at six weeks in the 4LB and control groups, respectively. The other patients did not fill out quality of life questionnaires as their ulcer was healed by week six. We chose six weeks as being the optimal time to measure quality of life during treatment.
Of the questionnaires used, the CIVIQ showed the most discernible clinical and statistically significant differences in perceived health status at six weeks, in preference to 4LB, most especially in the domains of physical activity and social functioning. There was a significant improvement in physical activity in the 4LB group with a median improvement of 18.7 after six weeks (31.25 vs 18.2), no difference was detected in the control group (p = 0.006, 4LB vs control). In the social functioning domain both groups baseline analysis were identical, again the greatest improvement after four weeks treatment was seen in the 4LB group, median improvement of 16.7 (50 vs 33.3) in 4LB and 8.3 (50 vs 41.7) in the control group (p = 0.001, 4LB vs control). For the global index domain the 4LB group experienced greatest improvement with a median difference of 10 at six weeks (32.5 vs 18.8) (p = 0.006, 4LB vs control). In support of this the SF-36 also displayed greater improvements in health benefits using 4LB. The most significant improvement after six weeks treatment was again seen in the area of physical function, the median improvement in the 4LB group was 15 (55 vs 70) whereas the control group showed a slight deterioration of 2.5 (52.5 vs 50) (p = 0.001, 4LB vs control). In the role-physical domain the baseline results for both groups were identical, again the most significant improvement after four weeks treatment was seen in the 4LB group, median improvement of 75 (25 vs 100) (p = 0.006, 4LB vs control).

**DISCUSSION**

Patients use the following words to describe life with a leg ulcer; pain, loss of mobility, disturbed sleep, offensive smell, fear, social isolation, anger, depression and negative self image. Most clinicians would accept that leg ulceration has a negative impact on patients’ health-related-quality-of-life (HRQoL) and various studies have shown this to be true. The first study to use HRQoL as an outcome measure, for patients undergoing treatment for venous leg ulcers was the Riverside leg ulcer project. This study assessed the effect of community leg ulcer clinics and concluded that effective treatment resulted in an overall improvement in patients’ QoL, with greatest improvements in the areas of pain, depression and hostility, particularly in patients whose ulcer healed. Few studies have examined the effects of treatment within randomised controlled trials. Franks et al conducted a randomised trial comparing the effect two types of four-layered compression bandage system had on patients’ QoL. This study showed no statistical difference between bandage systems presumably due to similar healing rates being achieved by both bandages. Improvement was directly related to ulcer healing rates with significant improvements in patients whose ulcer had healed, concluding that effective treatment is the key to improving QoL. These studies demonstrated that measuring health-related quality of life offers a holistic approach in evaluating various treatments, with the treatment which offers greatest healing rates being more likely to improve health related quality of life for patients. Although the concept of HRQoL may be difficult to measure, in a condition where the primary outcome, complete healing, may not be realised, QoL assessment of treatment is crucial.

In measuring HRQoL quantitatively two methods can be employed, generic or disease specific questionnaires. Generic questionnaires being general in nature can be used for any disease and thereby allow for comparisons between diseases, while disease specific questionnaires directly relate to the particular disease and show greater sensitivity to change than generic instruments. In this study, both methods have been used. The tools chosen were the generic Short Form 36-item Health Profile (SF-36), and the disease specific Chronic Venous Insufficiency Questionnaire (CIVIQ).

The findings here showed statistically significant differences between the two study groups in some SF-36 domains. Greater differences between groups may have been seen if the sample size was larger. This may be seen as a potential weakness in this study as the sample size chosen was calculated to detect differences in time to healing, but statistically significant differences were seen which indicate that this generic tool was successful in measuring quality of life changes.

The CIVIQ, being disease specific, showed slightly more clinical and statistically significant differences in favour of 4LB. This was especially true in the domains of physical activity and social functioning. The global index also showed a statistically significant improvement in favour of 4LB. The improvements in QoL detected in favour of the patients treated with 4LB may be attributed to improved healing rates which this group experienced, indicating that quality of life is directly related to rates of healing.
### Table 1.
**PATIENT PERCEIVED HEALTH STATUS (SCORES) BY RANDOMISED GROUP SF-36**

<table>
<thead>
<tr>
<th></th>
<th>BASELINE MEDIAN (INTER-QUARTILE RANGE)</th>
<th>WEEK 6 MEDIAN (INTER-QUARTILE RANGE)</th>
<th>DIFFERENCE IN GROUPS AT WEEK 6 MANN WHITNEY U TEST</th>
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<tbody>
<tr>
<td><strong>SF-36</strong></td>
<td></td>
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</tr>
<tr>
<td>Physical</td>
<td></td>
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<tr>
<td>Function</td>
<td>55 (35-80)</td>
<td>70 (45-85)</td>
<td>p=0.001</td>
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<tr>
<td>4LB Control</td>
<td>52.5 (25-80)</td>
<td>50 (25-80)</td>
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<tr>
<td>Role-Physical</td>
<td></td>
<td></td>
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<tr>
<td>4LB</td>
<td>25 (0-100)</td>
<td>100 (0-100)</td>
<td>p=0.006</td>
</tr>
<tr>
<td>Control</td>
<td>25 (0-100)</td>
<td>25 (0-100)</td>
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<tr>
<td>Bodily Pain</td>
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<tr>
<td>4LB</td>
<td>52 (42-84)</td>
<td>84 (61-100)</td>
<td>p=0.840</td>
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<tr>
<td>Control</td>
<td>51.5 (41-72)</td>
<td>72 (51-100)</td>
<td></td>
</tr>
<tr>
<td>General Health</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4LB</td>
<td>77 (67-82)</td>
<td>77 (62-87)</td>
<td>p=0.202</td>
</tr>
<tr>
<td>Control</td>
<td>72 (62-82)</td>
<td>72 (62-82)</td>
<td></td>
</tr>
<tr>
<td>Vitality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4LB</td>
<td>65 (55-75)</td>
<td>75 (60-80)</td>
<td>p=0.160</td>
</tr>
<tr>
<td>Control</td>
<td>60 (50-75)</td>
<td>60 (55-75)</td>
<td></td>
</tr>
<tr>
<td>Social Function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4LB</td>
<td>75 (50-100)</td>
<td>100 (75-100)</td>
<td>p=0.322</td>
</tr>
<tr>
<td>Control</td>
<td>75 (50-100)</td>
<td>87.5 (62.5-100)</td>
<td></td>
</tr>
<tr>
<td>Role-Emotional</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4LB</td>
<td>100 (0-100)</td>
<td>100 (100-100)</td>
<td>p=0.150</td>
</tr>
<tr>
<td>Control</td>
<td>100 (0-100)</td>
<td>100 (33.3-100)</td>
<td></td>
</tr>
<tr>
<td>Mental Health</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4LB</td>
<td>88 (80-92)</td>
<td>88 (80-92)</td>
<td>p=0.030</td>
</tr>
<tr>
<td>Control</td>
<td>84 (76-88)</td>
<td>88 (76-92)</td>
<td></td>
</tr>
</tbody>
</table>

6 week assessment: 4LB n=79, control n=91.
Higher SF-36 scores indicate better health status. The converse applies to the CIVIQ.

### Table 2.
**PATIENT PERCEIVED HEALTH STATUS (SCORES) BY RANDOMISED GROUP CIVIQ**

<table>
<thead>
<tr>
<th></th>
<th>BASELINE MEDIAN (INTER-QUARTILE RANGE)</th>
<th>WEEK 6 MEDIAN (INTER-QUARTILE RANGE)</th>
<th>DIFFERENCE IN GROUPS AT WEEK 6 MANN WHITNEY U TEST</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CIVIQ</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4LB</td>
<td>43.75 (25-62.5)</td>
<td>18.8 (6.3-37.5)</td>
<td>p=0.140</td>
</tr>
<tr>
<td>Control</td>
<td>50 (31.3-62.5)</td>
<td>31.3 (18.8-43.8)</td>
<td></td>
</tr>
<tr>
<td>Physical</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4LB</td>
<td>31.25 (12.5-50)</td>
<td>12.5 (6.3-37.5)</td>
<td>p=0.006</td>
</tr>
<tr>
<td>Control</td>
<td>37.5 (25-62.5)</td>
<td>37.5 (12.5-62.5)</td>
<td></td>
</tr>
<tr>
<td>Social</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4LB</td>
<td>50 (33.3-66.7)</td>
<td>33.3 (16.7-41.7)</td>
<td>p=0.001</td>
</tr>
<tr>
<td>Control</td>
<td>50 (33.3-66.7)</td>
<td>41.7 (25-58.3)</td>
<td></td>
</tr>
<tr>
<td>Psychological</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4LB</td>
<td>19.4 (11.1-33.3)</td>
<td>13.9 (11.1-25)</td>
<td>p=0.488</td>
</tr>
<tr>
<td>Control</td>
<td>22.2 (13.9-33.3)</td>
<td>19.4 (11.1-27.8)</td>
<td></td>
</tr>
<tr>
<td>Global</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4LB</td>
<td>32.5 (20.0-45.0)</td>
<td>18.8 (12.5-31.3)</td>
<td>p=0.006</td>
</tr>
<tr>
<td>Control</td>
<td>30.3 (22.5-48.8)</td>
<td>28.8 (18.8-43.8)</td>
<td></td>
</tr>
</tbody>
</table>
In assessing quality of life we chose to use quantitative analysis, another possibility would have been to take a qualitative approach and carry out interviews with sample patients from both groups. For this study we felt it would be more accurate to assess a large number of patients quantitatively in order to obtain a global view of patients with venous leg ulceration. Future research may be carried out to determine whether qualitative research produces similar results.

CONCLUSION

Leg ulcers greatly impact on patients’ day-to-day lives, reducing their quality of life. The aim of venous leg ulcer treatment is complete healing, however as this may not always be attainable quality of life must be recognised as an important outcome measure. This study examined the effect of treatment on patients’ quality of life. The results highlighted the quality of life benefits which 4LB provides, namely improved physical and social functioning, concluding that 4LB provides increased quality of life benefits when compared to alternative dressing options.

ACKNOWLEDGEMENTS

We gratefully appreciate the generous co-operation during this trial of the Public Health Nurses, Practice Nurses, and GPs in the Mid-Western Health Board and the Department of Mathematics and Statistics, University of Limerick.

REFERENCES


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Autologous stem cell transplantation in myeloma: the St James’s Hospital experience, 1997-2003

ABSTRACT
Background High-dose treatment with autologous stem cell transplantation (ASCT) has become the standard of care for patients with myeloma below the age of 65 years.
Aims We report an audit of 60 patients (median age: 52.5 years) who underwent ASCT in the National Bone Marrow Transplant centre in St James’s Hospital in Dublin between 1997 and 2003 inclusive.
Methods Clinical and laboratory data were retrieved from patient medical records and hospital information management systems.
Results Thirty-six patients had IgG, 11 IgA, 1 IgD, 9 light chain and 3 non-secretory MM. Fifty-seven (95%) patients received anthracycline-corticosteroid combination chemotherapy prior to autografting. There was no transplant-related mortality (TRM). Complete (CR) and Partial Responses (PR) were seen in 16 (29.6%) and 29 (53.7%) of those evaluable (n=54 (90%)). The actuarial Progression-Free (PFS) and Overall Survival (OS) rates at five years are 13% and 55% respectively.
Conclusion Centre outcome is comparable to published international series and supports the use of ASCT in the treatment of this malignancy.

INTRODUCTION
Myeloma is a malignancy of mature B-cells (plasma cells) and is characterised clinically by anaemia, bone pain and renal impairment. The median age at diagnosis is 65 years and it represents 10% of haematological cancers in most registries. The combination of melphalan and prednisolone (MP) has been widely used in the treatment of myeloma, yielding survival of approximately three years. Despite many trials of more complex chemotherapy regimens, meta-analysis failed to demonstrate that any were superior to MP in terms of OS. Interest therefore focused on exploiting the known dose-response effect seen with melphalan. The UK Royal Marsden Hospital group was the first to report the achievement of complete responses in a large proportion of those receiving higher doses. The subsequent addition of autologous marrow and myeloid growth factor support allowed dose escalation to 200mg/m². A seminal randomised trial leading to the more widespread acceptance of autografting in myeloma was published by the IFM French Myeloma Group in 1996. High-dose therapy was associated with a five-year Overall Survival of 52% compared to 10% in the conventional chemotherapy arm. The superiority of ASCT in term of PFS and OS has since been confirmed by other centres. In the UK myeloma VII trial, ASCT increased median survival by almost one year (54.1 months vs. 42.3 months).

Transplantation techniques continue to be refined. The choice of conditioning regimen, methods of processing of the stem cell product and aspects of supportive care have evolved over the last decade. Novel agents have also been introduced in the treatment of relapsed disease post-autograft. We present data on 60 patients with MM who have undergone HDT with ASCT at the National Bone Marrow Transplant centre between 1997 and 2003. Patient demographics, pre-transplant characteristics, engraftment data, post-autograft treatment details and survival rates are provided.

METHODS
Patients This study was approved by the hospital research ethics committee. Sixty patients with myeloma received HDT with ASCT at the National Bone Marrow Transplant centre at St. James’s Hospital between January 1997 and December 2003. Clinical details are shown in Table 1. Patients were referred to the use of ASCT in the treatment of this malignancy.
from nine hospitals: St James’s (n=18), Mid-West Regional, Limerick (n=9), Midland Regional, Tullamore (n=7), Waterford Regional (n=7), AMNCH, Tallaght (n=7), Beaumont (n=6), Letterkenny (n=3), Sligo (n=2) and the Royal Victoria, Belfast (n=1). Care of patients was shared between referring hospitals and St. James’s Hospital. All autograft procedure took place at St James’s Hospital.

Eighteen patients were transplanted between 1997 and 2000, and 42 patients between 2001 and 2003. The majority (95%) were treated prior to autografting with the conventional combination of an anthracycline and corticosteroid. Alkylator-based regimens such as Melphalan and prednisolone (MP) or ABCM (Adriamycin, BCNU, cyclophosphamide and melphalan) were given to ten (16.6%) patients. Most patients (81.6%) received a single line of chemotherapy (median of four cycles) before proceeding to ASCT. In terms of disease status after completion of chemotherapy, four (7%) achieved a complete response (CR - absence of monoclonal protein on immunofixation), 46 (76%) a partial response (PR - >50% reduction in paraprotein), four (7%) a minor response (MR - >25%, <50% reduction in paraprotein) and six (10%) stable disease (<25% reduction in paraprotein). The median interval between diagnosis and transplant was nine months (range: 5-25 months).

**Table 1**

<table>
<thead>
<tr>
<th>DEMOGRAPHIC AND CLINICAL DETAILS OF THE PATIENT POPULATION</th>
<th>NUMBER</th>
<th>Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PATIENTS</strong></td>
<td>60</td>
<td>100</td>
</tr>
<tr>
<td><strong>AGE (MEDIAN, RANGE)</strong></td>
<td>52 (38-66)</td>
<td>100</td>
</tr>
<tr>
<td>&lt;50 years</td>
<td>19</td>
<td>31.6%</td>
</tr>
<tr>
<td>51-60 years</td>
<td>30</td>
<td>50.0%</td>
</tr>
<tr>
<td>&gt;60 years</td>
<td>11</td>
<td>18.4%</td>
</tr>
<tr>
<td><strong>GENDER</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>39</td>
<td>65.0%</td>
</tr>
<tr>
<td>Female</td>
<td>21</td>
<td>35.0%</td>
</tr>
<tr>
<td><strong>ISOTYPE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgG</td>
<td>36</td>
<td>60.0%</td>
</tr>
<tr>
<td>IgA</td>
<td>11</td>
<td>18.3%</td>
</tr>
<tr>
<td>IgD</td>
<td>1</td>
<td>1.7%</td>
</tr>
<tr>
<td>Light chain</td>
<td>9</td>
<td>15.0%</td>
</tr>
<tr>
<td>Non-secretory</td>
<td>3</td>
<td>5.0%</td>
</tr>
<tr>
<td><strong>YEAR OF AUTOGRAFT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1997</td>
<td>2</td>
<td>3.3%</td>
</tr>
<tr>
<td>1998</td>
<td>8</td>
<td>13.3%</td>
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<tr>
<td>1999</td>
<td>4</td>
<td>6.7%</td>
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<tr>
<td>2000</td>
<td>4</td>
<td>6.7%</td>
</tr>
<tr>
<td>2001</td>
<td>13</td>
<td>21.7%</td>
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<tr>
<td>2002</td>
<td>10</td>
<td>16.6%</td>
</tr>
<tr>
<td>2003</td>
<td>19</td>
<td>31.7%</td>
</tr>
<tr>
<td><strong>PRIOR CHEMOTHERAPY</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAD</td>
<td>32</td>
<td>53.3%</td>
</tr>
<tr>
<td>Idarubicin-Dexamethasone</td>
<td>16</td>
<td>26.6%</td>
</tr>
<tr>
<td>Thalidomide-Dexamethasone</td>
<td>2</td>
<td>3.3%</td>
</tr>
<tr>
<td>Alkylators</td>
<td>10</td>
<td>16.6%</td>
</tr>
<tr>
<td>≥1 LINE OF CHEMOTHERAPY</td>
<td>11</td>
<td>18.3%</td>
</tr>
</tbody>
</table>

**Treatment**

Mobilised peripheral blood stem cells (PBSC) were used as the source of stem cells in all but the first ASCT in 1997, who received a combination of bone marrow and PBSC. Throughout the seven years, four different mobilisation regimens were used. Fourteen patients received IEV (ifosfamide, epirubicin and etoposide), 21 cyclophosphamide 4g/m²+G-CSF 5µg/kg and 24 cyclophosphamide 2g/m²+G-CSF 10µg/kg. One patient was mobilised with G-CSF only. Leucapheresis was commenced when the peripheral blood CD34+ cell count was greater than 20/µL. Harvesting was carried out on consecutive days aiming for a minimum target dose of 4.5x10⁶/kg CD34+ cells, sufficient to allow for two HDT. All PBSC products were cryopreserved with a final dimethyl sulfoxide concentration of 10% and stored at −190°C in vapour-phase liquid nitrogen. In 12 of the 60 autograft procedures, CD34+ selection was performed using the Isolex 300i system (Nexell Therapeutics Inc., Irvine, CA, USA), according to the manufacturer’s instructions.

The conditioning regimen prior to ASCT consisted of busulphan and cyclophosphamide in five early transplants (1997-1998). Since then, all patients received melphalan (140-200mg/m²) as a single agent. The dose has been divided in two and given intravenously over 30 minutes on Days -3 and -2. The melphalan dose was reduced from the standard of 200mg/m² for six (9.7%) patients with impaired renal function.
G-CSF (5µg/kg) (Neupogen, Amgen) was administered subcutaneously from Day +1 until two days after neutrophil engraftment (Absolute Neutrophil Count (ANC)>0.5x10^9/l). Routine laboratory investigations included daily Full Blood Count (FBC) and renal, liver and bone profiles. Valaciclovir (500mg OD PO) was given as anti-viral prophylaxis from Day 0. Co-trimoxazole (Septin, 960mg BD PO Mon, Wed, Fri) was given as anti-pneumocystis prophylaxis from the time of engraftment. Both these medications were continued for three months or until the peripheral blood CD4+ count was >200/µl. Mycostatin (1ml QDS PO) was given as anti-fungal prophylaxis. Broad-spectrum antibiotic treatment with the combination of piperacillin-tazobactam and ciprofloxacin was used in the event of neutropic fever. Aminoglycosides were avoided due to nephrotoxicity.

Response criteria
Disease response was graded by EBMT criteria. Complete Response (CR) was defined as the absence of a detectable monoclonal component in serum or in urine by immunofixation analysis, with <5% bone marrow plasma cells. A Partial Response (PR) was achieved when at least a 50% reduction in initial paraprotein levels was achieved and a reduction in light chain (Bence Jones) proteinuria by >90% or to <0.28/24h. A Minor Response (MR) was defined as a reduction in initial paraprotein levels by 25-49% and a reduction in light chain proteinuria by 50-89%, but exceeding >0.28/24h. Apart from CR, PR and MR, other categories included No response (NR) and Progressive Disease (PD), an increase in serum or urine paraprotein by 25%.

Relapse was defined as recurrence of monoclonal protein or bone marrow plasmacytosis if relapse was from CR, or a 25% increase from minimal tumour mass if relapse was from PR.

Statistical analysis
Data were collected to 1st February 2004. The Kaplan-Meier method was used to estimate probabilities of Progression-Free Survival (PFS, time to disease progression) and Overall Survival (OS, time to death).

RESULTS
Cell doses and engraftment
The median number of CD34+ cells infused was 3.95x10^6 CD34+ cells/kg (range: 2.4-18.75x10^6 CD34+ cells/kg).

The median time to neutrophil engraftment (>0.5x10^9/l) was ten days (range: 7-18). The median time to platelet engraftment (Plts>50x10^9/l) was 14 days (range: 9-39). No significant differences were seen in the times to engraftment when those of the 12 patients who received CD34+ selected autografts were compared with those of the remaining 48 patients who received unselected grafts. There was no transplant-related mortality.

Response to autograft
Data to evaluate response were available in 54 (90%) patients. The absence in certain referring hospitals of available bone marrow aspirate or serum electrophoresis results for the post-autograft period precluded assessment of disease response by EBMT criteria in six individuals. Complete (CR) and partial (PR) responses to the autograft were seen in 16 (29.6%) and 29 (53.7%) patients respectively. The overall response rate was (CR+PR) 83.3%.

Progression-free (PFS) and Overall Survival (OS)
The actuarial PFS rates at three and five years were 41% and 13% respectively (Figures 1 and 2). The actuarial OS rates at three and five years were 78% and 55% respectively. No significant differences were seen in the rates of either PFS or OS when those of the 12 patients who received CD34+ selected autografts were compared with those of the remaining 48 patients who received unselected grafts.

DISCUSSION
This is a retrospective assessment of 60 patients who underwent autografting for myeloma at the National BMT centre in St James’s Hospital between 1997 and 2003. Patients were referred from nine hospitals. The diagnosis was made and initial chemotherapy administered at the referring institution in all cases. Early liaison with the BMT centre facilitated scheduling of the mobilisation and ASCT procedure. An autologous BMT co-ordinator has been appointed to organise this tertiary referral service. The median age at ASCT was 52 years. Eleven patients (18.4%), however, were over 60 years of age, providing further evidence of the safety of this treatment in an older population. Recent guidelines from the UK Myeloma Forum and the International Myeloma Foundation advise that patients aged 60-70 years with good performance status may be considered suitable candidates for ASCT. There is no evidence, however, to support the use of ASCT in those over the age of 70 years, and toxicity is clearly increased. Patients who are candidates for autografting should not be exposed to alkylating agents such as melphalan, which are known to damage haemopoietic stem cells. Tricot et al found that even patients exposed to a median of only four months...
Figure 1 — Kaplan-Meier curve estimating probabilities of overall survival (OS, time to death).

Figure 2 — Kaplan-Meier curve estimating probabilities of progression-free survival (PFS, time to disease progression).
of prior alkylator therapy showed a significant delay in platelet recovery post-autograft when compared to those who were never exposed. In our cohort, only ten (16.6%) patients received alkylating agents prior to autografting, and of the five who received melphalan, the median number of cycles was three.

The VAD (Vincristine, Adriamycin and Dexamethasone) protocol was introduced by the MD Anderson group 20 years ago, and was associated with a higher response rate and more rapid disease control than MP. In the last three years, the use of the related IDEX (Idarubicin, Dexamethasone) regimen has become more widespread. Idarubicin is an oral anthracycline and facilitates the increasing trend towards out-patient-based administration of chemotherapy. Sixteen (26.6%) of the more recent patients received IDEX-based cytoreductive therapy pre-ASCT. Non-myelosuppressive induction therapy with oral dexamethasone alone also appears to be effective and has been shown not to compromise the efficacy of subsequent ASCT.

Evidence is also emerging that lack of response to induction chemotherapy does not seem to preclude a successful ASCT. Kumar et al at the Mayo Clinic compared 50 patients with primary refractory disease and 101 patients with chemosensitive disease in term of subsequent response to ASCT. Ten (20%) refractory patients and 35 (35%) in the chemosensitive group achieved CR. The estimated one-year PFS rates were 70% and 83%, respectively. These results suggest that the option of ASCT should be considered in all younger patients with myeloma regardless of response to initial induction therapy. Six (10%) patients in our cohort had refractory (i.e. stable) disease after initial induction chemotherapy. More prolonged follow-up will allow for the PFS rate of this group to be compared with that of those who responded to initial treatment.

In general, stem cells should be collected and cryopreserved as soon as the best possible response has been obtained. Mobilisation of PBSC can be achieved by chemotherapy, myeloid growth factors or a combination of the two as in our group. Three sequential mobilisation protocols were in use during this period: (i) (IEV) Ifosfamide, Epirubicin, Etoposide (VP16), (ii) Cyclophosphamide 4g/m2+G-CSF 5µg/kg, and (iii) Cyclophosphamide 2g/m2+G-CSF 10µg/kg. In an analysis of variables influencing the kinetics of engraftment, the minimal threshold dose of cells necessary for prompt engraftment was >2x10⁶ CD34+ cells/kg body weight in patients who had received up to two years of prior chemotherapy. The median cell dose returned to patients in our cohort was 3.95 x10⁶ CD34+ cells/kg.

Attempts have been made to purge myeloma cells from grafts using positive selection for CD34, an antigen expressed on stem cells but not by the myeloma clone. While this form of selection has been shown to reduce the malignant cell content of the graft by two to 4.5 logs without adversely affecting the rate of engraftment, long-term follow-up of a randomised study failed to show any survival advantage. It also appears that such selection is associated with a delay in immune reconstitution. As a result, only 12 of the early patients received CD34-selected grafts. The grafts from the remaining 48 patients did not undergo any manipulation.

Two regimens were employed for conditioning. Five early patients received busulphan and cyclophosphamide. The other 55 patients received melphalan (140-200mg/m²). A treatment-related mortality rate of 25% has since been reported in a Seattle series that used busulphan-based conditioning. In a randomised trial comparing melphalan alone with the combination of melphalan and TBI, there was no TRM in the melphalan arm.

Consensus now exists that single-agent melphalan (200mg/m²) is the recommended conditioning regimen. Although most (89%) patients received full dose melphalan (200mg/m²), the dose was reduced in six cases (three at 180mg/m² and three at 140mg/m²) due to renal impairment. Badros et al have shown that intermediate dose melphalan (140mg/m²) is as effective as full dose (200mg/m²) but is associated with less toxicity in patients with impaired renal function. Recent results from this group suggest that dialysis-dependent renal failure can be reversed by ASCT in some patients.

Patients received G-CSF (5µg/kg/day) from Day+1 until myeloid engraftment. Recovery of the neutrophil count (>0.5x10⁹/L) occurred at a median of Day +10 (range 7-18). In a recent single-centre report of 127 patients who underwent ASCT for myeloma where most (86%) did not receive G-CSF, neutrophil engraftment was achieved at a median of Day +16 (range 10-35). While no randomised data exist, the reduced duration of neutropenia may have contributed to the absence of TRM in our series. Fifty-four patients (90%) were evaluable for disease response post-ASCT. According to EBMT...
criteria, almost a third of patients (29.6%) achieved a complete response. The attainment of CR is predictive of longer PFS and OS. In a study of 59 patients, Nadal et al found those who achieved CR had a PFS (median 47 vs. 36 months) and an OS (median not reached (at 76 months follow-up) vs. 60 months) significantly longer than those attaining a lower degree of response. As most of the ASCT procedures were done in 2002-2003, the effect of attaining CR on PFS and OS in our cohort will be assessed after longer follow-up.

Autografting clearly represents a therapeutic advance. It is not, however, a curative treatment. Although the Kaplan-Meier curve for Overall Survival (OS) (Figure 1) appears to suggest a plateau after 50 months, this is more likely to reflect the small number of patients who have achieved this degree of follow-up at this point. The experience of all large autografting trials to date is one of progressive disease reactivation. Both PFS and OS decline steadily over time. For the bulk of patients, autografting therefore remains a palliative procedure. The median PFS was 31 months. Post-ASCT care includes monthly attendance at the haematology day-ward for intravenous zoledronic acid, a bisphosphonate shown to decrease the incidence of skeletal-related events (pathologic fracture, spinal cord compression, radiation therapy, or surgery to bone). Periodic clinical assessment is also required to detect any evidence of disease progression. The pattern of reactivation of disease post-ASCT is varied. In a follow-up of 560 patients in the Spanish myeloma transplant registry, 280 (52%) had relapsed or progressed at a median follow-up of 23 months. Most patients had a progressively increasing paraprotein in addition to different clinical symptoms, mainly osteolytic lesions. 40 (14%) patients, however, relapsed with multiple plasmacytomas only. Six (2%) patients fulfilled criteria for plasma cell leukaemia. A similar spectrum of presentations of relapse was seen in our cohort. This highlights the need for thorough post-ASCT assessment including questions regarding bone pain, examination for evidence of plasmacytoma, serial monitoring of any monoclonal paraprotein, blood film review and diagnostic imaging.

No tandem autografts were performed at St James’s Hospital during this period. Sufficient stem cells have, however, been collected to allow for the option of a second autograft in the event of disease reactivation in a medically fit individual who is felt to be appropriate for this option.

In our cohort, actuarial OS at five years is 55%. This reflects both re-treatment with conventional combination chemotherapy and the recent introduction of novel agents such as Thalidomide.

When employed in heavily pre-treated patients, this latter drug was reported as having a response rate of 32%. This represents the first compound in a new class of agent, immunomodulatory drugs (IMiDs), which target the myeloma clone through a number of pathways including anti-angiogenesis, disruption of the cell-stroma interaction and cytokine down-regulation. By combining IMiDs with other new drug classes, such as proteosome inhibitors, durable disease control may be a realistic goal.

In summary, autografting represents a significant advance in the care of patients with myeloma. When widely applied within a healthcare system, it has been shown to result in prolonged survival for the total patient population aged less than 60 years. The procedural complications and outcome data for our group are comparable with recently published series; the median survival of patients who underwent ASCT in the myeloma VII trial was 54.1 months. Future advances must address residual disease post-ASCT.

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Changing trends in the management of Infantile Hypertrophic Pyloric Stenosis- an audit over 11 years

ABSTRACT

Background This article is a follow-up to an audit performed by the Department of Surgery and published in the Irish Journal of Medical Science in 1996. This audit reviewed all cases of Infantile Hypertrophic Pyloric Stenosis (IHPS) operated on over 22 years up to 1991.

Aims We aim to demonstrate that radiologic investigations, namely barium meal and ultrasound, have been increasingly employed in the diagnosis of IHPS. In addition, ultrasound is now the investigation of choice.

Methods We have reviewed all cases of IHPS, at the same institution, over the subsequent 11 years, with reference to any radiological investigations performed. In the previous study, the diagnosis of IHPS was made clinically in 92.6% with the remainder diagnosed radiologically.

Results Over 11 years, 157 patients were diagnosed with IHPS. Male to female ratio was 4.06:1. Median age was four weeks (range 1-18 weeks). Twenty-four per cent had a barium meal, 36% had an ultrasound and 13% had both performed.

Conclusion We conclude a change in practice in the management of IHPS with radiology, particularly ultrasound, playing an increasing role.

INTRODUCTION

IHPS is a condition affecting young infants, in which the antrypyloric portion of the stomach becomes abnormally thickened and manifests as obstruction to gastric emptying.\(^1\) The incidence is approximately 2-5/1000 with a peak incidence of 3-6 weeks. The aetiology is unknown. Infants typically present with non-bilious, projectile vomiting. Clinical diagnosis relies upon the palpation of a thickened pylorus or olive. Barium meal features include a narrow and elongated pylorus; the so-called string sign. In addition there is compression of the duodenal bulb and indentation of the gastric antrum (shoulder sign). Ultrasound findings include an elongated canal of 15-18mm (Figure 1) and transverse muscle thickness above 3mm in diameter (Figure 2).\(^1\)

METHODS

Using the Hospital Inpatient Enquiry Database (HIPE), all patients with a diagnosis of IHPS from January 1992 to June 2003 were included. There were 157 patients; 126 male and 31 female (M: F 4.06:1). We then consulted the Radiology Information System (RIS) and determined which of these patients had radiology investigations performed, namely barium meal and/or ultrasound. For those patients who had radiology performed, we recorded the ultrasound measurements, where available, and whether the results were diagnostic.

RESULTS

Of 157 patients, 38 (24%) were investigated with barium meal and 56 (36%) with ultrasound. Twenty-one patients (13%) had both barium meal and ultrasound performed.

In the barium group of 38 patients, three patients were excluded, as one had their barium performed prior to admission, one barium meal was unreported and the other was performed post-operatively. Thirty-five (22% of total sample) patients of this group were eligible for consideration. Twenty-four (68% of these 35 patients) were reported as definitively diagnosing pyloric stenosis, with the remainder not yet reaching diagnostic criteria.

In the ultrasound group of 56 patients, two patients were excluded as one ultrasound was performed prior to admission and one was unavailable for...
reporting. This left 54 patients of whom 35 had ultrasound alone and 21 had both ultrasound and barium. In the group of 35, a definitive diagnosis was made in 30 (86%) cases with the remaining five patients thought to be evolving IHPS.

Of the group that had both barium meal and ultrasound (21 patients), barium was used only to confirm the diagnosis where ultrasound measurements did not yet reach diagnostic criteria. Also, one has to consider that IHPS is an evolving condition. Patients at the younger end of the age spectrum at the time of presentation may not initially meet ultrasound criteria. These patients could have either a barium meal or an interval ultrasound for confirmation.

DISCUSSION
Barium meal features of IHPS are widely accepted. There has been much debate as to the acceptable size criteria for ultrasound diagnosis of IHPS. Currently a pyloric muscle thickness of greater than 0.3mm is accepted in most centres. Early in its use, the required ultrasound measurements for diagnosis were higher. This partly explains our group of patients who had both barium and ultrasound performed, where initial measurements did not reach diagnostic criteria. Also, one has to consider that IHPS is an evolving condition. Patients at the younger end of the age spectrum at the time of presentation may not initially meet ultrasound criteria.

Figure 1 (far left) — LONGITUDINAL ULTRASOUND PYLORUS

Figure 2 — TRANSVERSE ULTRASOUND PYLORUS

Figure 3 — LINE GRAPH SHOWING CHANGING TRENDS IN THE ROLE OF RADIOLOGY IN DIAGNOSIS OF IHPS.
This study indicates changing trends in diagnosis of IHPS. In the series by Maher et al in this hospital, only 7.4% underwent upper gastrointestinal contrast studies and ultrasound was not used.5

In the subsequent 11 years (January 1992 to June 2003), this has increased to 24% having barium meal and 36% having ultrasound performed. The use of barium was at its highest early in the 1990s. With the exception of 2001, there has been a steady increase in the use of ultrasound over time. The decreased use of ultrasound in this year was due to local technical factors limiting service availability. Almost 90% of patients diagnosed with IHPS in 2002 had ultrasound performed (Figure 3). This reflects international trends, with fewer patients with IHPS diagnosed solely on clinical grounds and ultrasound playing an increasing role.6

Many patients now present early with symptoms of IHPS. Accurate clinical diagnosis in patients in whom a thickened antropyloric muscle is not readily palpable can be difficult. Delay in diagnosis can lead to electrolyte imbalance, making the patient a suboptimal surgical candidate. Ultrasound is fast and readily available. Ultrasound can make an accurate, early diagnosis, is non-invasive and does not involve ionizing radiation.

In the initial audit performed in this hospital, approximately 90% of the patients were diagnosed clinically whereas in the last year of our study almost 90% of patients had ultrasound performed. Ultrasound imaging is now the primary tool to diagnose IHPS.

REFERENCES


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Trends in Ophthalmic Surgery in Ireland

ABSTRACT

Aims This study was designed to document the changing trends in ophthalmic surgery in acute public hospitals in the Republic of Ireland over the years 1994 to 2001.

Method We obtained Hospital In-Patient Enquiry (HIPE) data returned from the major acute public hospitals to the Economic and Social Research Institute. We searched for cataracts, glaucoma, retinal detachment, strabismus, corneal transplant and repair of perforating injuries of the globe.

Results There was a 24% increase in the total number of the searched operations occurring during the study period, from 8,857 procedures in 1994 to 11,005 in 2001. In 2001, cataract surgery alone counted for 82% of all procedures performed. There was a large increase in cataract (49%) and vitreo-retinal procedures (41%) reported between 1994 and 2001. Conversely, a large fall in trabeculectomy (67%), strabismus (63%) and corneal transplant (52%) procedures occurred during the study period.

Conclusion These data suggest that surgical numbers in ophthalmology in Ireland are increasing and the relative proportions are changing.

INTRODUCTION

In recent years, there have been reports of a reduction in the number of surgical procedures for glaucoma performed in the United Kingdom.1,2 There are also reports of increases in cataract surgery being performed,3,4 as well as a reduction in strabismus operations.5 This information may be relevant for planning resource allocation in ophthalmology in Ireland. We studied the reported national figures for ophthalmic surgery in Ireland over the past eight years to report changes in emphasis in ophthalmic surgery.

METHODS

A search of national figures of ophthalmic operations in the Republic of Ireland was performed. We used Hospital In-Patient Enquiry (HIPE) data supplied to us by the Economic and Social Research Institute (ESRI), Dublin, Ireland.6

The HIPE system is a computer-based health information system designed to collect clinical data on discharges in acute hospitals in Ireland. It was established in 1971 and by 1990 had 45 participating hospitals with an estimated response rate of 54.8%. However, by 1999 there were 60 participating hospitals with an estimated response rate of 94.2%.6

Search results are accompanied by estimated coverage of the system for each year. The coding scheme used was the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9CM).6 HIPE data include both in-patient and day care surgery performed in theatre.

Search method

The ICD-9CM codes used for the search are illustrated in Table 1. Entries are coded as discharges with up to 4 procedures included for each event. The number of procedures performed was taken as the number of discharges that had the included procedures performed. For example, a retinal detachment case may have several procedures performed but nevertheless would only be included as one discharge.

All searches were for the years 1994 to 2001 inclusive. The search was performed in December 2002 to allow the greatest possible inclusion of data from 2001. These operations were chosen as they represent the bulk of the workload in ophthalmic surgery.

RESULTS

Overall, the total number of all discharges included was 76,337. There was a 24% increase in the number of procedures during the observed period, from 8,857 to 11,005.

The average sensitivity of coverage was 94.5% (range 91-96%) according to Department of Health estimates. The results of the search are shown in Table 2.
### Table 1
**ICD-9CM CODES AND DESCRIPTION OF DIAGNOSES AND PROCEDURES ASSOCIATED WITH COMMON OPHTHALMOLOGY SURGICAL PRACTICE**

<table>
<thead>
<tr>
<th>PROCEDURE</th>
<th>ICD-9CM DESCRIPTION OF PROCEDURE PERFORMED OR DIAGNOSIS</th>
<th>ICD-9CM CODE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Removal of an eye</td>
<td>Evisceration of eyeball</td>
<td>16.3</td>
</tr>
<tr>
<td></td>
<td>Enucleation of eyeball</td>
<td>16.4</td>
</tr>
<tr>
<td></td>
<td>Exenteration of orbital contents</td>
<td>16.5</td>
</tr>
<tr>
<td>Primary repair of a ruptured globe</td>
<td>Suture of corneal laceration</td>
<td>11.51</td>
</tr>
<tr>
<td></td>
<td>Suture of laceration of sclera</td>
<td>12.81</td>
</tr>
<tr>
<td></td>
<td>Repair of rupture of eyeball</td>
<td>16.82</td>
</tr>
<tr>
<td></td>
<td>Other repair of injury of eyeball or orbit</td>
<td>16.89</td>
</tr>
<tr>
<td>Corneal transplants</td>
<td>All forms of corneal transplant excluding pterygium excision with corneal graft</td>
<td>11.60 to 11.69</td>
</tr>
<tr>
<td>Strabismus operations</td>
<td>All types of ocular misalignment</td>
<td>378.00 to 378.9</td>
</tr>
<tr>
<td></td>
<td>Operations on extraocular muscles</td>
<td>15.0 to 15.9</td>
</tr>
<tr>
<td>Trabeculectomy</td>
<td>Trabeculectomy ab externo</td>
<td>12.64</td>
</tr>
<tr>
<td>Vitreo-retinal procedures</td>
<td>Repair of retinal detachment with scleral buckling and implant</td>
<td>14.4</td>
</tr>
<tr>
<td></td>
<td>Other repair of retinal detachment</td>
<td>14.5</td>
</tr>
<tr>
<td></td>
<td>Operations on vitreous</td>
<td>14.71</td>
</tr>
<tr>
<td></td>
<td>Other removal of vitreous</td>
<td>14.72</td>
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<tr>
<td></td>
<td>Other mechanical vitrectomy</td>
<td>14.74</td>
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<tr>
<td>Cataract extraction</td>
<td>Cataract</td>
<td>366</td>
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<tr>
<td></td>
<td>Congenital cataract</td>
<td>743.30-743.34</td>
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<tr>
<td></td>
<td>Cataract extraction</td>
<td>13.11-13.69</td>
</tr>
</tbody>
</table>

### Table 2
**NUMBER OF DISCHARGES WITH SEARCHED PROCEDURES RECORDED FROM HIPE DATA**

<table>
<thead>
<tr>
<th>YEAR</th>
<th>REMOVAL OF EYE</th>
<th>PRIMARY REPAIR OF PERFORATED EYE</th>
<th>CORNEAL GRAFT</th>
<th>TRABECULECTOMY</th>
<th>STRABISMUS</th>
<th>VITREO-RETINAL PROCEDURES</th>
<th>ACQUIRED CATARACT</th>
<th>CONGENITAL CATARACT</th>
<th>HIPE COVERAGE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1994</td>
<td>99</td>
<td>116</td>
<td>148</td>
<td>636</td>
<td>1213</td>
<td>575</td>
<td>6,024</td>
<td>46</td>
<td>91</td>
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<tr>
<td>1995</td>
<td>99</td>
<td>132</td>
<td>174</td>
<td>723</td>
<td>1069</td>
<td>646</td>
<td>6,377</td>
<td>37</td>
<td>95</td>
</tr>
<tr>
<td>1996</td>
<td>98</td>
<td>120</td>
<td>129</td>
<td>664</td>
<td>1,091</td>
<td>640</td>
<td>6,722</td>
<td>29</td>
<td>96</td>
</tr>
<tr>
<td>1997</td>
<td>104</td>
<td>94</td>
<td>118</td>
<td>579</td>
<td>923</td>
<td>701</td>
<td>6,737</td>
<td>25</td>
<td>96</td>
</tr>
<tr>
<td>1998</td>
<td>80</td>
<td>97</td>
<td>109</td>
<td>438</td>
<td>750</td>
<td>624</td>
<td>6,874</td>
<td>37</td>
<td>95</td>
</tr>
<tr>
<td>1999</td>
<td>107</td>
<td>115</td>
<td>94</td>
<td>312</td>
<td>731</td>
<td>732</td>
<td>6,955</td>
<td>36</td>
<td>95</td>
</tr>
<tr>
<td>2000</td>
<td>88</td>
<td>102</td>
<td>91</td>
<td>290</td>
<td>702</td>
<td>733</td>
<td>8,352</td>
<td>40</td>
<td>94</td>
</tr>
<tr>
<td>2001</td>
<td>69</td>
<td>112</td>
<td>71</td>
<td>209</td>
<td>691</td>
<td>811</td>
<td>9,011</td>
<td>32</td>
<td>95</td>
</tr>
</tbody>
</table>
Figure 1 — NUMBER OF DISCHARGES WITH PROCEDURES OF CATARACT SURGERY COMPARED TO TOTAL NUMBER OF ALL INCLUDED PROCEDURES FROM 1994 TO 2001

Figure 2 — NUMBER OF DISCHARGES WITH PROCEDURES OF TRABECULECTOMY OR STRABISMUS OPERATIONS PERFORMED FROM 1994 TO 2001
Cataract operations alone accounted for 75% of all the ophthalmic discharges retrieved. Comparing 2001 to 1994, there was a 49.5% increase in cataract surgery from 6,024 to 9,011 (Figure 1). There was a 41% increase in the number of vitreo-retinal discharges in the same period. Meanwhile, there was a 43%, 52% and 67% reduction in discharges with strabismus, corneal transplant and trabeculectomy procedures performed respectively (Figure 2). Little change was noted in the number of eyes needing enucleation or perforating eye injury repair.

DISCUSSION

This report studies the nationally recorded ophthalmology surgical practice acute hospitals in the Republic of Ireland. The figures used are the HIPE data returned by acute public hospitals in Ireland. These figures show some procedures are increasing in incidence while others decrease. This adds support to the accuracy of these figures.

Our figures show an increase in the occurrence of cataract surgery. This may reflect, among other things, the ageing population. The number of 60–64-year-olds in the Republic of Ireland (in thousands) has increased from 136.4 in 1995 to 148 in 2000 (Central Statistics Office, Dublin).

The overall number of these procedures performed has shown an increase. The number of day cases reported in all specialities in the Republic increased from 132,295 (23.5%) in 1994 to 246,531 (32.8%) in 1999. There has been a tendency towards dedicated day surgery units in Ophthalmology. This may have facilitated an increase in the number of cataract operations performed.

Cataracts in the paediatric population represent a difficult challenge in ophthalmology. The average number of operations performed for congenital cataracts was 35.2 (range 25 to 46). This probably suggests that treatment of this condition should be performed in specialised units.

The number of trabeculectomies performed has dropped in recent years, coinciding with the introduction of newer topical medications for glaucoma. In Scotland, operations for glaucoma fell 45.6% between 1994 and 1999, which closely reflects Irish data. The reduction in strabismus procedures may be due to better refractive management of children in the out-patients situation and better overall child health.

The decrease in trabeculectomy and strabismus operations has been more than compensated for by an increase in cataract numbers. The net result is an increase in demand for ophthalmologic services, both in Ireland and in the United Kingdom.

This information may help in the planning and provision of ophthalmology services in the future.

ACKNOWLEDGEMENTS

We wish to acknowledge the assistance given to us by Anne Clifton and Aisling Mulligan at the HIPE unit, ESRI, Dublin.

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Using HIPE data as a research and planning tool: limitations and opportunities

ABSTRACT

Background The Hospital Inpatient Enquiry (HIPE) system is an important information source for research and health service planning activities. However, as it was not designed explicitly for these purposes, some limitations exist.

Aims To make recommendations that would increase the value of HIPE as a research and planning tool.

Methods Experiences of using HIPE for research and planning exercises were analysed so as to identify its limitations and their impact on research and planning.

Results Limitations were identified regarding data quality, policy issues and the general system.

Conclusions To increase the utility of HIPE as a research and planning tool, a number of changes are recommended, including: expanding the system to cover private hospitals and outpatient and emergency services; adopting routine small area and socio-economic coding; adopting unique personal identifiers; publishing regular detailed reports with in-depth analyses; and considering making hospital identifiers available in certain circumstances.

INTRODUCTION

The Hospital Inpatient Enquiry system (HIPE) is a computer based health information system that collects data on discharges from 62 acute public hospitals in Ireland (Tables 1 and 2). It is the largest of eight national health information systems. The original objectives of HIPE as outlined in the recent HIPE report were to provide a standard minimum dataset on inpatient morbidity and mortality, to facilitate analysis of hospital activity, and to allow comparisons between countries. Arguably, one of the most important subsequent uses of HIPE data has been in the estimation of the casemix adjustment for acute hospital budgets. HIPE data have also been used for patient care studies, epidemiological studies, monitoring practice, planning, service provision, and quality assurance studies.

As HIPE was not explicitly designed as a research tool, limitations have been encountered. This paper examines the practical, system and policy limitations surrounding HIPE from the perspective of public health researchers with a view to suggesting changes which would increase the usefulness of HIPE as a research and planning tool, particularly in the context of the current health service reform programme. Reference is also made to the recently published National Health Information Strategy.

Practical issues

Data quality

There are three criteria by which data quality is assessed: coverage, completeness and accuracy. Coverage refers to the proportion of the total activity recorded by a system and relates to both the number of hospitals covered and data coverage within these hospitals. The HIPE report states that HIPE collects data from all acute public hospitals nationally although this has been amended on the HIPE website (http://www.esri.ie/) to reflect the inclusion of data from two private hospitals. However, there remain other private hospitals that are not included in HIPE. The term ‘acute hospitals’ is not well defined as can be seen from Tables 2 and 3 which highlight the discrepancies between the Department of Health and Children’s classification of an acute hospital and that used by HIPE. As overall coverage of the system is unclear this may lead to an underestimation of population based rates and selection bias. No mention of these potential problems is made in the HIPE report. Coverage in the HIPE report refers to data coverage, that is, the percentage of discharges from hospitals included in the HIPE system that are captured by HIPE. This has increased from 55% in 1990 to over 95% in 1998, partially due to improved training and the...
employment of dedicated HIPE coding staff within each hospital. The quantity of data collected has also increased with additional diagnosis and procedures fields, extra consultant fields, and recording of the number of intensive care and private care days. HIPE, however, does not record any activity in the outpatients or emergency departments. This limits the extent to which the full activity of hospitals can be examined. For example, a study using HIPE to assess the burden of alcohol on acute hospital services was limited to assessing the impact on hospital admissions only, in spite of the fact that a high proportion of accident and emergency contacts are alcohol related.

Completeness of data refers to the proportion of records that have an entry in any specified field. Incompleteness can render some fields useless. One solution is to make the entry of data for certain fields compulsory, although this can lead to the overuse of default codes. For example, in a study to develop a more sensitive empirically based model of demand for hospital inpatient care for small areas, it emerged that the use of “dump” postcodes in the UK resulted in biased data that had to be omitted. The HIPE report makes no mention of data completeness.

Accuracy refers to the extent to which completed records are valid, that is, whether they measure the characteristics that they were intended to measure. While HIPE validation is reported as taking place both at hospital level and centrally, there is no reference to validation using hospital charts, to an examination of inter-coder variation or to any external audit. An independent study at a large Dublin hospital in 1995 showed an inaccuracy rate for primary diagnosis of 41% and the omission of 44% of secondary diagnoses. Three more recent studies looking at the management of acute myocardial infarction, the epidemiology of leptospirosis and rotavirus, found discrepancies between their prospectively recorded or laboratory recorded figures and the HIPE figures. These findings highlight the fact that there is no method of detecting data that meet consistency checks but may be incorrect.

Events versus patients
The HIPE system records the number of inpatient and day-case events rather than the number of patients. While it is possible to identify some readmissions through individual hospital medical record numbers or through admission codes, the inability to be sure of identifying them all has caused difficulties in many studies. A unique personal identifier would enable readmissions to be easily identified from event level data and, if introduced for every citizen, for all medical, social and administrative data, a greater array of research and planning activities would be possible. Examples of studies which could have been better accommodated include development of a needs based resource allocation model using a population level database (O’Loughlin R. Unpublished thesis, TCD, 2004) and determination of incidence and prevalence of diseases, for example, leptospirosis, or opiate drug use.

Socio-economic group variable
The lack of an explicit socio-economic group variable reduces the usefulness of HIPE data in examining inequalities and in exploring the determinants of health. A report on inequalities in health in Ireland was unable to examine socio-economic gradients in hospital events. Medical card status is the only HIPE variable that could be used as a proxy for socio-economic group although the recent addition of HIPE fields that classify health coverage into private, medical card-holder or neither may provide a better proxy.

Small area coding
The only patient address information recorded by HIPE is county of residence. The lack of a small area identifier such as an electoral division code means that it is not possible to use spatial models that could help in the planning of services, or to differentiate between illness patterns at sub-county level. A National Hospitals Office is proposed as part of the health service reform programme. This may necessitate defining catchment areas for each acute hospital to assist with planning services. Experience has shown that lack of data coded to small area creates difficulties in defining hospital catchment areas. Small area coding of HIPE data would assist in the development of a small area based resource allocation model similar to the York model in England, and would eliminate the need to geo-code data for specific projects such as the recent examination of congenital anomalies and landfill sites.

System issues
Access and Confidentiality
Requests for HIPE data must be made in writing to the ESRI HIPE manager and these are dealt with while respecting confidentiality constraints protecting patient, doctor and hospital identification. In general, only access to aggregate statistics is provided by either the ESRI or the Public
Health Information System. Event data with a limited number of fields are occasionally provided and researchers are required to sign a conditions of use statement. In some circumstances additional data may be provided directly by the Department of Health and Children, particularly for work undertaken on their behalf. Contributors to HIPE, such as hospital based clinicians and managers, can obtain HIPE data for their individual hospital. Some health boards have access to HIPE data for their residents. However, data at health board level can only have limited use as there are no national data to which activities and outputs can be compared or to which reductions in inequalities can be measured.

**Reporting**

The 1990-1999 HIPE report, published in 2002, is the only official HIPE report ever published. It presents a series of frequency charts of discharges by hospital and Diagnostic Related Groups with no statistical analyses and limited commentary. As the data are not age, sex, or casemix adjusted, comparison between hospitals is not valid so its utility is limited. Reports pertaining to subsequent years have not yet been published. Annual reports, which are a feature of most other Irish databases, would be useful for identifying trends in hospital activity, for highlighting new developments, and for reporting on coverage, completeness and accuracy. Consultation with HIPE users is essential in order to maximise the effectiveness of the reports.

**Timeliness**

Timeliness of data is particularly important and HIPE data are theoretically available six months after the year’s end. In practice, the data may not be available for several more months. For research purposes, this timescale is not problematic but it may cause difficulties for service planners.

**Policy issues**

Hospital and consultant identifiers are not provided to HIPE users for confidentiality reasons. Another stated reason for not providing identifiers is to prevent the production of hospital or consultant league tables. The difficulty with league tables is that their results can be widely misinterpreted unless the data are properly standardised for patient variables such as age, sex, socio-economic group, casemix, and elective versus emergency surgery. However, there have been attempts to create league tables in Ireland from figures garnered under the Freedom of Information Act.

Positive developments from standardised league tables that are part of a performance indicators programme in the UK show that hospitals that performed well were rewarded with increased autonomy and hospitals that performed poorly were supported to improve standards. On the other hand, perverse incentives created by performance indicators exist; for example, reports of reduced surgery on high risk cases, and changes in recording practices to reduce severity adjusted mortality rates. It is therefore essential that clinicians are involved in discussions pertaining to how data they produce are used and presented. And it is of interest that Spiegelhalter et al., in their review of lessons learned from the Bristol inquiry, concluded that because ranks are highly sensitive to chance variability, ranking institutions is inappropriate. They recommend displaying risk adjusted trends in outcomes with 95% confidence intervals for institutions instead.

Anonymised data are normally sufficient for research purposes, but for planning purposes it would be preferable to have identifier data available but only with the agreement of the hospitals and consultants on access to and use of the data. Appropriately standardised comparisons between consultants and hospitals could help to improve quality, reduce access inequalities and standardise services both locally and nationally. For example, Spiegelhalter et al. have shown that statistical analysis of routine data sources was able to identify the excess paediatric surgical mortality in the Bristol Royal Infirmary.

Recent reports that have fed into the health service reform programme, such as the ‘National Task Force on Medical Staffing’ and the ‘Development of Radiation Oncology Services in Ireland’, required detailed information on throughput, accessibility and caseloads in order to inform planning decisions. Accurate HIPE data that identify hospitals and consultants will be required to evaluate these reforms and to continue to help inform decision making.

**DISCUSSION**

The acute hospital sector receives the bulk of health service funding and yet the system measuring its activity has several weaknesses. It is important that HIPE users have confidence in HIPE data and the recent HIPE report may have been a lost opportunity to adequately clarify the validation process. HIPE is a potentially valuable research and planning tool. While one of the original objectives of HIPE was to...
Table 1
DETAILS OF THE HIPE SYSTEM

<table>
<thead>
<tr>
<th>THE HIPE SYSTEM</th>
<th>DATA COLLECTED BY HIPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Computer based health information system</td>
<td>Administrative data</td>
</tr>
<tr>
<td>• Started in 1971</td>
<td>• Patient name (retained within hospital)</td>
</tr>
<tr>
<td>• Minimum data set</td>
<td>• Case reference number and hospital number</td>
</tr>
<tr>
<td>• Records inpatient and daycase discharge information</td>
<td>• Dates of admission and discharge</td>
</tr>
<tr>
<td>• 62 hospitals</td>
<td>• Dates of first and principal procedure</td>
</tr>
<tr>
<td>• Administered by the Economic and Social Research Institute (ESRI) for Department of Health and Children</td>
<td>• Day case indicator</td>
</tr>
<tr>
<td></td>
<td>• Admission type and admission source</td>
</tr>
<tr>
<td></td>
<td>• Discharge status and discharge destination</td>
</tr>
<tr>
<td></td>
<td>• General Medical Services status</td>
</tr>
<tr>
<td></td>
<td>• Admitting and discharge consultant (encrypted)</td>
</tr>
<tr>
<td></td>
<td>• Intensive care days and private care days</td>
</tr>
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</table>

Clinical data
• Principal and up to 9 secondary diagnoses (ICD-9-CM)
• Principal and up to 9 secondary procedures (ICD-9-CM)

Demographic data
• Date of birth, sex, marital status
• Area of residence by county

Table 2
NUMBER AND TYPE OF HIPE HOSPITALS

<table>
<thead>
<tr>
<th>TYPE OF HOSPITAL</th>
<th>NUMBER</th>
</tr>
</thead>
<tbody>
<tr>
<td>County</td>
<td>23</td>
</tr>
<tr>
<td>General</td>
<td>10</td>
</tr>
<tr>
<td>Regional</td>
<td>6</td>
</tr>
<tr>
<td>Orthopaedic</td>
<td>6</td>
</tr>
<tr>
<td>Maternity</td>
<td>5</td>
</tr>
<tr>
<td>Longstay</td>
<td>3</td>
</tr>
<tr>
<td>Cancer</td>
<td>2</td>
</tr>
<tr>
<td>Private</td>
<td>2</td>
</tr>
<tr>
<td>Infectious disease</td>
<td>2</td>
</tr>
<tr>
<td>Paediatric</td>
<td>2</td>
</tr>
<tr>
<td>ENT</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>62</td>
</tr>
</tbody>
</table>

Table 3
HOSPITALS WHERE A DISCREPANCY EXISTS BETWEEN DOHC* AND HIPE* CLASSIFICATION OF ACUTE HOSPITAL

<table>
<thead>
<tr>
<th>HOSPITAL</th>
<th>DOHC</th>
<th>HIPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ballina District Hospital, Co. Mayo</td>
<td>District</td>
<td>Acute (county)</td>
</tr>
<tr>
<td>Bantry General Hospital, Co. Cork</td>
<td>Acute</td>
<td>Not included</td>
</tr>
<tr>
<td>St. Mary’s Auxillary Hospital, Baldoyle, Dublin</td>
<td>Acute</td>
<td>Not included</td>
</tr>
<tr>
<td>Our Lady’s Hospice, Harold’s Cross, Dublin</td>
<td>Not included</td>
<td>Acute (long-stay)</td>
</tr>
<tr>
<td>St. Mary’s Hospital, Phoenix Park, Dublin</td>
<td>Not included</td>
<td>Acute (long-stay)</td>
</tr>
</tbody>
</table>
allow comparisons with other countries, not enough has been done by way of validation of the system and adjustments to take account of our mixed public-private hospital service to allow interpretable comparisons with other countries to be made.

The usefulness of the HIPE data could be improved by instituting the recommendations outlined below which have arisen from this paper.

We suggest that the Department of Health and Children should be responsible for the policy orientated recommendations, particularly those that have resource implications. These include expansion of the system to cover outpatient and emergency services, inclusion of data from all private hospitals, routine small area coding, adoption of a unique personal identifier and a socio-economic code. These measures would have the added benefit of facilitating comparisons with similar systems in other countries which have been hampered hitherto by the restrictive nature of the current HIPE system.

The ESRI operates the HIPE system on behalf of the Department of Health. To maximise the use of HIPE as a research tool and in particular as a planning tool, will require the development of a set of procedures in conjunction with participating hospitals and consultants. A balance will have to be struck so that data are published at the appropriate agreed level of anonymity. In addition, feedback mechanisms to hospitals and consultants need to be built in to maximise validity and completeness of data.

Further recommendations for the operators (ESRI) include regular reports with more in-depth analysis of national data, the provision of clear information on coverage, completeness and accuracy and a system of external audits.

In addition, we recommend that consideration be given to making the identification of hospitals and consultants available in some circumstances, particularly for quality control, risk assessment and service evaluation both locally and at national level. A debate is needed as to who is best suited to carry out this research and the new Health Information and Quality Authority may be well placed to do this. However, if work were to be contracted out to third parties, such as academic institutions, restrictions on access to data would have to be relaxed. The ability to conduct independent research is currently constrained due to access difficulties to individual level data.

We envisage that the National Health Information Strategy will provide a context for these recommendations. It is therefore essential that it is implemented immediately as its delay is limiting the development of a coherent and co-ordinated Irish health information infrastructure.

For the health services reform programme to advance, comprehensive, accurate and timely data will be required and HIPE will be an important source of such information. While a significant investment will be required to implement the recommendations arising from this paper, the improved quality and quantity of research are likely to make this investment worthwhile.

ACKNOWLEDGEMENTS

Thanks are due to Dr. Susan Smith for conceiving this paper, and to Dr. Fenton Howell, Ms. Anne O’Farrell and our colleagues in the Department of Public Health and Primary Care for their helpful comments.

REFERENCES


Correspondence to: Dr. Shane Allwright, Department of Public Health and Primary Care, Trinity College Centre for Health Sciences, Adelaide and Meath Hospital Incorporating the National Children’s Hospital, Tallaght, Dublin 24. Tel: 01 608 1087 / 1582 E-mail: sllwright@tcd.ie
Relating undergraduate musculoskeletal medicine curricula to the needs of modern practice

ABSTRACT

Background International studies have demonstrated significant discrepancies between undergraduate musculoskeletal curricula and the needs of modern medical practice. Aims To determine the prevalence of musculoskeletal disorders in primary care, General Practitioners, assessment of their undergraduate musculoskeletal training and that considered ideal for several clinical skills, and the relative importance of the ability to recognise selected clinical presentations. Methods A postal survey of 200 General Practitioners using a detailed questionnaire. Results The response rate was 50.5%, with respondents being an average 18.5 years in practice. They saw a mean 140.3 patients/week (range 10 – 270) of which 17.4% presented with musculoskeletal complaints (range 5-50%). Respondents felt their musculoskeletal education was poor, with a significant difference between it and their ideal (p=0.007). The most important skill for a graduating doctor was history taking, examination and appropriate investigation of a musculoskeletal problem. The most important clinical presentation was recognition of traumatic quadriplegia. Conclusions A large proportion of primary care in Ireland is devoted to musculoskeletal complaints, however, there are deficiencies perceived in undergraduate musculoskeletal education. A review of undergraduate musculoskeletal curricula, emphasising the clinically relevant aspects of this discipline is needed.

INTRODUCTION

Musculoskeletal complaints constitute a major reason for patients seeking medical treatment. This has been highlighted by the international designation of this decade 2000-2010 as ‘The Bone and Joint Decade’. This increased recognition of the importance of musculoskeletal medical practice has brought the issue of the adequacy of musculoskeletal medical education to the fore in current medical literature. As primary care physicians, it is general practitioners who typically have the initial responsibility for provision of care for many musculoskeletal problems. They may be able to manage many of these problems themselves or have recourse to referring certain patients for specialist orthopaedic or rheumatological assessment. International studies have demonstrated that symptoms of musculoskeletal problems are second only to respiratory system complaints as a reason for patients seeking medical attention. Although the specific number of patients presenting to an individual practitioner is dependent on a large number of variables, it has been shown that between 15 and 27% of patients presenting to their primary care physician do so with a musculoskeletal complaint. A sound knowledge of the basic issues and management of musculoskeletal problems is therefore essential for all medical practitioners.

Despite this it has been shown that 51% of general practitioners reported their training in orthopaedics to be inadequate for their current practice while paediatric trainees reported orthopaedics as being the most inadequate part of their training. These findings imply that many doctors feel they may be inadequately managing musculoskeletal problems due to a lack of training in this discipline.

The apparent disparity between the preparedness of medical graduates in this discipline and the prevalence of musculoskeletal complaints in the community prompted us to ascertain the prevalence of musculoskeletal complaints presenting to Irish general practitioners and to establish the attitudes of Irish general practitioners towards...
their own undergraduate training, what aspects of musculoskeletal training they consider most important, and the relative importance of knowledge of various specific musculoskeletal conditions.

**METHODS AND MATERIALS**

We performed a postal survey of 200 randomly selected general practitioners using a questionnaire. There were general questions regarding the prevalence of musculoskeletal disorders in their practice and other features of the practice (number of years in practice, whether group or individual, whether urban or rural, total number of patients seen per week and whether they had any special interest in musculoskeletal problems).

We then obtained each practitioner’s assessment of the training they obtained in medical school and that considered ideal for graduates. They were specifically asked to rate on a scale of 1 to 5 the relative importance of a range of clinical skills and areas of knowledge in musculoskeletal medicine (Table 1). Each topic therefore generated an overall score of between 1 and 5 when the means of these responses were calculated.

A further section was then devoted to the practitioners’ assessments of the relative importance of the ability to diagnose and treat 57 selected, representative clinical presentations (Table 2). This was also assessed on a scale of 1 to 5 depending on perceived importance.

The results were collated and statistical analysis was performed using a commercial programme (SigmaStat version 2.0).

**RESULTS**

There were 101 replies (50.5%). Further survey mailings were not performed. The respondents were an average 18.5 years in practice. Rural practices accounted for 43% and urban 57% of those who replied and 60.1% were in group and 39.9% in individual practices. They saw a mean 140.3 patients/week (range 10 – 270) of which 17.4% presented with musculoskeletal complaints (range 5-50%). A third (33%) claimed a special interest in musculoskeletal medicine. Further analysis of these special interests revealed 57% were specifically in sports related complaints, 24% were in back pain and 19% were in general and paediatric complaints.

Respondents felt musculoskeletal medicine to be important for students; however, the respondents felt their own musculoskeletal education was poor, with a significant difference between it and their ideal \( p=0.007 \), which was unrelated to time elapsed since graduation.

The most essential skills required were reported to be the ability to perform a history, examination and appropriate investigation of musculoskeletal problem (score 4.46) followed by the emergency management of fractures (score 4.44). Embryology was considered of academic interest only.

The least well taught topic was the correct technique and indications for soft tissue/intra-articular injections (score 1.77). Of note, all topics were rated as poorly taught except for anatomy and pathophysiology. Even these, however, only scored as adequate (score 3.11).

The importance of being able to manage 57 clinical musculoskeletal scenarios was also assessed, with none being perceived to be of academic interest only. Those considered essential were diagnosis and initial treatment of (in descending order) quadriplegia, a battered child, tendon or nerve injury, septic arthritis, congenital dislocation of the hip, degenerative disc disease or disc herniation of the lumbar spine, slipped upper femoral epiphysis, fracture distal radius or scaphoid, fractured neck of femur, unstable pelvic fracture, multiple injuries requiring assessment and treatment using ATLS principles and Perthes disease of the hip.

The only scenario reported to be of borderline usefulness was the ability to diagnose and manage a genetic condition affecting the musculoskeletal system such as muscular dystrophy.

**DISCUSSION**

The finding here that a large proportion of primary care is devoted to musculoskeletal complaints is consistent with the results of similar studies internationally.\(^2,3,8\) Given this relatively high prevalence, the importance of the ability to deal adequately with these complaints is obvious. However, there appear to be deficiencies in the undergraduate instruction received by the population sampled here, with a significant difference being reported between the quality of instruction received and that considered ideal. The general practitioners sampled here felt their undergraduate musculoskeletal instruction to be typically poor. Freedman et al specifically tested
the adequacy of medical school education among graduates, and found that 82% failed to demonstrate basic competency in a validated examination of fundamental concepts.\(^6\) As studies have shown that medical school represents the only training in musculoskeletal medicine received by up to 56% of all primary care physicians, there is obviously an imperative here to address the adequacy of the undergraduate curriculum.\(^4\)

The results of the current study clearly demonstrate that practitioners rate the teaching of practical skills such as clinical diagnosis, musculoskeletal interventions and emergency management as significantly more important than the more academic aspects of the topic such as genetics or biochemistry. These practical topics are not perceived as being well taught in the current system and new models of teaching and the emphasis on particular subjects in medical school need to be assessed. These findings are also supported by the great importance the practitioners placed on the ability to correctly diagnose and manage many acute and traumatic musculoskeletal disorders.

### Table 1

**QUESTIONNAIRE/RATING SCALE ON 12 CLINICAL SKILLS AND AREAS OF KNOWLEDGE IN MUSCULOSKELETAL TRAINING.**

<table>
<thead>
<tr>
<th>SUBJECT</th>
<th>Q. 1</th>
<th>Q. 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Musculoskeletal Anatomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmacology pertaining to musculoskeletal disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genetics of musculoskeletal disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pathophysiology of common musculoskeletal disorders (e.g. OA, RA, osteoporosis etc.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Embryology of the musculoskeletal system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurological disorders and their effect on the musculoskeletal system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biochemistry of musculoskeletal disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microbiology of infective musculoskeletal disorders (e.g. tetanus, septic arthritis, osteomyelitis etc.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>History, examination and appropriate investigation of musculoskeletal problem</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergency management of fractures (e.g. manage &amp; clear c-spine in trauma, emergency splintage of fractures etc.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demonstrate correct technique and explain indications for soft tissue/intra-articular injections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indications for and interpretation of Xrays</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### TABLE 2
RATING SCALE FOR CLINICAL PRESENTATIONS

**Question:** How important is it for a graduating medical student to be able to diagnose and appropriately treat a patient with the presenting complaints listed below?

1. 5 = Critical  
2. 4 = Very important  
3. 3 = Helpful  
4. 2 = Potentially beneficial  
5. 1 = Academic interest only

<table>
<thead>
<tr>
<th>Rating</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Low back pain radiating into foot (degenerative disc disease of the lumbar spine; disc herniation, radiculopathy)</td>
</tr>
<tr>
<td>2.</td>
<td>A dislocatable hip at birth (congenital dislocation of the hip)</td>
</tr>
<tr>
<td>3.</td>
<td>An inability to move his/her upper and lower extremity following a neck injury (quadriplegia)</td>
</tr>
<tr>
<td>4.</td>
<td>An acutely painful swollen joint (septic joint)</td>
</tr>
<tr>
<td>5.</td>
<td>Pain and swelling of a joint (OA, RA, gout, pseudogout)</td>
</tr>
<tr>
<td>6.</td>
<td>A child with inadequately explained injuries (battered child)</td>
</tr>
<tr>
<td>7.</td>
<td>Multiple injuries requiring assessment and treatment using ATLS principles</td>
</tr>
<tr>
<td>8.</td>
<td>A fracture through a growth plate (physeal injury)</td>
</tr>
<tr>
<td>9.</td>
<td>A deep laceration to the forearm and abnormal hand movement or sensation (tendon, nerve, muscle, vessel injury)</td>
</tr>
<tr>
<td>10.</td>
<td>Shoulder pain following an acute injury (AC joint disruption, shoulder dislocation, fracture clavicle or prox humerus)</td>
</tr>
<tr>
<td>11.</td>
<td>Haemodynamic instability and an unstable pelvis following a high energy trauma (unstable pelvic fracture)</td>
</tr>
<tr>
<td>12.</td>
<td>Hip/groin pain in a 10-year-old (slipped upper femoral epiphysis)</td>
</tr>
<tr>
<td>13.</td>
<td>Neck pain after being rear-ended in RTA (musculo-ligamentous sprain of the cervical spine)</td>
</tr>
<tr>
<td>14.</td>
<td>Wrist pain following a fall (fracture distal radius, scaphoid)</td>
</tr>
<tr>
<td>15.</td>
<td>Pain and swelling of elbow region after an acute injury (dislocated elbow, radial head #, olecranon #, supracleavicular #, distal humerus)</td>
</tr>
<tr>
<td>16.</td>
<td>Pain in the hip region following an acute injury (inter/subtrochanteric #, femoral neck #, dislocated hip, acetabular #, pubic rami #)</td>
</tr>
<tr>
<td>17.</td>
<td>Low back pain after lifting an object (acute lumbar strain, disc herniation)</td>
</tr>
<tr>
<td>18.</td>
<td>Swelling and pain in the knee following an acute injury (ant. cruciate lig. tear, medial collateral lig. tear, meniscal tear, tibial plateau #)</td>
</tr>
<tr>
<td>19.</td>
<td>Paediatric multiple trauma victim</td>
</tr>
<tr>
<td>20.</td>
<td>Pain and swelling in the ankle region after an acute injury (lat. ankle ligament sprain, ankle #, osteochondral #, tibial plafond #)</td>
</tr>
<tr>
<td>21.</td>
<td>Chronic low back pain (lumbar strain, spondylolisthesis)</td>
</tr>
<tr>
<td>22.</td>
<td>Chronic neck pain (whiplash, arthritis, cervical stenosis)</td>
</tr>
<tr>
<td>23.</td>
<td>Hip/Groin pain in a 6-year-old (Perthes disease)</td>
</tr>
<tr>
<td>24.</td>
<td>A grossly swollen foot which is minimally painful and a history of diabetes (diabetic neuropathy)</td>
</tr>
<tr>
<td>25.</td>
<td>Pain and/or numbness in one hand (carpal tunnel syndrome, nerve compression syndromes)</td>
</tr>
</tbody>
</table>
### TABLE 2 - CONTINUED

#### RATING SCALE FOR CLINICAL PRESENTATIONS

<table>
<thead>
<tr>
<th></th>
<th>Clinical Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>26.</td>
<td>Knee pain (patello-femoral pain syndrome, osteoarthritis, meniscal tear, RA, tendonitis, bursitis)</td>
</tr>
<tr>
<td>27.</td>
<td>Pain in the shoulder (subacromial impingement, adhesive capsulitis, rotator cuff tear, AC joint arthritis)</td>
</tr>
<tr>
<td>28.</td>
<td>Neonate failing to move arm after birth (brachial plexus injury)</td>
</tr>
<tr>
<td>29.</td>
<td>A painful deformed upper arm following an injury (humer al shaft #)</td>
</tr>
<tr>
<td>30.</td>
<td>Pain and deformity in the forearm following acute injury (radius &amp; ulna #, nightstick #, Galleazzi #, Monteggia #)</td>
</tr>
<tr>
<td>31.</td>
<td>Hip/groin pain (osteo or rheumatoid arthritis)</td>
</tr>
<tr>
<td>32.</td>
<td>Pain over the distal forearm and wrist (De Quervains tenosynovitis, scaphoid non-union, radiocarpal arthritis)</td>
</tr>
<tr>
<td>33.</td>
<td>A toddler with a painful elbow after being picked up (pulled elbow)</td>
</tr>
<tr>
<td>34.</td>
<td>A child with an acute limp (greenstick #, transient synovitis)</td>
</tr>
<tr>
<td>35.</td>
<td>Polarticular arthritis (RA, ankylosing spondylitis)</td>
</tr>
<tr>
<td>36.</td>
<td>A painless curvature of the spine (idiopathic scoliosis)</td>
</tr>
<tr>
<td>37.</td>
<td>Pain over the lateral elbow (lateral epicondylitis)</td>
</tr>
<tr>
<td>38.</td>
<td>Muscle and joint pain throughout the body (fibromyalgia, flu, myositis)</td>
</tr>
<tr>
<td>39.</td>
<td>Heel swelling and pain after a fall from a height (calcaneus #, heel bruise)</td>
</tr>
<tr>
<td>40.</td>
<td>Hand pain after striking an object/person (boxers #)</td>
</tr>
<tr>
<td>41.</td>
<td>Finger pain after accidentally striking it (phalanx #, subungual haematoma)</td>
</tr>
<tr>
<td>42.</td>
<td>A non-tender soft-tissue mass (soft-tissue tumour)</td>
</tr>
<tr>
<td>43.</td>
<td>Painful foot following an injury (phalanx #, Lisfranc #, metatarsal #)</td>
</tr>
<tr>
<td>44.</td>
<td>Pain and swelling in a number of joints (polarticular arthritis, JRA)</td>
</tr>
<tr>
<td>45.</td>
<td>A child with abnormal looking feet (in/out-toeing, metatarsus adductus)</td>
</tr>
<tr>
<td>46.</td>
<td>A deformed foot at birth (clubfoot)</td>
</tr>
<tr>
<td>47.</td>
<td>Instability and recurrent dislocations of the shoulder</td>
</tr>
<tr>
<td>48.</td>
<td>Forefoot pain following repetitive stresses to the area (stress #)</td>
</tr>
<tr>
<td>49.</td>
<td>Chronic pain in the heel region (plantar fascitis, heel pain syndrome)</td>
</tr>
<tr>
<td>50.</td>
<td>An osseous lesion on plain x-ray (bone tumour)</td>
</tr>
<tr>
<td>51.</td>
<td>A history of recurrent ankle sprains (chronic lateral ankle instability)</td>
</tr>
<tr>
<td>52.</td>
<td>A deformed great toe including a painful medial 'bump' (hallux valgus)</td>
</tr>
<tr>
<td>53.</td>
<td>Nodularity on the palm and finger contractures (Dupuytren's contracture)</td>
</tr>
<tr>
<td>54.</td>
<td>A congenital spinal abnormality (congenital kyphosis, Scheurmann's etc)</td>
</tr>
<tr>
<td>55.</td>
<td>A history of cerebral palsy</td>
</tr>
<tr>
<td>56.</td>
<td>Deformity of the sternoclavicular joint (SC joint subluxation)</td>
</tr>
<tr>
<td>57.</td>
<td>A genetic condition affecting the musculoskeletal system (osteogenesis imperfecta, Ehlers-Danlos syndrome, muscular dystrophy)</td>
</tr>
</tbody>
</table>
Although not the primary objective of the current study, many also referred to a lack of formal training in this specialty during their postgraduate vocational training. In this regard, many of the respondents, particularly those with a special interest in musculoskeletal problems, indicated that they had pursued postgraduate courses of their own volition. However, they also expressed concern at the difficulty in finding suitable courses for their perceived needs. It therefore appears that there are deficiencies in musculoskeletal medicine training across the whole spectrum of medical education.

As mentioned earlier, one third of the general practitioners claimed a special interest in musculoskeletal medicine. Although studies such as this are prone to a selection bias based on the interests of those surveyed, this figure is nonetheless an indication of how prevalent musculoskeletal problems are. The preponderance of those with a special interest, furthermore, identified sports injuries and back complaints as their area of interest. This would indicate that a significant proportion of the problems presenting to general practitioners fall into one of these categories. Unfortunately, undergraduates typically have little exposure to these conditions as these are largely managed on an outpatient basis. Also, the relatively new discipline of sports medicine in particular has not been the focus of much attention in traditional texts and curricula. However, such special interests aside, the overall results here indicate the rather urgent need to reassess the whole range of undergraduate musculoskeletal medicine education as currently provided by orthopaedic and rheumatologic academic services. A more effectively co-ordinated interaction between primary care training and these services also needs to be achieved. The results further emphasise that curricula need to be implemented with an emphasis on the common conditions encountered in the community.

In conclusion, we have found that musculoskeletal complaints constitute a significant proportion of the workload of general practitioners. Their dissatisfaction with the undergraduate training received however indicates the need for a review of undergraduate musculoskeletal curricula, with an emphasis possibly on more common outpatient problems, emergencies and physical examination and diagnosis. There may also be a place for changes in postgraduate vocational training in musculoskeletal medicine and the provision of relevant postgraduate courses for those practitioners wishing to develop a special interest.

ACKNOWLEDGEMENT

The authors would like to acknowledge the assistance of the Irish College of General Practitioners in the performance of this study.

REFERENCES


Correspondence to: Dr. Kevin J. Mulhall, Maree Road, Oranmore, Co. Galway, Ireland. E-mail: kjm@indigo.ie
Using HIPE data as a research and planning tool: limitations and opportunities: A Response

The paper by O’Loughlin et al (2005) raises a number of issues in regard to the operation of the Hospital Inpatient Enquiry that require clarification and/or a response. In our view, there are many potential applications for these data that are not explored in this paper; our comments here, however, are of necessity limited to those issues raised by O’Loughlin et al (2005) in an attempt to ensure that a more balanced perspective on the operation of this system may be portrayed.

**INTRODUCTION**

While O’Loughlin et al (2005) recognises in the introduction that the Hospital Inpatient Enquiry is intended to provide a “standard minimum dataset on inpatient morbidity and mortality” subsequent comment would seem to assume a broader set of objectives for this system. It is important, therefore, to reiterate at the outset that the HIPE system is intended to collect information on discharges treated in the inpatient setting. Notwithstanding the desirability of being able to track individuals through the health system, with it’s establishment the HIPE system was never intended for this purpose. While the ‘inpatient’ setting has been broadened in recent years to include day case activity, it was never intended that the HIPE system would collect information in the outpatient, A&E or community settings. Again, while the establishment of information systems in such settings might be desirable, such an initiative demands consideration of a whole range of factors specific to the relevant areas.

In Table 1, O’Loughlin et al (2005) list what they call ‘Data collected by HIPE’. This listing is incomplete and out of date. In Table 1 here, a complete and up to date listing of data collected by HIPE is presented.

**Practical Issues**

**Data quality**

It is extraordinary that nowhere in the paper by O’Loughlin et al (2005) is there any mention of the HIPE software (Windows HIPE and Windows HIPE Reporter). Custom designed software for data entry and reporting of HIPE data have been produced by the ESRI’s HIPE & NPRS Unit. An independent review of clinical coder training programs and data quality audit procedures commissioned from the University of Sydney in 2004 went so far as to state that “the ‘ace’ in the Unit’s pack of data quality initiatives is the HIPE computer system”: Every HIPE hospital uses the same software, standardised to the same version for the entry of HIPE data. This software is updated regularly. Integrated within this software are a whole range of procedures directed at safeguarding data quality. Automated edits and validations enable hospitals to correct errors at the source and are performed on individual data fields as data are entered in the system. There are also inbuilt combination checks between two or more data fields and final cross comparisons between all data fields when data entry for the episode of care has been completed. Table 2 gives an indication of the range of data quality and consistency checks integrated within the HIPE software. Messages are displayed to prompt or guide the user in correcting any errors. Fields are also colour coded and ‘red’ indicates the field with an error.

Flags are inbuilt to the data entry software to reject certain codes or coded combinations. They also allow users to confirm, endorse or explain their choice of codes. Some fields allow the user to enter a textual explanation of why they selected a certain code (particularly the .9 unspecified codes). Two special flags, audit and report flags, are automatically triggered when users select certain codes. Queries are marked in logs and the logs can be viewed and accessed centrally by the HIPE & NPRS Unit for analysis.

In addition to the edits built into the HIPE computer system, approximately 140 validation checks are routinely performed on national data by the HIPE & NPRS Unit. These cover a range of coding conventions and guidelines. If any problems are found, the Unit produces query reports for hospitals to verify and correct. Routine quality checks are also applied to administrative and demographic data in addition
RESPONSE

to analyses of compliance with the guidelines published regularly in Coding Notes and the HIPE instruction manual.

Requests for data quality audits can originate from a number of sources, including hospitals, the Department of Health & Children, clinicians, researchers and staff of the Unit. Audit methodology is determined by the purpose of the audit. In-house auditing software has been developed which facilitates extraction of data from the national file, the analysis of data as required and standardisation of the format of reports.

In addressing the issue of coverage, O’Loughlin et al (2005) express concern at “discrepancies between the Department of Health and Children’s classification of an acute hospital and that used by HIPE” and list the five hospitals concerned in Table 3. It should be noted here that the two hospitals not included in the HIPE system opted out many years ago. The three hospitals in HIPE considered to be long stay or district have been retained within the system in the interests of maintaining a data flow that might prove useful for the area concerned. To put this issue in perspective, however, it should be noted that these five hospitals combined had estimated discharges of 5,240 in 2004 while the national returns to HIPE for 2004 (estimated end

<table>
<thead>
<tr>
<th>Table 1</th>
<th>DATA COLLECTED BY THE HOSPITAL INPATIENT ENQUIRY*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ADMINISTRATIVE DATA</strong></td>
<td><strong>CLINICAL DATA</strong></td>
</tr>
<tr>
<td>• Patient name (retained within hospital)**</td>
<td>• Principal** and up to 19 secondary diagnoses (ICD-10-AM wef 01/01/2005)</td>
</tr>
<tr>
<td>• Case reference number and hospital number**</td>
<td>• Principal and up to 19 secondary procedures (ICD-10-AM wef 01/01/2005)</td>
</tr>
<tr>
<td>• Dates of admission and discharge**</td>
<td>• Date of transfer to Pre-Discharge Unit (optional)</td>
</tr>
<tr>
<td>• Dates of first and principal procedure</td>
<td>• Admission Mode</td>
</tr>
<tr>
<td>• Day case indicator**</td>
<td>• Waiting List Indicator</td>
</tr>
<tr>
<td>• Admission type and admission source**</td>
<td><strong>DEMOGRAPHIC DATA</strong></td>
</tr>
<tr>
<td>• Discharge status and discharge destination**</td>
<td>• Date of birth**, sex**, marital status**</td>
</tr>
<tr>
<td>• General Medical Services status**</td>
<td>• Area of residence by county**</td>
</tr>
<tr>
<td>• Medical Card Number (GMS patient number)</td>
<td>** Completion of these data fields is mandatory</td>
</tr>
<tr>
<td>• Admitting and discharge consultant (encrypted)**</td>
<td>** Completion of these data fields is mandatory</td>
</tr>
<tr>
<td>• Intensive care days and private care days**</td>
<td>** Completion of these data fields is mandatory</td>
</tr>
<tr>
<td>• Public Care days (optional)</td>
<td>** Completion of these data fields is mandatory</td>
</tr>
<tr>
<td>• Infant admission weight (for all neonates and low weight infants)</td>
<td>** Completion of these data fields is mandatory</td>
</tr>
<tr>
<td>• Date of transfer to Pre-Discharge Unit (optional)</td>
<td>** Completion of these data fields is mandatory</td>
</tr>
<tr>
<td>• Admission Mode</td>
<td>** Completion of these data fields is mandatory</td>
</tr>
<tr>
<td>• Waiting List Indicator</td>
<td>** Completion of these data fields is mandatory</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2</th>
<th>SUMMARY OF DATA QUALITY AND CONSISTENCY CHECKS INTEGRATED WITHIN THE HIPE SOFTWARE</th>
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<tbody>
<tr>
<td>ITEM</td>
<td>ICD-9-CM</td>
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<td>Sex checks</td>
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<tr>
<td>Admission type checks</td>
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<tr>
<td>Discharge code checks</td>
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</tr>
<tr>
<td>Checks on use as Principal Diagnosis/Procedures</td>
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<tr>
<td>Checks on use as Secondary Diagnoses/Procedures</td>
<td>216</td>
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<tr>
<td>Checks on Age</td>
<td>1664</td>
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<tr>
<td>Checks on LOS</td>
<td>17216</td>
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<tr>
<td>Rare Diagnosis</td>
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</tr>
<tr>
<td>Complete record checks</td>
<td>114</td>
</tr>
<tr>
<td>Total</td>
<td>35718</td>
</tr>
</tbody>
</table>

* Data elements in italics are in addition/different to the data listing presented in Table 1 of O’Loughlin et al (2005).
** Completion of these data fields is mandatory.
May 2005) were 962,785 discharges. The presentation of HIPE data are differentiated by Acute (length of stay 0-30 days) and Extended Stay (length of stay > 30 days) discharges specifically to take account of the fact that a small number of hospitals with long stay patients were historically included within this system. While the achievement of 100% cover is the objective for the HIPE system, the returns to date for 2004 are at the 96% level.

O’Loughlin et al (2005) present as a criticism that “HIPE, however, does not record any activity in the outpatients or emergency departments”. As noted above, this was never an objective put forward for the HIPE system. Any decision regarding the development of national databases in these areas will have to be informed by a range of factors including the objectives to be achieved, the costs involved and the priorities for such an investment given competing alternative demands for scarce resources within the health system. Again, to gain an appreciation for the scale of such an undertaking, it is worth noting that in 2004 there were approximately 2.4 million attendances at outpatient departments and 1.2 million attendances at casualty departments. The range of information to be collected, as well as potential applications for such data, would have to be addressed before the large scale investment of resources in these areas could be justified.

In commenting on completeness of data, O’Loughlin et al (2005) note that incompleteness can render some fields useless and that one solution is to make the entry of data for certain fields compulsory. They neglect, however, to report that this is exactly what happens in the HIPE data entry system. In Table 1, completion of the data elements marked with a double asterisk are treated as mandatory by the national file unless these data fields have been returned to the HIPE & NPRS Unit or included on the national file unless these data fields have been completed.

In the section on data accuracy, O’Loughlin et al (2005) quote a 1995 study of one Dublin hospital and studies of three different conditions. The authors do not report on a whole range of initiatives since the mid-1990’s including the advancements with computer-based edits/checks within the HIPE data entry system, improvements in training, support and guidelines for coders, or the 18 chart-based audits that have been conducted on HIPE data since 2001. The independent review of clinical coder training programs and data quality audit procedures commissioned from the University of Sydney in 2004 has also not been referenced or referred to in any way by these authors. The Bramley and Reid Report (2004) was funded by the Department of Health and Children and commissioned by the ESRI’s HIPE & NPRS Unit. A range of objectives were addressed by this review including an evaluation of the policies and procedures being applied within HIPE for the purpose of auditing and improving the quality assurance of coded records. A wide ranging set of recommendations have been proposed by this report and these now constitute an essential input to the agenda for the future development of the HIPE system.

The improvement of data quality and the development of more effective data quality initiatives will always be a challenge for HIPE as with other data systems. This objective is, however, accorded the highest priority in all developments being considered for this system. While recognising that much remains to be done, it is also important to acknowledge improvements achieved in recent years thanks to the commitment of those working at all levels within the system and increased investment by the Department of Health and Children in the HIPE system. When compared with the quality assurance initiatives being pursued by an agency like the Canadian Institute for Health Information (CIHI), those applied within HIPE compare favourably as, for example, both HIPE and CIHI support a coding query database, an abstracting manual, education programmes, abstracting software, system edits and re-abstraction studies.

Another important initiative for the HIPE system not mentioned by O’Loughlin et al (2005) is the introduction of ICD-10-AM for morbidity coding beginning January 2005. This development followed from the conduct of a review of morbidity coding schemes internationally and the completion of a pilot study in Ireland to determine the best available option for use within the HIPE system. As the ICD-9-CM system had been in place since 1990, the introduction of ICD-10-AM involved the implementation of an extensive training programme for all clinical coders nationally, together with the introduction of such initiatives as the ebook for use in coding morbidity data. In addition to updating the clinical coding systems to the ICD-10 level, this development also provides opportunities for skill and
knowledge transfer between the National Centre for Classification in Health in Australia and the Irish HIPE system. Data quality tools used in Australia like the Performance Indicators of Coding Quality (PICQ) 2004 and the Australian Coding Benchmark Audit have already proved to be a useful resource for the development of data quality checks and audit software within the Irish system.

Events versus patients
There is no doubt that the inclusion of PPS Number on HIPE would greatly enhance the range of potential uses for these data. Use of PPS Number is, however, currently confined to specified agencies within the public sector and any further extension of its use requires legislative provision and consultation with the Department of Social and Family Affairs. In the Health Information Strategy there is, however, a commitment to the introduction of a system for unique identification within the health sector using PPS Number. Delivery on this commitment will, of course, have to ensure that the necessary safeguards are in place to protect patient privacy.

Socio-economic group variable
When the HIPE system was originally introduced in the 1970s, a data variable for occupation was included. Prior to the ESRI taking management responsibility for HIPE, this variable was regrettably dropped in the 1980s due to the very low level of response achieved. There is an annual review of the data elements collected within HIPE and the inclusion of a variable to enable the assignment of socio-economic group has been considered on a number of occasions. When data changes to the HIPE system are considered, however, a number of factors have to be taken into account. Firstly, data can only be collected for the HIPE system if they are collected initially by hospitals. Where a number of changes to the system are being considered, priorities must be assigned to determine which changes are considered more urgent or important. Finally, there is a cost to each change to the HIPE system both in terms of the workload generated for those collecting and inputting the data and also because of software changes that have to be made locally and nationally. While the inclusion of a variable to facilitate improved measures of socio-economic status remains an objective for the HIPE system, the inclusion of information on public/private status and medical card status should facilitate an assessment of equity issues within the system as currently structured.

Small area coding
In the interests of protecting patient and doctor confidentiality, the Department of Health and Children agreed in the mid 1990s that consultant codes would be encrypted and patient name and address would not be collected on the national database. In the absence of address, it is therefore not possible to determine a small area identifier for discharges on the HIPE system nationally. Given the information held locally on patient address, individual hospitals could, of course, choose to include a small area identifier on their Patient Administration Systems (PAS). The recent government announcement regarding the development of a post code system would, however, be expected to enable some advancement on this issue if, when available, the post code of the patient can be collected on the HIPE system.

System issues
Access and Confidentiality
In the past, all health boards requesting access to HIPE data for their residents have been provided with data sets and software to facilitate analysis of these data. All health boards have now been provided with data sets for their residents and these will be updated annually. Comparable, national level data can, and have been, provided to health boards and other users on request.

Each year, a Shared Information System is developed and circulated to all hospitals involved in the national casemix programme. This data set includes data that the hospitals have agreed to share amongst those participating in the programme. Using this system, it is therefore possible for an individual hospital to benchmark performance against other peer hospitals for the same conditions.

Reporting
To date, the resources available to the HIPE system have been concentrated on improving coverage, quality, timeliness and access to the data. Within the HIPE & NPRS Unit at the ESRI, approximately 1.5 FTEs have been allocated to data management and analysis functions. The responsibilities of these staff include processing data received from over 60 hospitals on a monthly basis and preparation of the national file for the Department of Health & Children together with report development and responding to data requests. In 2004, 119 such requests were received from a range of sources including clinicians, hospitals, health agencies, government departments,
researchers, voluntary organisations etc. Many of these requests result in the publication of HIPE data in academic journals and other sources. Given the constraints on the resources available, combined with increasing demands for access to data, it is regrettable that it has not been possible for the HIPE & NPRS Unit to produce more analytic reports on the system. Beginning in 2005, however, the Department of Health & Children have made funds available for an additional resource to work on data management and analysis so it is hoped that within the next year, further reports on the system will be available for publication.

**DISCUSSION**

Most of the issues requiring clarification that are summarised in this section, in O’Loughlin et al (2005)\(^1\), have already been addressed. Just two outstanding points remain to be considered. Firstly, private hospitals cannot currently be compelled to participate in the HIPE system. Private hospitals have been invited to be involved in the HIPE system and two have agreed to be so involved on a voluntary basis. In the interests of completeness for hospital activity data at a national level, the inclusion of private hospitals in the system is an objective to be supported and actively pursued. It is worth noting, however, that the largest area of activity in the private hospital sector is the provision of maternity services and data on all births nationally are collected by the National Perinatal Reporting Scheme, also managed by the ESRI’s HIPE & NPRS Unit\(^2\).

Finally, it seems extraordinary that the only mention of the resource requirements for implementing the recommendations put forward by O’Loughlin et al (2005)\(^3\) is in the last sentence of the paper where it is noted that “While a significant investment will be required to implement the recommendations arising from this paper, the improved quality and quantity of research are likely to make this investment worthwhile.” Given competing demands for resources across the health system, any request for increased investment needs to be quantified and the likely returns estimated if a case for greater investment of public funds in health information systems is to have any chance of success.

Greater use of HIPE data for research and planning is fully supported by all involved in the operation and development of this system. It is therefore all the more regrettable that, while aspiring to support these objectives, O’Loughlin et al (2005)\(^4\) present a paper that portrays an out-of-date view of the HIPE system, criticises HIPE for limitations on functionality that are outside the scope of the system objectives and puts forward a number of recommendations that could not be implemented in the current health information environment.

There is no denying that there are deficiencies with many aspects of the operation of the HIPE system. Recognising that the system needs further development and improvement need not, however, be inconsistent with an appreciation for the many improvements introduced within HIPE in recent years. A number of these improvements noted here, including significant developments in quality assurance, audit, coder training programmes, coverage, completeness, access etc have enhanced the value of this system for the many potential applications for the data collected. As the only source of data on the work undertaken in the most expensive part of the health system, it is essential that the HIPE system is developed in a stable and coherent manner with continued support for all involved in all aspects of the system. While increased resources will achieve improvements like the collection of an expanded range of data and improved tools for monitoring data quality, optimum data quality standards can only be achieved where all involved in data reporting, coding and collection are facilitated in taking ‘ownership’ of the data they return to the HIPE system.

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3. Coding Notes is a quarterly newsletter produced by the ESRI’s HIPE & NPRS Unit for coders and others involved in the HIPE system.

7 Murphy, D., M.M. Wiley, A. Clifton, D. McDonagh Updating Clinical Coding in Ireland: Options and Opportunities, The Economic and Social Research Institute, Dublin, September 2004.


ACKNOWLEDGEMENTS

The very substantial commitment of all involved in the Hospital Inpatient Enquiry to the achievement of the system objectives of complete coverage of HIPE data of optimum quality in a timely manner is greatly appreciated. For assistance provided in the preparation of this paper, sincere thanks to Professor Brendan Whelan, Director ESRI and Deirdre Murphy, Brian McCarthy, Aisling Mulligan and Jacqui Curley in the ESRI’s HIPE & NPRS Unit.

Correspondence to: Professor Miriam Wiley, The Economic and Social Research Institute, 4 Burlington Road, Dublin 4. Tel: +353 1 667 1525, Fax: +353 1 668 6231, email: miriam.wiley@esri.ie
Small bowel obstruction secondary to a giant enterolith complicating Crohn’s disease

ABSTRACT

Background Enterolith formation associated with Crohn’s disease is a very uncommon clinical entity.

Aim To describe a case of sub-acute small bowel obstruction secondary to a giant enterolith in a patient with Crohn’s disease.

Results A 54-year-old male with a history of Crohn’s disease presented with sub-acute small bowel obstruction secondary to a giant enterolith. The diagnosis was confirmed utilising plain film radiography and computed tomography.

Conclusion Plain film radiography and computed tomography play a central role in establishing the diagnosis of this rare complication of Crohn’s disease and assist in planning surgical intervention.

CASE REPORT

A 54-year-old male presented to a university teaching hospital with a one-week history of nausea, vomiting, central abdominal pain and increasing abdominal distension. The patient was diagnosed as having Crohn’s disease in 1981 and had undergone a right hemicolectomy for complications of the disease one-year following diagnosis. Physical examination demonstrated signs of dehydration, abdominal distension and central abdominal tenderness. Laboratory investigations demonstrated a normal haemoglobin, white cell and platelet count. Biochemistry and C-reactive protein were normal. A plain abdominal radiograph showed dilated loops of small bowel. The patient was admitted for the management of sub-acute small bowel obstruction. This was initially felt to be related to adhesions or stricture formation as a complication of Crohn’s disease. A nasogastric tube was placed and the patient received intravenous fluids and intravenous steroids. Contrast-enhanced computed tomography (CT) was performed which demonstrated proximal small bowel dilatation and a large intraluminal filling defect in the proximal ileum (Figure 1). No abnormality was identified in the hepato-biliary tract. Forty-eight hours following admission, the patient’s symptoms of central abdominal pain recurred. A laparotomy was performed which revealed a 7 x 6-cm hard mass in the lumen of a segment of proximal ileum affected by Crohn’s disease. The enterolith was removed and a strictureplasty was performed. The patient made an uncomplicated postoperative recovery and was discharged five days following surgery.

DISCUSSION

The association between enterolith formation resulting in small bowel obstruction in patients with Crohn’s disease is a very uncommon clinical entity. In patients with Crohn’s disease, enterolith
formation may occur within a pre-stenotic segment of bowel affected by regional enteritis. The presence of an enterolith in patients with Crohn’s disease may be the first manifestation of chronic inflammatory complications of regional enteritis. Complications of enterolith formation in this clinical setting include abscess formation and bowel perforation. Enteroliths causing small bowel obstruction may closely resemble gall stone ileus as a clinical entity and should be considered in the differential diagnosis.

Plain radiographs will demonstrate features of small bowel obstruction and may show the presence of lamellated calcifications within the enterolith. Ultrasound may demonstrate the presence of highly echogenic intraluminal mass with acoustic enhancement. The findings on contrast-enhanced computed tomography (CT) of this condition may mimic a small bowel intussusception. The preferred management of this rare complication of Crohn’s disease is only available from few case reports. If conservative management is unsuccessful, manual destruction and “milking” of the shattered obstructing enterolith down to the colon has been advocated as the least invasive surgical method. If this is unsuccessful, an enterotomy may be performed, preferably at a point remote from the site of obstruction, in order to make an incision in a non-inflamed segment of bowel. If a complicated enterolith is present, resection of the diseased segment of bowel is necessary.

CONCLUSION
Enterolith formation associated with Crohn’s disease is a very uncommon clinical entity. Plain film radiography and computed tomography play a central role in establishing the diagnosis of this rare condition and assist in planning surgical intervention.

REFERENCES

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Giant solitary non-parasitic cyst of the liver

ABSTRACT

Background Cystic diseases of the liver and intrahepatic biliary tree are uncommon. The majority of cases are detected only when patients become symptomatic, or as an incidental finding on radiological imaging.

Methods We discuss the case of a 25-yr-old female with a centrally located giant liver cyst causing obstructive jaundice, and briefly discuss the management options in the treatment of this uncommon problem.

Results and Conclusions Intervention is recommended in patients with symptomatic simple cysts of the liver. Surgical cystectomy is the treatment of choice for large deep seated cysts.

INTRODUCTION

Cystic lesions of the liver can be classified into four main groups based on aetiology: congenital, neoplastic, inflammatory and traumatic. Congenital liver cysts are the most commonly encountered, and include simple cysts and polycystic liver disease. Primary cystic neoplasms of the liver are rare, and include biliary cystadenomas and cystadenocarcinomas. Inflammatory liver cysts are associated with an infectious aetiology from bacterial and parasitic origin, such as hydatid cysts. Traumatic cysts occur following a significant injury resulting in subcapsular haematoma formation, or disruption of the intrahepatic biliary tree.

The majority of cases of congenital liver cysts are asymptomatic. They are usually discovered incidentally on radiological imaging, or rarely when they become symptomatic. We present an unusual case of a young female who presented with obstructive jaundice due to a centrally located giant non-parasitic cyst of the liver. The aetiology and management of this uncommon problem are discussed.

CASE REPORT

A 25-year-old female presented with a three-week history of epigastric discomfort, dyspepsia, abdominal bloating, and jaundice. On further questioning she had noticed a fullness in her right upper abdomen over the previous nine months. She had no history to suggest biliary colic or ascending cholangitis. She denied weight loss. On examination, she was jaundiced. Her vital signs were normal. A large tender mass was palpable in the right upper quadrant. Investigations confirmed cholestatic liver function tests with an elevated serum bilirubin (290μmol/L), a low serum albumin (29g/L) and an abnormal coagulation profile with an INR of 1.4. An abdominal computed tomography (CT) scan demonstrated a massive centrally located liver cyst compressing the liver parenchyma with hilar obstruction (Figure 1). The right kidney was displaced downwards into the pelvis (Figure 2). Hydatid serology was negative. At laparotomy, a massive central liver cyst containing a mixture of cyst fluid and old haematoma was demonstrated with atrophy of both hepatic lobes (Figure 3). A total cystectomy and cholecystectomy was performed with excision of redundant liver folds. An intraoperative cholangiogram demonstrated normal biliary anatomy. The histology was consistent with a solitary bile duct cyst. A repeat abdominal CT scan four weeks later demonstrated rapid regeneration of the liver with a small collection at the site of cyst removal. On follow-up she remains well, with no evidence of cyst recurrence.

DISCUSSION

Simple cysts of the liver are usually asymptomatic, and detected incidentally during abdominal imaging. They are thought to arise due to aberrant development of intrahepatic bile ducts, and usually do not communicate with the biliary ductal system. Simple cysts can be single or multiple, and range in size from millimetres to >20cm in diameter. Symptoms are rare, but can occur if the cyst becomes complicated as a result of intracystic bleeding, rupture, or secondary bacterial infection. Compression of adjacent structures can occur including compression of the inferior vena cava causing lower extremity oedema, compression of the portal vein resulting in portal hypertension, or compression of the biliary tree resulting in
cholestasis. Only 16 cases of enlarging non-haemorrhagic simple liver cysts causing obstructive jaundice have been reported in the English literature, most of which were centrally located.\(^1\)\(^-\)\(^3\) Other possible presentations include rupture into adjacent bowel or biliary tree, or development of carcinoma. Treatment is recommended only in symptomatic patients. Management options include aspiration, aspiration and injection of a sclerosing agent into the cyst cavity (absolute alcohol, minocycline hydrochloride or doxycycline), fenestration (laparoscopic or open) with marsupulization, total cystectomy, hepatic resection and orthotopic transplantation.

Simple percutaneous aspiration is associated with risk of infection, and recurrence is invariable. Aspiration and percutaneous instillation of a sclerosant has been demonstrated to be safe and effective.\(^1\)\(^,\)\(^2\)\(^,\)\(^4\) However, multiple treatments may be required to achieve resolution and there is a high risk of recurrence. This method is contraindicated if the cyst communicates with the biliary tree, when hydatid disease is suspected or in the presence...
of malignancy. Fenestration can be performed if >50% of the surface area of the cyst is superficial. Laparoscopic fenestration can be carried out successfully for superficial cysts located within the anterior liver segments (segments III, IV, V, VI). It is of limited value when the cyst is located in segments VII or VIII, as adequate drainage would be difficult to achieve. If >50% of the surface area of the cyst remains, or the majority lies within the hepatic parenchyma, ablation of the residual cyst lining by direct cautery, argon beam coagulation, topical sclerosant, or omentoplasty may reduce the risk of recurrence. Small cyst cavities can persist, and recurrences do occur.

In the case of giant liver cysts, the resultant fluid loss and secretion following cyst fenestration can exceed the resorptive capacity of the peritoneal surface resulting in ascites. Surgical cystectomy has been recommended as the treatment of choice for giant deep seated liver cysts. However, this procedure is hazardous due to an increased risk of injury in the presence of distortion of large vessels and bile ductal elements traversing a thin compressed liver parenchyma. Postoperatively, synthetic function of the liver may be compromised, and recovery can be prolonged. Partial hepatectomy may be indicated in the treatment of complex recurrent cysts, the localised form of Caroli’s syndrome, and type III polycystic liver disease.

Biliary cystadenomas are rare neoplasms, and patients usually present with non-specific symptoms. The majority of cases occur in middle-aged women. An abdominal CT, or ultrasound demonstrating a thick walled or multiloculated cyst with solid intracystic components should raise a suspicion for a cystic neoplasm. Neither preoperative imaging nor histology can reliably distinguish biliary cystadenoma from cystadenocarcinoma. Because of the risk of malignancy and the inability to accurately determine tumour type preoperatively surgical resection is recommended.

CONCLUSION

Intervention is recommended in patients with symptomatic simple cysts of the liver. Surgical cystectomy is the treatment of choice for large deep seated cysts. This case illustrates the mode of presentation, and management options in a young patient with a symptomatic giant non-parasitic cyst of the liver.

REFERENCES


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Tel.: 0044 2073464801 Fax: 0044 2073463575 E mail: otucker@rcsi.ie
Massive retroperitoneal ganglioneuroma presenting with small bowel obstruction 18 years following initial diagnosis

ABSTRACT

Background Ganglioneuroma is a rare tumour of neural crest origin, which arises from maturation of a neuroblastoma. While previously considered to be non-functioning, they are now known to be frequently endocrinologically active.

Aims and Methods We report a case of a massive retroperitoneal ganglioneuroma presenting with small bowel obstruction in an adult, 18 years after initial diagnosis. Urinary dopamine levels were elevated, but other catecholamines were within normal limits. This is the first report in the English-language literature of a retroperitoneal ganglioneuroma presenting with or causing intestinal obstruction. We also review the metabolic, radiological, and histological features of these tumours. Relevant publications were identified from a Medline search using the MeSH headings ‘ganglioneuroma’, ‘retroperitoneal neoplasms’ and ‘intestinal obstruction’, and also from the reference lists of retrieved articles.

Conclusions Ganglioneuroma can grow to a massive size and present in a varied manner. It should be included in the differential diagnosis of any large retroperitoneal or mediastinal mass, including those causing bowel obstruction.

CASE REPORT

We report a 21-year-old female who presented to the Accident and Emergency Department with a 14-hour history of colicky epigastric pain and vomiting. Of note in her background she had a biopsy of a benign abdominal tumour aged 3 years. On examination she was tender in the epigastrium, and an ill-defined mass could be palpated extending from the pelvis to above the umbilicus. Vital signs were normal, as was her white cell count. CA125, CA19.9, and alphafetoprotein were all within normal limits. A plain film of abdomen revealed a huge mass that displaced dilated loops of small bowel into the upper abdomen (Figure 1). CT of abdomen showed a 26cm x 13cm complex soft tissue mass originating from the retro-peritoneum and occupying most of the abdomen and pelvis (Figure 2). It encased the aorta and inferior vena cava, both of which were pushed anteriorly. One small area of calcification was seen. There was no evidence of intra-spinal involvement. A working diagnosis of small bowel obstruction was made and the patient was treated conservatively.

She had previously presented as a 3-year-old with a large abdominal mass. Laparotomy and open biopsy were performed, but no attempt was made to resect the tumour. Histology then showed a ganglioneuroma. She was followed-up with serial ultrasound, until she was lost to follow-up at the age of twelve.

On this occasion ultrasound-guided percutaneous biopsy was performed and histology showed mature ganglion cells (Figure 3), which strongly expressed neurofilament markers and were Bielschowsky silver positive. Some of the ganglion cells were binucleate, and surrounded by mature perineurial cells as well as well-developed axons. There were no primitive cells and no necrosis. The cell proliferation index (as judged by MIB 1 immuno-labelling) was very low (<1%), consistent with benign ganglioneuroma. The original biopsy was reviewed, and showed almost identical features. A 24-hour urine collection showed elevated dopamine excretion, while other catecholamines were within normal limits (Table 1). Clinical examination and radiological investigation failed to detect any metastasis.

The patient’s symptoms failed to resolve with conservative treatment and she underwent a laparotomy, at which a massive intra-abdominal tumour was found (Figure 4), displacing small and
large bowel proximally. An adherent segment of small bowel was non-viable and a partial small bowel resection with primary anastomosis were performed. Whilst bowel function was slow to return to normal, her in-hospital stay remained complication-free.

**DISCUSSION**

Ganglioneuroma represents the benign end of the spectrum of primitive neuroepithelial tumours, which also includes neuroblastoma (highly malignant) and ganglioneuroblastoma (intermediate). Geographical or racial predilection is not reported in the literature, although ganglioneuroma is more commonly diagnosed in countries such as Japan where infants are screened for neuroblastic tumours. There appears to be no gender preference. Neuroblastoma and ganglioneuroblastoma represent the second most common group of solid extra-cranial neoplasms of infancy and childhood.

Neuroblastoma and ganglioneuroblastoma represent the second most common group of solid extra-cranial neoplasms of infancy and childhood. They account for approximately 8% of malignancies in these age groups. They may be found in association with a number of syndromes including Beckwith-Wiedemann, von Recklinghausen’s disease, Hirschprung’s disease, opsoclonus-myoclonus, heterochromia iridis, watery diarrhoea or Cushing’s syndrome. They arise from neural crest cells and occur more commonly in the mediastinum, retroperitoneum and adrenal glands, with occasional cases reported in the neck or spinal canal. The differentiation of neuroblastoma into ganglioneuroma is well-described and is more common in younger patients, but most tumours arise de novo. Much less commonly, malignant transformation of ganglioneuroma into neuroblastoma is described in the adult.

The presentation of neural crest tumours varies greatly, from asymptomatic tumours discovered incidentally on imaging studies or mass screening, to a palpable mass, scoliosis, neurological symptoms or even respiratory distress. To our knowledge, there are no reports in the English-language literature of retroperitoneal ganglioneuroma presenting with or causing small bowel obstruction. Neuroblastoma staging systems can also be applied to ganglioneuroma: using the International Neuroblastoma Staging System our patient’s tumour was Stage 3, as it was a unilateral tumour infiltrating across the midline. In general ganglioneuromas may be treated by complete excision, however in the case described the tumour was unresectable.

Although catecholamine secretion is common in neuroblastomas, ganglioneuromas were formerly thought to be endocrinologically inactive. However, one series of 46 patients found elevated plasma or urinary catecholamines in 39%. Another series of 25 patients found a trend for metabolic activity to correlate with tumour size. Ganglioneuromas have rarely been reported as being VIP-secreting, when they are frequently associated with severe watery diarrhoea. $^{1}$ $^{125}$I-mIBI uptake has also been well described in ganglioneuroma, tending to occur in functionally active tumours. On this occasion scintigraphy was not required for diagnosis.

CT is the radiological investigation of choice when establishing the diagnosis of ganglioneuroma, as the appearances can be characteristic and are well described. In this case, findings were consistent with those previously reported: that of a round or oval tumour encasing the great vessels with or without calcification and a tumour capsule. Where intra-spinal involvement is suspected, MRI should be performed as it is superior to CT in this regard.

Ganglioneuroma is a benign neoplasm consisting of relatively mature ganglion cells arranged in groups, surrounded by a Schwann cell-rich stroma. They are most commonly asymptomatic. Less than 30% are adrenal in origin, the remainder are located in the posterior mediastinum, retroperitoneum or other sites including the small and large intestine. The gross appearance is usually of a sharply circumscribed mass without a true capsule and a cut surface, which is grey/tan with some gelatinous firm and whorled regions. At light microscopy, ganglioneuromas have a variable number of mature ganglion cells. The cells may be binucleate and misshapen. The stroma consists of Schwann cells and variable amounts of collagen. Immunohistochemical identification of neurofilament and S100 is useful in the diagnosis and the cell proliferation index marker.

<table>
<thead>
<tr>
<th>24-HOUR URINARY CATECHOLAMINE COLLECTION</th>
<th>NMOL PER 24 HRS</th>
<th>NORMAL RANGE (NMOL PER 24 HRS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine</td>
<td>7376</td>
<td>653-2700</td>
</tr>
<tr>
<td>Adrenaline</td>
<td>25.6</td>
<td>27-100</td>
</tr>
<tr>
<td>Noradrenaline</td>
<td>208</td>
<td>118-500</td>
</tr>
</tbody>
</table>
Mib, as judged by Ki 67 immunolabelling, is a useful indicator of cell turnover. It is of interest that in this tumour there was no change in either maturity or cell proliferation index in either biopsy, despite an eighteen-year interval between the two. The Shimada classification is widely used to determine the degree of differentiation in neuroblastic tumours. The most malignant is a stroma-poor neuroblastoma of undifferentiated subtype whilst the most benign is ganglioneuroma, which is devoid of any undifferentiated subtype. The classification has prognostic significance, as do other biological characteristics such as presence or absence of chromosome 1p, ploidy, and MYCN amplification.

Ganglioneuroma is a rare benign tumour of the mediastinum, retroperitoneum and other tissues, which can grow to a massive size and present in a varied manner. It should be included in the differential diagnosis of any large mediastinal or retroperitoneal mass, including those causing bowel obstruction. Management involves total excision where possible, while inoperable tumours such as that described above must be managed conservatively.

**REFERENCES**

CASE REPORT


Correspondence to: Professor H.P. Redmond, Department of Surgery, Cork University Hospital, Wilton, Cork, Ireland. Tel: 00 353 21 4922371 Email: ecronin10@hotmail.com
The rise of Troponin

Dear Editor

In recent years the use of Troponin testing to monitor myocardial damage has become more pervasive and prominent, replacing the old style CK-MB measurement. Troponin elevation is a marker of cardiac injury and high risk; it is also raised in a minority of acute coronary syndrome patients. However, it is important for clinicians to realise that a single rise in Troponin levels is of indeterminable significance. An appropriate series of tests over time, fitting in with the right clinical picture is of most value. The Troponin complex in striated muscle fibres has three distinct subtypes and c-troponin-I is believed to be the one present only in cardiac muscle. Consequently, c-troponin-I is released when there is an assault to the myocardium and this is what laboratory testing picks up. (some labs may measure the troponin-T sub unit, this however has been found to be less specific and less sensitive).

Interpretation of results can be confusing and there are several caveats to be aware of. A positive c-troponin-I level means that cardiac muscle contents have leaked out of cells. The primary reason why this occurs is in response to injury. There are multiple causes of cardiac muscle injury that includes acute coronary events, but there is also a whole spectrum of disorders that can cause a rise in troponin. The largest study of this subject showed that all of the following were associated with elevated c-troponin-I levels. Pulmonary embolism, congestive cardiac failure, cardiomyopathy, myocarditis, rhabdomyolysis, chest contusions, sepsis, mural thrombi, prosthetic heart valves, neoplasms, radiation-induced coronary stenosis, homocystinuria, SLE and rheumatoid arthritis. Surprisingly, high troponin levels have also been found in Cocaine abusers and marathon runners.

Some of these are obviously significant while others merely represent a normal response to a physiological event. C-troponin-I can therefore be distinctly elevated in many ‘non-cardiac’ disorders. The rise is evidence of cardiac damage per se and the relative importance of this should be determined by the state of the patient. The Troponin test is a valuable and sensitive one but always needs to be assessed in the cold light of the clinical scenario as its specificity to acute coronary syndromes can be questionable, especially on a one-off basis. Perhaps the advancement of this ultimate biochemical test leads us round in full circle when we attempt to clarify its rise. That is, to a thorough clinical history taking.

REFERENCES:
2. Clinical usefulness and prognostic value of elevated cardiac troponin I levels in acute pulmonary embolism. Am Heart J. 2003 May;145(5):821

Correspondence to: Dr. Paul Grant, Timaru Hospital, Timaru, South Canterbury, New Zealand.
E-mail: drpaul.grant@orange.net
Eureka! Osteoporosis Diagnosed!

Dear Editor

Archimedes famously made observations about buoyancy during ‘hydrotherapy’ – after which he ran naked from his bath proclaiming ‘Eureka!’ We have made our own observation on the relationship of buoyancy and bone density.

A 78-year-old frail lady was receiving inpatient rehabilitation including hydrotherapy for osteoarthritis, which curtailed independent living. At the ward round, the physiotherapist reported particular difficulties with the patient’s therapy because of ‘osteoporosis’. Assuming that now even trained staff members were confusing the terms osteoarthritis and osteoporosis, the therapist was challenged to explain. “She was difficult to manage in the hydrotherapy pool,” she replied – “because she floats.” Subsequent bone density measurement confirmed severe osteoporosis with Z-scores (T-scores) of -1.7 (-3.6) at the femoral neck and -2.9 (-5.0) at the lumbar spine.

This interesting clinical observation demonstrates the Archimedes principle: an object immersed in fluid will float if it is less dense than the fluid. The human skeleton contributes approximately 20% to total body weight. It would be naive to assume a direct correlation between bone density and buoyancy, as other factors including fat and muscle bulk are also relevant but clearly physiotherapists delivering hydrotherapy have spotted a relationship. An increased awareness of osteoporosis in all staff is vital as insufficiency fractures cause increased morbidity and mortality. Novel strategies to heighten awareness of osteoporosis have included recruiting hairdressers in Manchester. \(^1\) In this case, vigilant physiotherapist identified a patient with osteoporosis that might otherwise have been overlooked.

REFERENCES

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125 Years of Caring in Dublin
Our Lady’s Hospice, Harold’s Cross 1879-2004

Tim Healy
Published by A & A Farmer November 2004
Cost €10

Since its foundation in 1879, Our Lady’s Hospice has been an intimate part of the lives of the people of Dublin. Dr. Tim Healy has chosen to write a history that captures the foundation of Our Lady’s Hospice by the Religious Sisters of Charity, and traces its evolution into a modern centre that delivers geriatric, rheumatology and palliative care to the people of Dublin and beyond. Using internal records from the hospice and interviews from current and retired staff, he eloquently captures this transition.

The Hospice for the Dying (title until 1969) was founded in response to the suffering of patients in 19th century Dublin. In the early chapters of the book, Dr. Healy captures the meagre social conditions and attitudes that existed in Dublin, which lead initially to the establishment of a 40-bedded unit at Our Lady’s Mount. Many hospitals at that time had a policy of refusal of admission for patients who were beyond hope of recovery and the hospice would have provided a place of care for these people. Earliest admissions to the hospice consisted mainly of tuberculosis patients who were offered a ‘clean bed and a faint smell of soap and carbolic’. The Sisters worked long hours but delivered care in a cheerful and pleasant manner. The last case of tuberculosis was admitted to the hospice in 1958. Cancer replaced tuberculosis as the main reason for admission in the latter half of the 20th century. Scattered throughout the book are anecdotal tales of patients and staff, which gently reminds us of the humanity and suffering of the people who came in contact with the Hospice.

This is a comprehensive and historically rich text and easily readable. Dr. Healy in a narrative style reminds us that the present-day delivery of holistic care to patients by a large multi-disciplinary team is deeply rooted in the type of care delivered by the Sisters in the previous century. This text provides readers with an insight into one of the great institutions of Dublin and would interest anyone whose life has been touched by the care offered there.
A Life in Medicine
A biography of Malachy Smyth

Aubrey Malone
€9.99 / Stg£6.88 (Proceeds to victims of tsunami disaster fund.)

From happy childhood and pleasant schooldays with the Christian Brothers in Monaghan to impecunious student life in University College Dublin, Malachy Smyth graduated to the wards of English hospitals just in time to be called up for service with the Royal Air Force in Africa and the Middle East, most memorably in a detention camp after Rommel’s defeat at El Alamein. A study grant brought him to the Royal College of Surgeons in Edinburgh, followed by marriage to Lucy O’Hara of Sligo in 1952, and surgical training in Hull and Leeds. Toronto and Utica in upstate New York beckoned, and so successful was his orthopaedic practice that he was appointed to the Workers Compensation Board, which eventually became his sole source of income when he could no longer afford insurance costs. Even so, life was pleasant with golfing weeks in Florida, until Lucy’s stroke made them decide to return to Ireland in 1994 to Rosses Point where her father had left her some land. When she died in 1999 Malachy moved back to live with his married brother in Monaghan.

Malachy had the unique pleasure of serendipitously discovering that the paper had been reprinted as a classic in Clinical Orthopaedics and Related Research (1977; 129: 9). And because the wrong M J Smyth had been identified in the eulogy, he had the rare distinction of being able to say with Mark Twain that the rumour of his death was greatly exaggerated. But the accolade seems to have been celebrated with heady wine, for he has adopted a proprietorial role over pain, in all its manifestations, regardless of Bonica, Wall and Melzack. Two hundred years after the Galvani-Volta controversy, he muses about ‘what kind of electricity comes from a nerve end’, unaware that the Nobel Prize in 1991 went to Neher and Sakmann for the answer.

With chronology the surgeon must also have implied accuracy and precision. So scarlet are the misprints that one wonders if the proofs were read. As a result this is the story of a life well lived but not well written. ‘A Life’, in fact, is a ghosted autobiography with a difference: the ghost materialises as the author who fails to curb the third-person egocentricity. The retired doctor dredged his memory banks enthusiastically for Aubrey Malone but advised him not to worry too much about chronology. Taking him at his word perhaps was not the wisest choice to make. The kernel of the story is the work with Verna Wright at Leeds on prolapsed discs published in Journal of Bone and Joint Surgery (1958; 40A: 1401). The paper’s introductory sentences about deciding to test the ‘well established clinical syndrome’ associating sciatic pain with herniation of a vertebral disc seem to have been forgotten or mislaid in the biography. A few days after operation, taking up the slack in a nylon loop which had been passed around the freed spinal root could rekindle the preoperative pain; the patients, who ‘took a co-operative and intelligent part’ in the procedure, were suitably impressed.
Access to Health Services for Transsexual People

Eoin Collins and Brian Sheehan
Published by The Equality Authority
Download at: www.Equality.ie/research

This well-researched, well-argued and well-expressed report paints a picture only too familiar both to those seeking sexual and reproductive health services and to those trying to provide them.

This report came about following regular meetings between the Transgender Equality Network Ireland and the Equality Authority. It addresses the health services provisions for transsexuals in Ireland, including differences across health board areas. It documents transsexual people’s perspectives on access to health services and makes recommendations based on these findings.

A chapter describing the increasing international recognition of transsexualism as a medical condition requiring specific treatments and the increasing legal recognition of gender change shows how far we have to go in Ireland to catch up.

In addressing the health service provisions in Ireland feedback was obtained from the health boards and from relevant professional medical bodies such as the Irish College of Psychiatrists. This revealed that policy and practice around the health needs of transsexual people is underdeveloped. In particular: most health boards focussed on access to genital reassignment surgery abroad; there appeared to be little or no particular experience or expertise in meeting the needs of transsexual people and there did not appear to be procedures for onward referral to specialist services.

Seventeen transsexual people participated in the research. Their perspectives on doctors’ and counsellors’ responses to their needs are described. These include negative reactions, lack of knowledge about the condition and lack of knowledge of specialised services. These responses caused anxiety, despondency and depression. Where respondents did eventually manage to access appropriate services the impact was always positive.

All involved in this report have helped to lift the veil of ignorance, prejudice and indifference in relation to transsexualism. This report could go a long way in convincing health professionals to take transsexual people more seriously and to work together to improve services. Perhaps even those who do not “believe” in the condition will at least be persuaded to refer transsexual people to those who do.

Gagna A. & Ch. Van Heck Prize 2006

APPLICATION FIELD
The Gagna A. & Ch. Van Heck Prize is awarded to a researcher or physician whose work has contributed to the treatment of a currently incurable disease, or has significantly contributed to research into such an outstanding progress.

AMOUNT The Prize will amount to 75,000 Euro.

NOMINATIONS
This triennial and international Prize, awarded for the second time in 2006, is reserved for a work submitted by one or two researcher(s).

Nominations must be received by the Secretary general of the National Fund for Scientific Research, F.N.R.S., rue d’Egmont 5, BE - 1000 Brussels, Belgium, by Oct. 3, 2005.

The person proposing the nomination must provide a memorandum in English on the candidate’s merits.

REGULATIONS
The complete regulations can be obtained from the secretariat of the F.N.R.S., rue d’Egmont 5, BE - 1000 Brussels, Tel.: 32 (0) 2.504.92.11, Tel. Prize: 32 (0) 2.504.92.40, Fax: 32 (0) 2.504. 92.92, e-mail: mairesse@fnrs.be, website: www.fnrs.be
IRISH JOURNAL OF MEDICAL SCIENCE
DOCTOR AWARDS 2005

In association with the Royal Academy of Medicine in Ireland

Open to all those involved in medical research
Saturday, 19th November 2005, Burlington Hotel, Dublin

CLOSING DATE EXTENDED 29th JULY 2005

The Irish Journal of Medical Science Doctor Awards 2005 will be presented by Eireann Healthcare Publications, in association with the Royal Academy of Medicine in Ireland, to doctors who have had clinical research papers published in an indexed journal anywhere in the world, between July 2004 and June 2005.

An adjudicating panel from the Royal Academy of Medicine in Ireland will choose the three finalists in each category.

The aim of the Irish Journal of Medical Science Doctor Awards is to recognise excellence in clinical research by all medical doctors working in Ireland.

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Awards will be presented in the following categories:

- Anaesthesia
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- Endocrinology & Diabetes
- Immunology
- Nephrology
- Neuroscience
- Oncology
- Psychiatry
- Respiratory Medicine
- Rheumatology
- Surgery
- Urology
- Women’s Health
- Best overall paper
- Best paper published in the Irish Journal of Medical Science
- Lifetime Achievement Award

APPLICATION FOR THE IRISH JOURNAL OF MEDICAL SCIENCE DOCTOR AWARDS

The awards are open to all those involved in medical research who have had a clinical research paper published in an indexed journal between July 2004 and June 2005. The research must have been totally or significantly carried out in Ireland.

- All entries must be submitted on disk and accompanied by six reprints of the published paper.
- Each entry form must contain the name, address, and email address of the applicant.
- The applicant must ensure that they are able to attend the award ceremony and, if unable to attend, must nominate someone to attend in their place.

Please return by 12 noon on 29th July 2005, if entering the same work in more than one category, six copies must be submitted for each category.

Name of submitting author: .................................................................
Name of senior author: ........................................................................
Department in which work was wholly or substantially carried out: ....
Address of submitting author: ...............................................................
Address of submitting author (July – December 2005): ..........................
Tel: ...................................................................................................
Fax: .................................................................................................
Mobile: ............................................................................................
Email: .............................................................................................
Title of paper: ..................................................................................
Publication: ....................................................................................
Impact factor of publication if known: ..............................................
Identify source of funding (where applicable): ...................................

Please select your particular category:

- Anaesthesia  
- Cardiology  
- Endocrinology & Diabetes  
- Immunology  
- Nephrology  
- Neuroscience  
- Oncology  
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- Best paper published in IJMS

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The Lifetime Achievement Award seeks to recognize the efforts of individuals who have contributed significantly to clinical research in Ireland over the last 20 years. Nominations are sought from colleagues and peers.

Name: ............................................................................................
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Reasons (if necessary please attach additional sheet): ......................
Nominee’s name: ........................................................................
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Nominee’s address: .......................................................................
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Terms and conditions apply. The adjudicating panel reserves the right to assess papers under categories different to those selected by entrants. Medical professionals may enter as many categories as they wish, provided they abide by the terms and conditions as set out at the top of this application form.

PLEASE NOTE: all entries must be submitted on disk and accompanied by six reprints of the published paper.