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Contents continued from front cover

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The Ulster Medical Journal

The Journal of the Ulster Medical Society. First published in 1932.
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THE ULSTER MEDICAL JOURNAL

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The Ulster Medical Journal, Volume 65, No. 1, May 1996.

Editorial

Mesotheliomas all : long before their time

In 1935 in the Ulster Medical Journal, Campbell and Young[1] reported a cluster of three cases of pleural tumour which they had observed in Belfast within five months. They concluded that each was a primary tumour of the pleura and they entitled their paper: *"A Primary Tumour (Mixed-Cell Sarcoma) of the Pleura"* The case reports are predominantly pathological, the gross appearance of the tumours and the histology are described and illustrated. In two cases neither sex nor occupation is given, the third case was a woman school teacher.

It was possible through the records system of the Department of Pathology of the Royal Victoria Hospital to locate the tissue blocks and cut fresh sections, nearly sixty years later. On review of the histology two of the cases (A1026 and A1014) were typical tubulo-papillary mesotheliomas. In one case (A1026) asbestos bodies are identified in the adjacent lung tissue. In the third case (A1143) the histological diagnosis was less certain: the tumour was composed of spindle shaped cells which could represent an undifferentiated carcinoma of lung or a spindle cell mesothelioma. So far as one can tell from Campbell and Young's paper, this was probably the case of the school teacher. All cases were scrutinized using a new immunohistochemical marker – HBME-1[7] which has just been made available. This new marker was positive in all three cases confirming them as mesotheliomas. It is remarkable that antigen preservation is maintained in paraffin blocks over a 60 year span.

As early as 1928 Professor Young,[2] then working at the Western Infirmary of Glasgow, had observed three similar cases. Both Doctor Campbell and Professor Young were earnest and distinguished workers, but the clustering does not seem to have suggested to them the possibility of an environmental agent being a factor in the causation of the tumour, even though both Glasgow and Belfast were in those days shipbuilding centres of world importance. Twenty-three years later Doctor W. T. E. McCaughey,[3] of the Department of Pathology in the Royal Victoria Hospital, published an account of eleven diffuse and two focal primary tumours of the pleura – another example of a cluster in Belfast. As Professor P. C. Elmes relates in this journal in 1977, the association of the pleural tumours with asbestos exposure became clear with the observations of Wagner[4] and his associates in South Africa. The work of Elmes[5] and his colleagues was to revolutionise health concepts of the worker in the asbestos industry in Belfast, and farther afield.

Professor James Cuming was Professor of Medicine in the Queen's College, Belfast. In 1884 in his address to the annual meeting of the British Medical Association[6] he said: "Symptoms without morbid anatomy are misleading and inadequate for the purposes of the physician. This has been only too well demonstrated in the records of medicine; but it is no less certain that morbid anatomy without symptoms, that is without giving a due and a preponderating weight to the origin and progress and vital character of the disease, will lead to error hardly less disastrous". The history of asbestos related disease in its clinical, pathological and environmental aspects illustrates the truth of Cuming's observation.

The Department of Pathology at the Royal continues this tradition of interest in mesotheliomas and in asbestos related diseases in general. In 1986, the Asbestos Research Laboratory was set up for analysis of asbestos fibres using scanning electron microscopy with EDXA and image analysis techniques. Over 600 cases of asbestos related disease are now in its records – representing a significant data base of asbestos-related disease.

J. S. Logan
H. Bharucha
J. M. Sloan

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The Ulster Medical Journal, Volume 65, No. 1, May 1996.

Editorial

The Thirtieth Anniversary of Pre-hospital Coronary Care in Belfast

Pre-hospital coronary care was introduced at the Royal Victoria Hospital, Belfast, on 1 January, 1966. The 20th Anniversary of this event was marked by a *Festschrift* in honour of the originator of this revolutionary approach, Professor Frank Pantridge. The proceedings of this international symposium were later published by Dr John S. Geddes under the title of "The Management of the Acute Coronary Attack".[1] Publications elsewhere[2] as early as 1972 had attested to the success of coronary ambulances in the Asian-Pacific area.

The original concept of mobile coronary care envisaged by Pantridge and Geddes involved the use of a rota of junior hospital doctors and nurses trained in coronary resuscitation. However shortly after the 1967 publication of their original work, Cobb[3] in Seattle studied the feasibility of training non-physicians to provide initial management of certain medical problems outside hospital. He chose to use firemen because of their very rapid response – three minutes on average. The development by Pantridge of a portable defibrillator soon afterwards greatly facilitated this development. Thus in the USA doctors and nurses were replaced to a very large extent by trained paramedics and lay people. Prompt defibrillation delivered by paramedics, intermediate emergency medical technicians and basic emergency medical technicians taught to recognise and treat ventricular fibrillation by direct current countershocks, had proved effective in lowering morbidity and mortality. This allowed Dr Richard S. Crampton[4] of the University of Virginia to state at the 1986 Symposium that the innovative treatment begun by Pantridge and his associates two decades previously had led to an extraordinary widespread remodelling of emergency services and clinical practice in the United States.

Also at the 1986 *Festschrift* Dr Charles Wilson presented data from two catchment areas in Northern Ireland showing the effect of the presence or absence of mobile coronary care (MCC). The availability of MCC in Ballymena was associated with a community mortality rate 33% lower than in Omagh, though the populations were otherwise demographically similar. He noted that one third of the difference was apparent at the end of the first hour after the onset of symptoms, at which time the proportion of patients admitted was 10 times greater in Ballymena than in Omagh. Thus, many more patients in Ballymena received acute coronary care before lethal symptoms could supervene. The remaining two-thirds of the difference occurred over the next month. Wilson attributed the reduction in early deaths to prevention of death by arrythmia by timely therapeutic intervention, while the later benefit could be attributed to early treatment limiting myocardial necrosis.

Subsequently the treatment of the acute coronary attack in the community by trained paramedics was introduced in Ballymena in 1986, and reported by McRea, Hunter and Wilson[6] in 1989, facilitating the wider spread of community treatment of the acute coronary attack.

In this issue of the Ulster Medical Journal Pantridge and Wilson provide a dispassionate history of pre-hospital coronary care over the 30 years since its first introduction. They discuss its surprisingly slow introduction and spread in the United Kingdom compared with early and enthusiastic acceptance across the Atlantic.

The equipping of ambulances with defibrillators was an important step forward and has led to an increase in successful recovery from cardiac incidents in the community. This must have made a contribution to the decrease of over 30% in the age-standardised mortality rate of males aged 40 to 69 between 1986 and 1992 (Monica project).[7]

There is still no room for complacency. The Northern Ireland mortality from acute cardiac events remains much higher than that of other European countries, especially that of France which has a similar prevalence of risk factors. Pantridge and Wilson point out that only a small

percentage of the lives saved can be attributed to resuscitation from cardiac arrest and much more complete medical care directed towards limitation of myocardial damage is essential. The success of thrombolytic therapy in acute myocardial infarction increases the desirability of early medical treatment before transfer to hospital. All areas in Northern Ireland are now served by mobile coronary care units. The scene is set for another radical leap forward in the management of the acute coronary attack. In this 30th Anniversary Year of the introduction of pre-hospital coronary care, let us all support the Pantridge Foundation of Northern Ireland, set up to further develop coronary care in the community and spearhead research into this major cause of morbidity and mortality.

MARY G McGEOWN

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A NOTE FROM THE EDITOR

There are several sound reasons why the journal now appears on A4 sized paper. There is ample room for a two column format, section headings are easy to identify, and there is more scope for figures and graphs .

And, supplies of the old paper were running low . . .

J M GIBSON

The Ulster Medical Journal, Volume 65, No. 1, pp. 5-18, May 1996.

Disease oriented medicine: the metabolic model

D R Hadden

Presidential Address, 12th October 1995

When you elected me to be your President for this year – an event which was initiated by a letter from the President before last – Professor Robin Shanks – I was certainly honoured, and challenged, but I made a mental note that I should be forward looking, and practical, and above all, medical in any remarks I would offer by way of a presidential address. Professor Philip Reilly delivered a thoughtful dissertion on the development of the branch of the practice of medicine which we now know and respect as general practice.[1] He recalled how there was a tendency to lurch from one problem to another in the administrative arrangements, and to take shelter in any port in a storm: the present arrangements for the practice of primary care medicine, or family practice, are the outcome of much deliberation and foresight, and the overall respect and admiration for doctors in that most general of all medical disciplines at the present time is a compliment to the professional wisdom of the founding fellows of what became the Royal College of General Practitioners. They set a high standard, and the profession has followed their example.

The Ulster Medical Society is not heavily encumbered by a mission statement or a business ethic, and its constitution is more concerned with good organization than high sounding phrases about the practice of medicine in Ulster. But the 19 original founding fathers who met at a house in High Street in Belfast in September 1806 to establish the Belfast Medical Society – there may not have been any more than that in those days in Belfast where the population was only about 20,000 – were concerned with meeting each other and continuing their medical education in the most practical way. The subsequent history of the Society, and of the development of Belfast medical and surgical practice, and of the Belfast Medical School, has been carefully documented. Professor Desmond Montgomery in his Presidential Address to the Society in 1975, 20 years ago – 'The Ulster Medical Society – Quo Vadis?,[2] the year we moved into our new rooms in the Whitla Medical Building - believed that we were coming to terms with the challenge of specialization, and adapting ourselves to the changing pattern of medicine. He saw the Society as fulfilling an integrative role for a divided profession, always striving to maintain the highest ideals of the art and practice of medicine. It is in that forward looking perspective that I hope to consider some of the challenges of medicine that lie ahead of us.

THE PAST

"'Tis the sunset of life gives me mystical lore,
And coming events cast their shadows before".

Thomas Campbell, 1777-1844

Lochiel's Warning.

Thomas Campbell was also the source of the one liner "*'Tis distance lends enchantment to the view*" – and we must guard at looking backward through tinted spectacles, either rosy or black: but it is reasonable to see if the events which took place did in fact cast a shadow in time, and whether medical planning was ever successfully proactive rather than reactive.

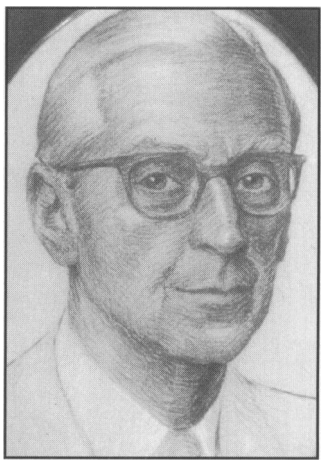

Fig 1 Robert Evans Hadden, BA, MD, FRCGP, Portadown, 1902-1978.

Sir George E Clark Metabolic Unit, Royal Victoria Hospital, Belfast BT12 6BA.

David R Hadden, MD, FRCPEd, FRCP.

It was my father, Dr Robert Evans Hadden, of Portadown, who talked to me about these matters: in the 1940's, when all sorts of things were happening, a far greater change in medical practice than is occurring now. It is interesting to realize that it was in the King's speech on VJ Day, 16th August 1945, that the first small reference to the National Health Service crept into a Government statement, carefully camouflaged between social security and industrial injury compensation. My father was a fellow of this Society, as was his father before him – the journey from the country into Belfast was always tedious for those who lived outside the centre: he was nevertheless a good attender, and found the Society an important source of continuing education. The Health Service committees at that time seemed to have just as much trouble as their counterparts today in trying to foresee the future: they frequently got it wrong, particularly with medical student numbers, and with the steady growth of specialization. He had given his Presidential Address in 1960 to the Northern Ireland Branch of the British Medical Association on the subject of poetry in medicine, with particular reference to 'The Testament of Beauty' by Dr Robert Bridges, Poet Laureate[3]: perhaps it needs a Trinity College Dublin graduate to bring back the broader educational values which are stultified by our present highly specialized A level examinations and medical school entrance criteria.

General medical practice at that time had many problems, but in retrospect, I remember the happy times and we seemed to have good holidays, and the sun shone and the snow snowed and the frost froze at the appropriate seasons. Many doctors at that time were so fearful of, and so unhappy with the National Health Service that they advised their children to have nothing to do with it.

Those of us who persevered despite the doom and gloom did so with the support and encouragement, not of committees or books of rules, but of those elders and betters whom we knew and trusted. Perhaps it was always so.

Practical genetics is a fascinating discipline, and pedigrees of diseases can be traced through many generations. It is more difficult to be sure of diagnostic criteria in earlier cases such as the difficulty in establishing a retrospective diagnosis of porphyria in the case of George III's illness, even when the abnormal colour of the royal urine was recorded carefully by the otherwise incompetent (or perhaps more kindly expressed as inadequate) physicians of the day. This family tree shows a condition which has recurred through five generations, and not all branches have been shown in full (Fig. 2). In earlier generations it was rather intermittently expressed, and appeared to be sex linked to males. In later generations female cases occurred. Some early females married males who expressed the condition. This would fit a genetic

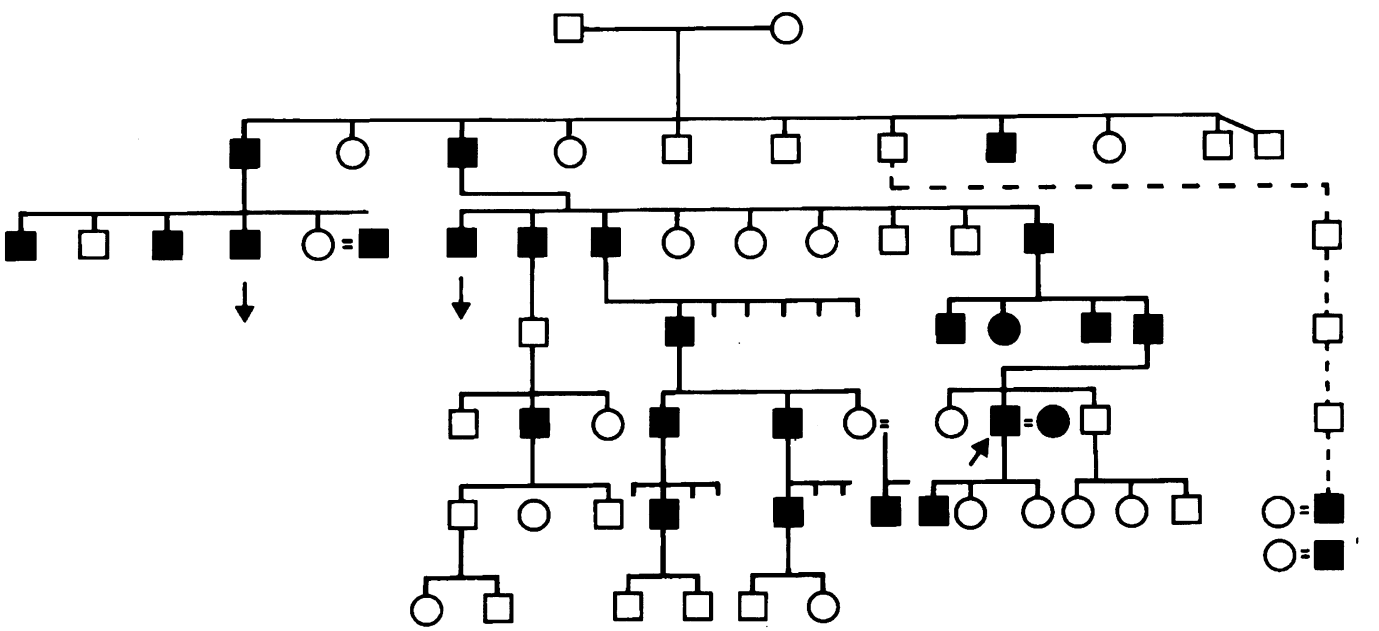

Fig 2 A family tree.

explanation with a dominant transmission, but it is of course entirely an environmentally determined condition – at least the study and practice of medicine is thought to be such. The affected members of this pedigree probably all felt that they made the decision to study medicine of their own free will: Darwin and natural selection would not allow any genetic explanation, but Lamarck and his discredited theory of the inheritance of acquired characteristics would have recognised some possibility of the transgenerational passage of environmental factors. This latter concept, now dignified by the term 'imprinting' and the Barker hypothesis,[4] may be allowed some respectability, and it has been further studied by Professor Joseph Hoet and his team in Belgium.[5] Robert Bridges expressed the message succinctly and elegantly in his Testament of Beauty as an *"atomic mechanism with unlimited power to vary the offspring in character, by mutual inexhaustible interchange of transmitted genes"*.

But would these early doctors have foreseen the problems ahead in 1840? Could the crisis of the Irish potato famine have been predicted? Dr David Hadden (third sibling of the second generation shown) studied medicine as an apprentice to his elder brother in Wexford, and took the examinations of the Apothecarys Hall in Dublin in 1839: the rules of his apprenticeship make strange reading: the Medical Acts later in the 1840's abolished this method of becoming a doctor, and Dr Hadden himself clearly felt the need of a more established degree as he took the MRCS London and the MD Glasgow by examination in 1846, even though his dispensary practice in Skibbereen, Co Cork, was then in the centre of the worst area for the famine.

As an aside, the profession in Ireland was even then concerned with financial matters, and more urgently the alarming mortality among medical men themselves. Dr William Wilde presented a memorial to the Lord Lieutenant in 1847 signed by 1160 practitioners, "It is right to draw your Excellency's attention to the fact that statistical returns for upwards of twenty-five years exhibit a fearful mortality from fever among the medical men of this country and recent events have shown that from the same cause we have to deplore the loss of many of the best and most efficient practitioners who contacted typhus fever in the discharge of their duties among the sick poor. We most strongly, but respectfully, protest against the ... five shillings per day ... offered by the Board of Health for the discharge of that onerous responsibility and dangerous duty". To which they received the reply that "the lordships of the treasury are of the opinion that the remuneration is as high, as under the circumstances of the case, as they should be justified in granting". The average income of a dispensary doctor at that time was about seventy pounds a year.[6] Dr Hadden's response to all this is not recorded, but his patients must have felt strongly about it, for in 1860 they presented him with a service of silver and a purse of 200 sovereigns, which must have been of considerable benefit in his financial affairs (Fig. 3).

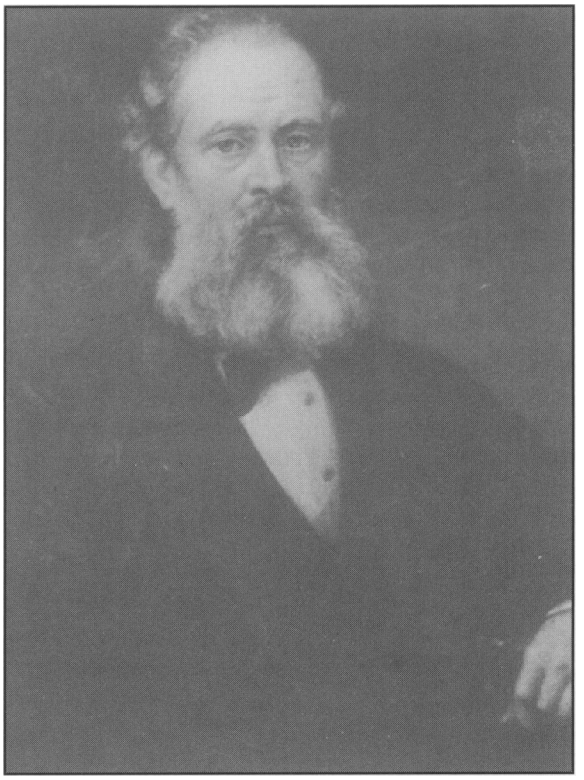

Fig 3 David Hadden MD, Skibbereen, 1817-1878.
Reproduced from E O'Brien, A Crookshank, G Wolstenholme. A Portrait of Irish Medicine, Dublin, Ward River Press, 1984: 130. The original portrait is in the Masonic Hall, Skibbereen.

The practice of medicine in Ireland was entirely empirical, whether by Dr David Hadden in dispensary practice in Skibbereen, or by the leaders of the profession like Graves and Corrigan in Dublin, or by the 19 worthy doctors in Belfast who founded this Society. "These are awful times – never did you see the like, what the end of them will be God only knows – let us watch and be sober": these premonitions are just as relevant today as they were when they were written to the first male member shown on the pedigree on the occasion of his marriage in 1808. Some of the medical members died young and their families had to emigrate to a new life in America, where they often did well – still in medicine. Some had less successful careers,

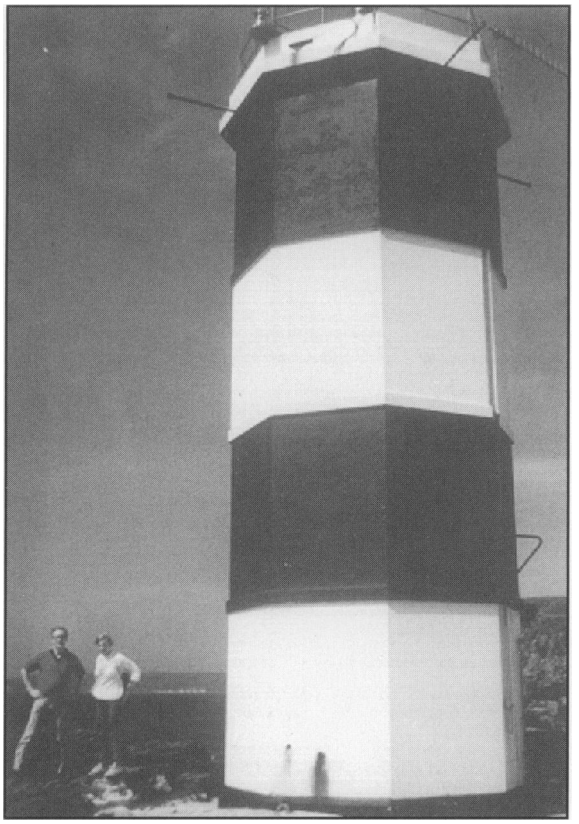

Fig 4 The lighthouse at Rue Point, Rathlin Island, 1988.

and one at least even came to a bad end: one was a ship's doctor, Dr William Edward Hadden, my grandfather, who was shipwrecked on Rue Point, (Fig 4) Rathlin Island in 1886 and that is why I am here in Ulster tonight. One of the American connection, Dr John Hadden, has become a distinguished expert in the immunopharmacology of cancer,[7] and will address this Society on this topic. But none could have foretold two world wars, nor was their medical education appropriate to deal with the problems specifically due to war or famine. A study of the past, whether within a small family or as part of the larger community of doctors, does not identify any common theme of prescience, but always suggests that given a good education, perhaps particularly a good practical Irish medical education, North or South, the practising doctor can adapt to the problems that arise.

THE PRESENT

"Reading maketh a full man,
Conference a ready man,
Writing an exact man"

Francis Bacon, 1561-1626

Reading, conferring and writing about a subject are all essential elements in the search for knowledge, and only by increased knowledge, properly applied, can treatment be improved. Specialization in medicine has come about in a number of different ways, which have led to rather different approaches by the groups of doctors involved (Table 1).

An age-related approach has led to neonatal, paediatric and geriatric medicine: children are special because they are small, even very tiny, and need smaller equipment and smaller doses of medicine. They also have parents who want to be part of the action. At the other end of the age range, elderly people have special problems of frailty and the difficulty of living alone – they also have carers, although these may not be their own relations. So these age-related specialties often focus on the broad spectrum of care without necessarily emphasising the detail of individual disease processes or what causes them.

Gender-related medicine is virtually confined to female reproduction, which involves obstetrics and gynaecology: the diseases that develop in women are important because of their effect on the reproductive process and its subsequent long- term effects. Recent trends include the investigation and management of impaired reproduction or infertility, which has taken on the male component as well. The study of male genito-urinary medicine might in some ways be considered the male counterpart of gynaecology, and the long-term effects of sexually transmitted diseases may be of equal importance to the traditional problems of female reproduction.

Organ-related medicine is also easy to identify. The eye, the ear, the heart, the gut, are all clearly defined, with easily measured physiological functions. The mind is also an organ, though measurement is more difficult. Each of these organs can be the seat of different disease processes, so the specialist must be to some extent multidisciplinary although they will not get to the broader limits of the several disease processes with which they interface.

Procedure-related specialists include anaesthetists, radiologists, radiotherapists and chemotherapists - now becoming known as oncologists as their skills are confined to cancer therapy. The laboratory-based specialties are also essentially procedure-based, such as biochemistry with its complex measurements, and pathology with its histological examinations.These procedures allow a detailed knowledge of a number of specific aspects of disease processes, but still do not encompass the full spread of a particular pathological process.

TABLE I

A classification of types of medical practice

Age-related	Neonatal	Diagnosis-related	General medicine
	Paediatric		General surgery
	Geriatric		Family practice
Gender-related	Gynaecology		
Organ-related	Ophthalmology	Disease-related	Rheumatology
	Otology		Haematology
	Cardiology		Tuberculous diseases
	Gastroenterology		Ischaemic heart disease
	Psychiatry		Endocrinology
Procedure-related	Anaesthetics		Diabetology
	Radiotherapy		
	Chemotherapy		
	Biochemistry		
	Pathology		
	Emergency medicine		

Diagnosis is still the most important process in medical care and treatment, whether established in primary care as it frequently is, or uncovered after complex specialist investigations in hospital practice. Diagnosis-related medicine will include the present broad fields of general medicine and general surgery, and both of these relate closely to family practice and primary care medicine, although the present-day family doctor will have a major role in the prevention of disease, as much as or even more than in its diagnosis.

Disease-oriented medicine first appeared with the treatment of tuberculosis, and the success of that exercise, particularly the work of the Northern Ireland Tuberculosis Authority between 1946 and 1959, has been documented by H G Calwell and D H Craig in the booklet 'The White Plague in Ulster' – in 1946 twenty people were dying from tuberculosis each week, and by 1959 this had fallen to two per week and has continued to fall, though not unfortunately to disappear altogether.[8] There were several reasons for that success, not least the discovery of effective drugs: but tuberculosis remains a scourge in other countries and the great value of a focused and authoritarian approach to disease control must not be forgotten.

I first realized I was practising disease-oriented medicine in 1960, when I became senior house officer to Dr Desmond Montgomery and Dr John Weaver in the Sir George E Clark Metabolic Unit at the Royal Victoria Hospital. This had been opened three years earlier, in 1957, by Professor Charles Best of Toronto, who was famous as one of the team who discovered insulin – now recognised to include Banting, Best, Collip and Macleod.[9] It was then, and is now, one of the very few units specifically devoted to metabolic diseases – what has now come to be known as endocrinology and diabetes. The phrase 'metabolic' is rather specific to Northern Ireland, and comes from the biochemical background of Dr J A Smyth who was physician in charge of the biochemical department and had not had direct control of inpatient beds to treat the increasing number of patients referred to him with diabetes of all types. A large diabetes clinic for outpatients had grown up, since the first use of insulin in Belfast, but this was accommodated initially on a row of chairs outside the biochemistry laboratory and later in the basement of the original outpatient hall, now still the department of dietetics.[10] When one of the Clark family of the Workman Clark shipyard left the then large sum of

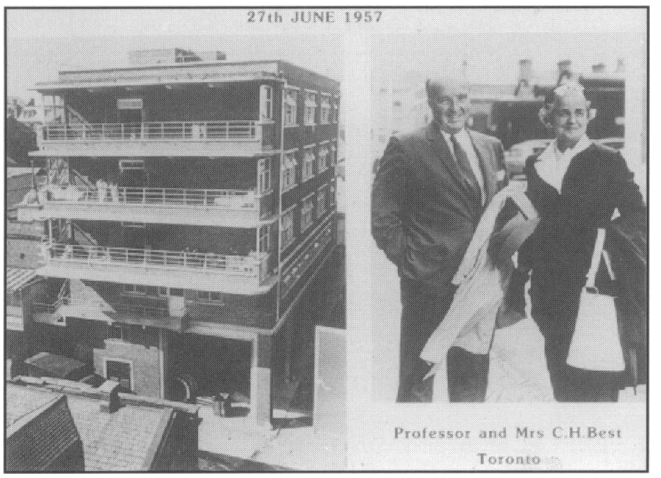

Fig 5 The Sir George E Clark Metabolic Unit, Royal Victoria Hospital, Belfast. Opened by Professor Charles Best, 27 June 1957.

£10,000 to the Royal Victoria Hospital it was in recognition of the work done for diabetes over the years; the building was designed to incorporate outpatients in a carefully organised progressive consultation system with full time clerical, nursing and dietetic staff, and for 30 beds on two floors upstairs for inpatients. (Fig 5)

No other hospital in the United Kingdom has a Metabolic Unit quite like ours, and we must cherish it and look after the concept whatever comes in the future. Our outpatients are now seen in the new general outpatient building which is much too far away; the regional endocrine laboratory was accommodated in the ground floor of the Metabolic Unit for twenty years but has now moved to the new Kelvin laboratory building. The space is now being re-opened as the Diabetes/Endocrinology Day Centre, with facilities for diabetes nurse specialists, dietitians and dedicated patient education facilities. We will also have proper accommodation for the secretarial and clerical staff, and for the computerised diabetes and thyroid registers.

In 1960, endocrinology was the most exciting field in medicine, with new hormones and new diseases and new drugs to treat them being discovered each year. The pioneering work of Montgomery and Welbourn in bilateral adrenalectomy for Cushing's Syndrome had established Belfast as a centre for the new specialty,[11] and when the facilities of the Metabolic Unit became available, with the biochemical expertise developed by D W Neill, the situation was ripe for rapid development and all of us who were junior staff in those days benefited greatly. Cortisone had recently been discovered and the adrenal steroids made enormous therapeutic advances possible, although controlled double blind trials were certainly not undertaken and many misjudgements must have been made. It was perhaps Desmond Montgomery's insistence on long-term review of these Cushing's Syndrome patients, who were maintained on cortisone acetate and came to a special clinic which still exists, called the Adrenal Clinic, once a month, that started one line of disease-oriented medicine. By following the patients it became clear that a few would develop excess ACTH secretion, and eventually succumb to a locally aggressive pituitary basophil tumour – the world knows this as Nelson's Syndrome, but we in Belfast know that it was first recognised by Montgomery and Gleadhill and their colleagues.[12] Some of these early patients still survive 40 years later, and still come to the Adrenal Clinic: the natural history of a disease takes a lifetime to identify, and will involve the professional lifetimes of several medical attendants. Good records, and the passage of interest and enthusiasm from one doctor to the next, are necessary for long-term studies.

Thyroid disorders were probably the reason for the term 'metabolic' – special single rooms were built for measurement of basal metabolic rate, which was the only test for hyper- or hypothyroidism: the old BMR machine still exists but it was a poor and inaccurate measure. The duty of the senior house officer was to creep into the room early in the morning, with the patient sedated and the blinds down, and gently put in a large rubber mouthpiece and ask the patient to breathe normally into a canister of soda lime: not an easy thing to do even in a physiology laboratory, and certainly alarming first thing in the morning in a strange hospital. But it is surprising how good the results were, and even the subsequent development of radio-iodine neck uptakes and then accurate assays for serum thyroxine and TSH have not entirely removed the concept of measuring the end organ action of the thyroid hormone by some index of oxygen consumption.

Hypothyroidism had first been treated in Ireland in 1892 by Dr Thompson of Feeny, Co Londonderry, whose history was identified by the late Dr Mary Logan[13]: hyperthyroidism proved a more difficult therapeutic task, and although subtotal thyroidectomy was surgically possible in the 1930's, even post-war it was still a formidable procedure. The development of antithyroid drugs and the introduction of therapeutic radio-iodine has made a cure of Grave's disease a much more straight-

forward, and more certain, procedure. The long-term recall of many of these radio-iodine treated patients became unnecessary when the metabolic unit thyroid computer review service was introduced in the 1970's, and although many general practitioners are now sufficiently well organised to provide this service themselves, some patients still are pleased to feel they have contact with the Metabolic Unit, even if only by computer-generated letter.

The overall change in management of hyperthyroidism between 1970 and 1990 is shown in Table II.[14] The great reduction in subtotal thyroidectomy and its replacement by radio-iodine means that a two-hour day procedure with only a few subsequent hospital reviews should be sufficient. The staff of the Metabolic Unit are registered for this radio-isotope administration, and the concept of disease oriented medicine means that we are still interested in the long-term outcome. In the early days we used smaller doses, but the tendency to relapse, with need for more hospital attendances pointed to the use of larger ablative doses, and when Dr Atkinson and Dr Kennedy returned from the USA in 1980, and brought this more radical approach, both Dr Weaver and I were happy to go along with it. Thyroid cancer management requires even larger doses and close co-operation with the endocrine surgeons – initially Mr Willoughby Wilson, and now Mr Colin Russell.

It was Mr Russell's interest in thyroid cancer that has resulted in a long-term investigation of a widely distributed kinship of the MEN 2 syndrome (Multiple Endocrine Neoplasia type 2): members of this family have developed malignant medullary thyroid cancers, with or without adrenal phaeochromocytomas. The search for effective endocrine tumour markers – initially with serum calcitonin, and subsequently with the interest of Dr Patrick Morrison the demonstration of genetic markers on chromosome 10 has meant that members of these families can now be identified with a high degree of accuracy to be either at risk or not at risk of thyroid cancer.[15] The family tree shows that the genetic marker has been 100% accurate in known cases, but the problem of management of children in the next generation who are genetically positive but have absolutely no evidence of thyroid cancer, means that the skills and wisdom of the thyroid surgeon are still needed. The disease-oriented approach to these patients means that one team keeps in touch with all members of the family, so that consistent advice is given, although with most careful confidentiality between different branches of the family. Even in well integrated families there are personality difficulties, and it can be difficult and at times disappointing when people known to be at risk refuse to come for even simple treatments or tests. Pre-clinical diagnosis is not always popular, and this aspect of medicine in the future will tax our successors just as much as some of the tragedies of today.

My own interest in research in the Metabolic Unit started off at a very early stage in wondering why some babies born to diabetic mothers were so large. The theory of Dr Jorgen Pedersen in Copenhagen was that maternal hyperglycaemia caused fetal hyperglycaemia and subsequent endogenous fetal hyperinsulinism which caused fetal overgrowth: my somewhat naive concept was that the mother's growth hormone might also be too high, and account for the impaired maternal glucose tolerance in the

TABLE II

Hyperthyroidism in Northern Ireland. A therapeutic audit of the numbers of patients treated by three different methods over two six-year periods. (Based on data from Hadden D R, McDevitt D G ,1974 and subsequent analysis.)

	1966-71	*1986-91*
Carbimazole	3,127	2,739
(standardized treatment years)		
Radio-iodine	633	1,063
Subtotal thyroidectomy	295	60
	4,055	3,862

first place. With the enthusiastic support of Dr Graham Harley, and the encouragement of Dr Montgomery who had already set up their combined metabolic antenatal clinic with the intention of simplifying the clinical attendances of the diabetic mothers, we set off on an odyssey which still continues.[16] Glucose tolerance tests in pregnancy have proved to be a never-ending search for international agreement, and have introduced me to the medical and political interactions of a number of countries round the world.[17] We hope that Belfast will be one of the central points and the laboratory for the Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) study, one of the largest co-operative international studies ever undertaken, on 25,000 normal pregnant women each of whom will have a glucose tolerance test, in 25 different countries, simply to sort out the ethnic and environmental differences. Once that is done, the disease-oriented approach will allow careful monitoring of what is most likely the real cause of the explosion of non-insulin dependent diabetes throughout the developing world. The trans-generational effect of maternal hyperglycaemia has been shown to affect the second and third generation in animal models, and to be responsible for both obesity and diabetes in the first generation in human studies. Whether the Barker hypothesis of maternal malnutrition as a cause of many of the ills of the offspring when they grow up will be confirmed is still uncertain, but there is major evidence to support the diabetes effect.

The road to measurement of maternal plasma growth hormone was long and difficult. I made my own human growth hormone from pituitary glands collected in the mortuary. I made antibodies to it in rabbits, and set up radio-immunoassays which largely did not work. I was fortunate to be able to go to the Johns Hopkins Hospital, Baltimore, USA, and work in the Endocrine Unit under Dr Sam Asper and Dr Thad Prout, who had also trained Dr Weaver before me. The endocrine link with the Johns Hopkins Hospital extends further back, to the time when the then Dr John Henry Biggart studied the neuropathology of the posterior pituitary in the 1930's.[18] The assay for growth hormone came with me, and diverged into studies as to why it did not work, which led to the first clear identification of a growth hormone binding protein.[19] This was received with much disbelief by the originators of radio-immunoassay techniques in the USA, Berson and Yalow, but I was encouraged to find they spent the next two years repeating my work in order to try to disprove it,[20] and even more to find the growth hormone binding protein rediscovered in Chicago by Dr Gerhard Baumann 22 years later.[21] The pathophysiological role of this substance still remains unclear. Dr J K Nelson followed me in Baltimore, and ultimately a method of assaying growth hormone in serum was developed which has proved robust and consistent in clinical practice. It does not seem to be important as a cause of big babies.

After return to Belfast for a year, my metabolic story took a curious, but entirely logical turn when the opportunity arose, through the good offices of Professor Graham Bull and the Medical Research Council, to become a temporary member of the scientific staff and, in fact, the only qualified doctor at the MRC Infantile Malnutrition Research Unit in Kampala, Uganda. This was then a very famous unit, where most of the scientific work on malnutrition had been undertaken, with careful analysis of the differences between kwashiorkor and marasmus: there were close links with Professor R A McCance and Dr Elsie Widdowson, although they stayed most of the time safely at home in Cambridge.[22] The question was whether growth hormone, and insulin, played any part in the endocrine response to malnutrition, and whether it might be possible to explain and hopefully prevent the sudden deaths that occurred during re-feeding of these malnourished children.[23] (Fig 6)

Uganda in 1965 was a delightful country: the Medical Research Council ran a first class research unit: the work went well and I learnt a lot of paediatrics and basic nutrition, which has left me with the life-long determination to improve the teaching of nutrition in our own medical schools. Even after a famine, a rapid increase in mortality from diabetes and the present day Northern Ireland epidemic of ischaemic heart disease which may well be entirely nutritionally based – there was no ischaemic heart disease in the African population of Uganda in 1965 – there is still no formal teaching, or department of nutrition, at The Queen's University of Belfast.

On return to the Department of Experimental Medicine in Cambridge I was one of the last fellows to work under Professor R A McCance, the distinguished but eccentric professor who had been born and brought up in Woodburn House, Dunmurry. His early interest in the growth of babies has laid many of the foundations for the present interest in the relation of size at birth and

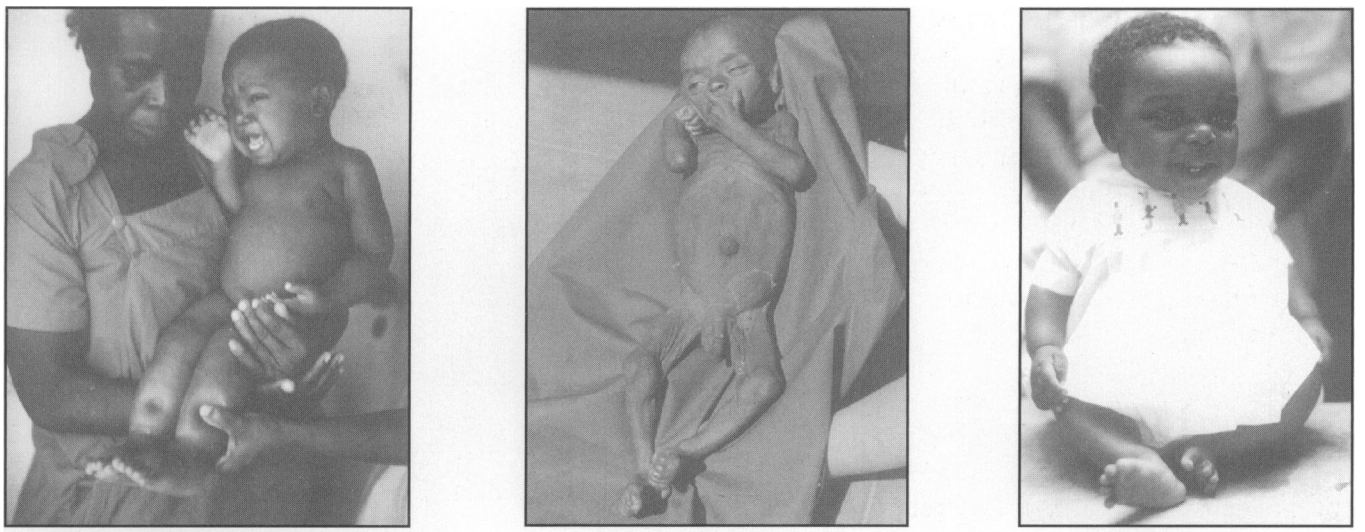

Fig 6 Children at the MRC Infantile Malnutrition Research Unit, Kampala, Uganda, 1965. (i) Kwashiorkor: showing oedema of legs, pallor of skin, with poor hair growth, due to dietary protein deficiency. (ii) Marasmus: starvation of all nutrients, due to social problems. (iii) The same child as in (ii), after normal feeding and about to be discharged.

subsequent disorders in adult life.[24] Growth hormone and insulin were certainly affected by the malnourished state, and showed a patho-physiological adaptation: as might be expected, the best way to avoid serious events during recovery was to proceed slowly and not to give too much by way of either nutritional or hormonal supplements. These basic clinical concepts had been reinforced by the nutritional studies on pigs under McCance's supervision (Fig. 7).

At the same time as these laboratory investigations there was much clinical interest in the use of growth hormone in helping short statured children to grow more normally. Human pituitary glands had continued to be collected carefully at autopsy and stored, and were eventually pooled with similar collections at the MRC pituitary peptide laboratory in Cambridge. The Medical Research Council, and subsequently the Department of Health, drew up most stringent rules for deciding which children would be eligible for this rare and expensive therapy, which had to be given by daily injections, but which certainly worked and produced considerable growth spurts in growth hormone deficient children.[25] I sat on these committees in London, and the constant problem in the 1970's was that there was not enough human pituitary growth hormone to satisfy the demand both from paediatric endocrinologists and from parents of the small children. When a child was accepted for treatment, the enthusiasm always overcame any reservations about possible long-term side effects from a hypothetical slow virus.

In 1985, the first case of Creutzfeldt-Jakob disease was recognised in a person who had received human pituitary growth hormone 20 years before. This is a rapidly fatal progressive dementia and ataxia: there have now been 15 cases among the 1,850 children who received the human growth hormone between 1960 and 1985. There have been none among the 40 children treated in Northern Ireland. No further treatment with this human product was given after May 1985, and it was fortuitous that genetically engineered biosynthetic growth hormone identical to the human molecule became available within six months of the withdrawal notice. But these people are justifiably concerned about their future, and the ultimate outcome is not yet clear. Several of the Northern Ireland patients have become pregnant in the natural course of events, and no problems have arisen in the children. The benefit of the disease-oriented approach in the Metabolic Unit is that I am still able to look after these people, and keep in contact with them at least annually as far as possible. In Great Britain the greater separation between paediatrician and adult endocrinologist meant that most of the early growth hormone treated children who had grown up had stopped attending hospital, and it has proved remarkably difficult to contact some of them again, even in these circumstances.

Another angle on the disease-oriented approach to diabetes is the long-term review we know as the Belfast Diet Study. Those of you who refer diabetic patients to the Royal Victoria Hospital will know that we have a "we try harder" approach to reducing

Fig 7 Three pigs, all one year old. The smallest has been on minimal food intake (marasmus), the pale-skinned one on the right has been protein deficient (kwashiorkor). I took this photograph under Professor R A McCance's supervision, at the Department of Experimental Medicine, Cambridge.

energy intake and advising sensible eating for non insulin dependent diabetes. Belfast has a mild degree of fame on the international diabetes circuit for this approach, and specialists from other countries, especially the USA and Germany, will still stop and ask how we achieved such good results on diet alone? The answer they suggest is that there must be something special about the diabetic people in Belfast – perhaps our dietitians deserve the credit too. But like all long-term studies, even where the patients live longer than the doctors, there is still a down side, and there is no doubt that the prevalence of death from myocardial infarction is still considerably higher in these patients after 10 years than in the population of Northern Ireland.[26] This hospital-based diabetes study will become one of the markers for the future management of this disease in family practice, and the risks of this so-called mild disease must be fully understood by patient, nurse and doctor. The most recent analysis of the Belfast data shows a strong relationship between high blood glucose levels identified as a continuous variable during the ten-year review period and either death from or the occurrence of a myocardial infarction. Macrovascular disease in non insulin dependent diabetes is the real problem.

There is not time to discuss a number of other disease-oriented concepts in endocrinology. Metabolic bone disease, from hyperparathyroidism to osteoporosis, is a slow moving but crucial problem which requires a long-term approach to assess results. The management of female hirsutism and the polycystic ovarian syndrome are still under investigation. And the problem of what happens to children with an inborn errors of metabolism such as phenylketonuria, when they grow up, will be the subject of the next meeting of this Society.

In retrospect, considering these past 40 years in the present tense, we were a fortunate group of medical students. We arrived at a time when scientific medicine was taking a great leap forward and we were able to participate in that leap. We had a scientific education from the combined clinical

course at Queen's University, and we were encouraged to carry out clinical research projects. (Fig 8) So I have no problem in maintaining an optimistic stance as we try to look into the future.

Fig 8 The Teaching Hospital – a logo for the Royal Victoria Hospital designed by Professor D A D Montgomery and drawn by the hospital artist, George A Smyth, 1975.

THE FUTURE

"Say not the struggle naught availeth
The labour and the wounds are vain,
.....
In front the sun climbs slow, how slowly!
But westward, look, the land is bright!"
Arthur Hugh Clough 1819-1861

The future of disease-oriented medicine is to abolish the disease. This is certainly a possibility for all the endocrine and metabolic disorders, particularly those which have an autoimmune basis such as insulin dependent diabetes and both hyper- and hypothyroidism. All that is needed is a means of preventing the initiation, or of the progression, of the activity of the activated T-cell lymphocytes in the cascade of events which leads to the production of antibodies to the specific hormone, such as islet cell antibodies in diabetes. There are a number of studies in progress in this field, of which we are participating in one called ENDIT – a study of the effect of nicotamide in this process – jointly with Dr Dennis Carson at the Royal Belfast Hospital for Sick Children. The identification of children at risk for insulin dependent diabetes because of the presence of islet cell antibodies, even though their blood glucose is completely normal, leads to a number of both ethical and management problems, as there is no clear way ahead at present. The most important fact is that not all these children will actually develop the disease, and in some way nature overcomes the incipient autoimmune process in some of them. That spontaneous cure is what we are looking for. The future management of diabetes may well be a complex matter of identification of the condition before it occurs, and some form of immune modulation to prevent the progression and encourage the remission of the process – all without the classical marker of a high blood glucose and the rather dramatic symptoms that used to go with it. This form of pro-active prevention will need a dedicated team, and an efficient process of identification, education and review – the concept of a diabetes prevention clinic, or even a computerised postal review process, is not yet with us. The experienced family doctor will recognise the difficulty of practising preventive medicine, even when the interaction is as simple as an inoculation to prevent diseases that used to be lethal.

These concepts should also be possible for the prevention, or at least the prevention of progression of the several diseases due to activation of a genetic process in a clone of cells in the anterior pituitary gland. Cushing's disease is due to the inappropriate activation of the gene for ACTH production in the anterior pituitary on chromosome 12: it is not a malignant tumour, but expresses itself because of the profound effect of the excess ACTH on the production of cortisol in the normal adrenal. Even if inactivation of the abnormal gene (without complete suppression of the normal ACTH producing basophil cell mechanisms) is not immediately possible, the concept of targeted radiotherapy or chemotherapy to the anterior pituitary using specific antibodies to the abnormal hormone producing cells is tantalizing, though still ineffective. The role of the neurosurgeon in the cure of Cushing's syndrome, so well practised in Belfast by Colin Gleadhill, Derek Gordon and Tom Fannin and John Grey is still necessary, but like the changing role of the thyroid surgeon, no operation is forever.[27] The recognition by Professor Brew Atkinson that some patients with pituitary dependent Cushing's syndrome may be intermittent, or cyclical,[28] indicates that there must be other as yet unrecognised processes involved in switching

on and switching off the pituitary trophic hormones, which may lead to drugs with as striking an effect as that of bromocriptine in hyper- prolactinaemia.

In the absence of total prevention of the disease, our present aim is to prevent the complications. For diabetes this means returning the blood glucose to normal, and keeping it there. The discovery of insulin in 1921 produced the means to do this, and we are still learning how to use this potent cure; the problem is that as the only potent drug which is self-administered by people with the disease, and which has such an unpleasant and potentially lethal side effect, it is human nature not to want to push the dose too close to the borderline between normoglycaemia and hypoglycaemia. The late Dr Jack Smith was remembered by his patients for insisting that they kept their blood glucose normal, and for insisting that it was measured in the laboratory before he saw them – this early insistence is largely responsible for the overall better level of control of hyperglycaemia which can still be shown in comparisons between diabetic patients in Northern Ireland and those in less well organised places – for example in the South of England, where many diabetic people were rather left to their own devices with only occasional contact with a family doctor and only the unsatisfactory measurement of urine glucose as a yardstick of success.

Good organization is essential, and the record cards introduced by Professor Montgomery in 1958 are still the basis of management in the Royal Victoria Hospital and most others in Belfast: the computerised patient management system pioneered at the Royal, but developed jointly by the Northern Ireland Diabetes Group, will produce the means of auditing the success of this long-term and rather intensive form of preventive epidemiology. The development of measures of control of hyperglycaemia by identifying the amount of glucose stuck non-enzymatically on to the haemoglobin (by Dr Laurence Kennedy), or other protein molecules (by Dr Tim Lyons), has produced a much better long-term assessment.[29] Dr Laurence Kennedy should get the credit for introducing this measurement into hospital practice in 1980, when he returned from the USA, and the early work in Belfast, including the demonstration by Dr David McCance that long-term prospective control of glycosylated haemoglobin will prevent the microvascular complications, was one of the first real proofs of the importance of good control.[31] We always knew it to be so, but it had been very difficult to prove. Eventually the Diabetes Control and Complications Trial in the USA has confirmed the Belfast studies, by a prospective randomised trial. The evidence is available and our only problem is to deliver the goods.

Dr Patrick Bell had demonstrated that excellent control could be achieved by special insulin infusion pumps,[32] and these were part of the very expensive DCCT study. In Europe, where we are rather in advance of US medicine in many ways at a pharmaceutical level, it was soon realized that the pen injectors would allow multiple insulin doses to be given with minimal inconvenience to the person with diabetes, and that these simple devices were much preferable to the expensive and more complicated pumps. The Northern Ireland Committee of the British Diabetic Association, which is about to open an office in Belfast, and a number of Department of Health and Regional Board committees will help to organise the dream of achieving a disease-oriented diabetes treatment programme in which we can all take part – general practitioner, diabetes physician, specialist nurses, dietitians, chiropodists, and people with diabetes.

The immediate future is therefore a process of facilitation of the delivery of a drug discovered over 70 years ago. The encouraging resurgence of interest in diabetes management in family practice, and the development of shared care and outreach clinics should assist this in the short term, and there is much work to be done by us all. If we are successful, our colleagues who have provided such important services in fixing up the ravages of persistent hyperglycaemia may be less heavily involved. I have not had time to discuss the importance of these complications, but the ophthalmologists under Professor Archer and his team; the experts in end-stage kidney disease at the Renal Unit in the Belfast City Hospital who follow the recipes for success laid down by Professor Mary McGeown; the extraordinary vascular surgical repairs and when necessary the preventive amputation of digits undertaken by Mr Barros D'Sa and his colleagues; the preventive approach to foot ulceration with neurological measurements and the provision of practical footwear and foot care by skilled chiropodists; and the cardiological management of diabetes-related ischaemic heart disease which is now the ultimate killer in the great majority of our patients: all of these hard working and uncomplaining colleagues in our practice of disease- oriented diabetic medicine could and should be put out of business!

I have not referred to some of the present day problems of medical organization such as funding, or purchaser-provider splits, or priorities, or resource allocation, or even medical fees, because like the doctors who coped with the problems of fever and famine 150 years ago, the practice of medicine is always with us: future developments will certainly change what we do, but both specialization and generalization will persist beyond the year 2000. The new building for the Royal Victoria Hospital, which will incorporate a new Metabolic Unit, will allow our team to continue to practise our form of disease oriented metabolic medicine. The next generation of endocrinologists will still need the enthusiastic co-operation of colleagues in all branches of medicine, and from all parts of Northern Ireland. The next millennium is almost with us, and "the land is bright".

ACKNOWLEDGEMENTS

I recall these moments in the ongoing passage of time which is the essence of disease oriented medicine. The strength of the metabolic model has been the sense of continuing team work amongst us all, at medical, nursing, secretarial, clerical, laboratory and administrative levels, with all the professions allied to medicine, and all the educational and scientific colleagues who have participated in these studies. I have referred eclectically to research undertaken at both clinical and laboratory level over the years by a great number of friends and colleagues: I trust they will forgive my too brief references to themselves, and there are many others whose work has impacted with that of the Metabolic Unit to whom there has been insufficient time to refer. The close relationship between the Royal Victoria Hospital and The Queen's University of Belfast has been a benefit to both: the research undertaken has been funded by many sources, and we are grateful to all. Our patients, who have more reason than any of us to be concerned about the disease-oriented model, will be grateful above all to two very long-term members of the team, Sister Maureen Murphy in the outpatient clinic, and Sister Reta Humphries in Ward 25. They have set a very high standard.

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The incidence and distribution of leukaemia and lymphoma within Northern Ireland in the period 1989-1993

R J Q McNally, R A Cartwright, A Staines, S Kuterescz, D Rowland

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SUMMARY

This is the first attempt to systematically record haematological malignancies in Northern Ireland. The methods are identical to a similar effort in other parts of the UK,[1] except that an independent cross check with a cancer registry source was not possible. In addition problems with the census may create differences. Generally, the rates for the leukaemias are slightly lower than in England and Wales, except for acute lymphoblastic leukaemia whilst non-Hodgkin's lymphoma rates are higher. It remains to be seen how stable this situation is as further data are accumulated.

INTRODUCTION

The Northern Ireland Leukaemia Research Fund Data Collection Study started in 1989 as an independent collection system. At that time there was no Health Service cancer registration scheme in Northern Ireland. The aim was to give an accurate picture of the descriptive epidemiology of haematological malignancies in Northern Ireland. The data come from a special collection of material from the diagnostic laboratories of collaborating haematologists and histopathologists around the province. The method of collection was the same as that used in parts of Great Britain.[1] A previously published study in Northern Ireland[2] (the Podar report) concentrated on those leukaemias which are associated with ionising radiation, and used several incomplete registration sources to retrospectively obtain incident cases.

Using these data, variations in the incidence of disease by age, sex and area can be described. This is of intrinsic interest and may also be of value in generating hypotheses about the causes of the diseases studied.

Incidence rather than death certificate data are used because there is concern over both the accuracy of death certificates and their validity as a measure of disease incidence. Therapeutic advances have led to marked changes in the survival pattern of both leukaemias and lymphomas, with greater survival rates leading to marked decline in mortality.[3] Death certificates were used in the Podar report[2] to examine mortality in the leukaemias linked with ionising radiation.

METHODS: Background

Seven disease groupings were used, namely:–

(1) Acute Myeloid Leukaemia (AML),
(2) Chronic Myeloid Leukaemia (CML),
(3) Myelodysplasia (MDS),
(4) Acute Lymphoblastic Leukaemia (ALL),
(5) Non-Hodgkin's Lymphoma (NHL),
(6) Hodgkin's disease (HD), and
(7) Multiple Myeloma (MM).

These groupings were chosen because they provided sufficient numbers of cases for a critical statistical analysis.

Incidence data are reported in 5-year age groups up to 79 years.[4] In common with the GB Leukaemia Research Fund atlas,[1] no incidence data on the over 80's are reported because of lack of diagnostic accuracy and ascertainment problems. Further detail is given in the full report.[4]

Leukaemia Research Fund Centre for Clinical Epidemiology, University of Leeds, 17 Springfield Mount, Leeds LS2 9NG.

R J Q McNally, BSc, MSc, DIC, PhD, Senior Statistician.

R A Cartwright, MA, MB, BChir, PhD, FFPHM, FFOM, Director.

A Staines, BA, MB, BCh, BAO, MSc, MFPHM, MRCPI, Clinical Research Fellow.

S Kuterescz, BSc, Programmer/Analyst.

D Rowland, BSc, MSc, Computing Manager,

Correspondence to Dr McNally.

Local government district populations from the 1991 census were used in the analysis.[5] However, since no post-enumeration survey was carried out, the quality of data is likely to be poor in certain areas and certain age-groups due to under-enumeration.[6]

METHODS: Data Collection

Hospitals likely to diagnose or treat haematological malignancies were identified and the help of their haematologists and histopathologists sought. A central hospital in each area whose consultant staff were prepared to oversee the activity of a Belfast based, Northern Ireland Leukaemia Research Fund funded clerical officer, was identified. The clerk's duty was to collect and record information on every new case falling within the agreed diagnostic groups presenting at the hospitals. Each clerk had a limited number of hospitals to visit to collect data. This was recorded on standard forms and was completed for all new registrations after 1st January, 1989. Included for each patient were full name, sex, date of birth, home address and postcode at diagnosis, exact diagnosis and the date it was made. Copies of relevant haematology or histopathology reports were sent with the registration form to the Leukaemia Research Fund centre in Leeds. All the haematologists and histopathologists in Northern Ireland were involved in this study.

The exact system for case identification from each hospital laboratory was adapted to local practices relating to the reporting and storage of diagnostic information. Whenever there was doubt regarding the validity of a registration, the information was sent to Leeds for a decision. In addition the returns made by each clerk were relayed back for subsequent rechecking and for the addition of missing data. The work of the data collection clerks was controlled by regular contact with Leeds. Also, detailed procedures have been compiled hospital by hospital and kept up to date.

On receipt, the identification information was checked and the address postcode confirmed. A matching and identification program enabled the personal details to be checked to discover if the patient had been registered already. If not, or if the previous registration related to another diagnosis, the registration was completed. A second diagnosis was normally registered only if a malignant progression appeared to be ruled out.

The computer software has numerous logical checks. Also, all new input data are proof read by two clerks. Cases with missing information are reviewed, duplicate registrations are checked for discrepant information and decisions about registration made.

Unfortunately, as there was no formal cancer registration scheme in Northern Ireland when the study was set up it has not been possible to perform cross-checking for this time period.

STATISTICAL ANALYSIS

Since cancer incidence rates show marked variation with age and sex, it is necessary to standardise the rates so as to ensure that regional differences are not merely a reflection of differences in the age-sex structure of the population. In computing figures for the entire Northern Ireland study area (see Tables 1, 2 and Figures 1 of the full report[4]), the direct method of standardisation has been used, and overall incidence rates standardised to a uniform population are presented.

Elsewhere in the full report,[4] indirect standardisation is used, because we are seeking to make comparisons between the 26 Northern Ireland districts, and such comparisons are subject to smaller random variation when this method is used. Age-sex specific rates for the entire area of Northern Ireland are computed and used to generate expected numbers of cases for each district. The ratio of observed to expected for the district is its Standardized Morbidity Ratio (SMR), which is given as a percentage.

A district with an SMR of 100 has the same number of cases as if the provincial age and sex-specific rates had applied. Any process of computing a standardised ratio involves calculating an average of the ratios applicable to individual age-sex strata. This will not be appropriate if geographical changes of risk themselves show age or sex variation. Differences between the observed case counts, and the expected values are reported in terms of "p-values".[4]

If age-standardised rates, or SMR's, are mapped, then there is a tendency for those areas with few events to yield extreme values owing to Poisson variation. These areas are then given undue prominence. One proposed solution is to include some measure of statistical significance in the information to be mapped.[7] Indeed, most atlases have exclusively mapped p-values. However, this confuses statistical significance with biological importance and gives undue prominence to areas of high population in which quite modest deviations of the rate from the overall value may achieve a high level of statistical significance.

TABLE I

Age-specific incidence rates and uniform standardised incidence rates (per 100,000 person years) by disease grouping, pooled over both sexes. The number of cases is in parentheses.

Age	*AML*		*CML*		*MDS*		*ALL*		*NHL*		*HD*		*MM*	
0-4	1.4	(9)	0.0	(0)	0.0	(0)	7.4	(47)	1.3	(8)	0.0	(0)	0.0	(0)
5-9	0.2	(1)	0.0	(0)	0.0	(0)	2.9	(19)	0.0	(0)	0.9	(6)	0.0	(0)
10-14	0.6	(4)	0.5	(3)	0.2	(1)	1.7	(11)	0.3	(2)	0.6	(4)	0.0	(0)
15-19	0.8	(5)	0.0	(0)	0.2	(1)	1.9	(12)	1.1	(7)	2.2	(14)	0.0	(0)
20-24	1.1	(7)	0.2	(1)	0.0	(0)	0.6	(4)	1.1	(7)	2.9	(18)	0.0	(0)
25-29	0.8	(5)	0.0	(0)	0.2	(1)	0.5	(3)	1.3	(8)	2.5	(15)	0.0	(0)
30-34	1.2	(7)	0.4	(2)	0.2	(1)	0.7	(4)	0.9	(5)	3.2	(18)	0.2	(1)
35-39	1.0	(5)	0.4	(2)	0.4	(2)	0.6	(3)	2.4	(12)	1.2	(6)	0.8	(4)
40-44	1.6	(8)	0.4	(2)	0.4	(2)	0.2	(1)	5.9	(29)	2.0	(10)	0.2	(1)
45-49	1.1	(5)	0.2	(1)	0.4	(2)	0.2	(1)	9.8	(44)	1.1	(5)	2.9	(13)
50-54	1.6	(6)	1.3	(5)	1.3	(5)	0.3	(1)	13.3	(51)	1.3	(5)	2.9	(11)
55-59	4.5	(16)	2.5	(9)	2.0	(7)	0.0	(0)	16.0	(57)	1.7	(6)	5.6	(20)
60-64	4.6	(16)	0.9	(3)	5.3	(18)	1.2	(4)	22.8	(79)	2.6	(9)	10.7	(37)
65-69	7.4	(24)	0.9	(3)	10.5	(34)	1.2	(4)	34.8	(113)	3.1	(10)	11.7	(38)
70-74	4.6	(12)	1.2	(3)	15.0	(39)	1.2	(3)	37.2	(97)	0.8	(2)	21.1	(55)
75-79	8.4	(17)	0.5	(1)	18.9	(38)	0.0	(0)	45.7	(92)	2.5	(5)	21.8	(44)
Uniform Standardised Rate	2.6	(147)	0.6	(35)	3.4	(151)	1.3	(117)	12.1	(611)	1.8	(133)	4.9	(224)

A compromise is an "empirical Bayes" version of the SMR.[8] A probability model is adopted for the prior distribution of the true relative risks across the map. The influence of this model upon the estimation of the relative risks follows from "Bayes theorem". The method for estimating the parameters of this prior distribution is termed the "empirical Bayes" method

Two types of map are illustrated in the full report.[4] Both use "empirical Bayes" methods.[8] The first is a map of relative risk (RR) estimates which lie intermediate between the area-specific SMR and the mean of all the age-adjusted relative risks included in the map. Estimates are shrunk towards the mean; this shrinkage is substantial for RR's based upon small numbers of events while those based upon large numbers remain close to the corresponding SMR's. Using small areas, this approach may be modified so that shrinkage is towards a "local" mean based upon adjacent areas, and this method was used in the second map.[4] Comprehensive results are given in the full report.[4] GENSTAT V was used to carry out all analyses.[9]

RESULTS AND DISCUSSION

ACUTE MYELOID LEUKAEMIA

There were 147 cases. Age-specific incidence rates show higher rates in the first five years, followed by a decline (Table I). The pooled rates do not exceed those observed in cases aged 0-4 years until the 40's. There is a female excess in those aged 5-35 years roughly similar rates in both sexes between 35 and 55 yrs and a male predominance emerges in the over 55's. There is no evidence for a temporal trend. There is no evidence for between-district heterogeneity in the SMR's (Table II). There is not much variation in the "shrunk" RR's.

However, for the adjacency smoothed RR's, the highest rates tend to be concentrated in the South East of the province, particularly in the County Down area, Belfast Lough and the Mourne mountains. The lowest rates occur in the north of the province, and County Fermanagh.

CHRONIC MYELOID LEUKAEMIA

There were 35 cases. Age-specific incidence rates (Table I) show a female excess in the under 20's, a

TABLE II

SMR's by district of residence and disease grouping, pooled over both sexes. The number of cases is in parentheses. Significantly high or low SMR's are indicated by stars.[10]

District	*AML*		*CML*		*MDS*		*ALL*		*NHL*		*HD*		*MM*	
Derry	116	(9)	106	(2)	147	(10)	87	(7)	115	(34)	103	(8)	88	(9)
Limavady	124	(3)	358	(2)	188	(4)	42	(1)	55	(5)	122	(3)	94	(3)
Coleraine	63	(3)	173	(2)	20	(1)*	56	(2)	108	(22)	117	(5)	80	(6)
Ballymoney	88	(2)	0	(0)	0	(0)	56	(1)	63	(6)	196	(4)	58	(2)
Moyle	0	(0)	0	(0)	0	(0)	0	(0)	50	(3)	0	(0)	88	(2)
Larne	139	(4)	0	(0)	33	(1)	148	(3)	89	(11)	40	(1)	88	(4)
Ballymena	75	(4)	0	(0)	109	(6)	50	(2)	102	(23)	84	(4)	145	(12)
Magherafelt	32	(1)	0	(0)	32	(1)	69	(2)	95	(12)	167	(5)	108	(5)
Cookstown	111	(3)	0	(0)	112	(3)	119	(3)	120	(13)	118	(3)	172	(8)
Strabane	95	(3)	0	(0)	164	(5)	35	(1)	79	(10)	101	(3)	154	(7)
Omagh	125	(5)	108	(1)	227	(9)*	82	(3)	88	(14)	80	(3)	34	(2)
Fermanagh	78	(4)	250	(3)	147	(8)	268	(11)**	102	(22)	90	(4)	87	(7)
Dungannon	98	(4)	307	(3)	148	(6)	167	(6)	103	(17)	80	(3)	116	(7)
Craigavon	74	(5)	61	(1)	90	(6)	106	(6)	108	(30)	126	(8)	50	(5)
Armagh	43	(2)	90	(1)	64	(3)	75	(3)	110	(21)	70	(3)	116	(8)
Newry & Mourne	165	(12)	0	(0)	42	(3)	105	(7)	90	(26)	132	(9)	115	(12)
Banbridge	161	(5)	269	(2)	63	(2)	82	(2)	108	(14)	106	(3)	84	(4)
Down	115	(6)	323	(4)*	76	(4)	67	(3)	126	(27)	105	(5)	77	(6)
Lisburn	126	(11)	47	(1)	85	(7)	120	(9)	109	(38)	84	(7)	89	(11)
Antrim	53	(2)	0	(0)	86	(3)	123	(4)	118	(18)	106	(4)	75	(4)
Newtownabbey	128	(9)	0	(0)	58	(4)	97	(5)	79	(23)	78	(5)	104	(11)
Carrickfergus	133	(4)	272	(2)	67	(2)	170	(4)	104	(13)	143	(4)	67	(3)
North Down	126	(9)	118	(2)	113	(9)	148	(7)	77	(24)	83	(5)	86	(10)
Ards	97	(6)	135	(2)	123	(8)	67	(3)	87	(23)	73	(4)	187	(18)**
Castlereagh	46	(3)	194	(3)	125	(9)	76	(3)	78	(22)	167	(9)	38	(4)*
Belfast	98	(28)	61	(4)	116	(37)	96	(19)	114	(139)	87	(21)	117	(54)

* $p<0.05$
* * $p<0.01$

male predominance in the 20-50 year olds, and roughly equal rates in the over 50's, with a slow increase with age. There is no evidence of an increase with time. There is no evidence for between-district heterogeneity from the male and female SMR's, but possible evidence from the pooled SMR's (p=0.065 – Table II). In particular, Down has a significantly raised pooled SMR (p=0.05), and Dungannon has a significantly raised male SMR (p=0.02). However, these observations should be treated with caution, owing to the small number of cases.

The male shrunk RR's were much more heterogeneous than the female RR's. Highest rates occurred in Fermanagh, Dungannon, Banbridge, Down, Castlereagh, Carrickfergus and Limavady, whilst very low shrunk RR's were observed for Ballymena, Newtownabbey, Belfast and Newry and Mourne. The smoothed RR's were in general agreement with the shrunk RR's, particularly concerning the highest rates. However, the lowest rates appear to be concentrated in two distinct areas – the North East of the province and the Mourne region.

MYELODYSPLASIA

There were 151 cases (Table I). There is a marked predominance of males aged over 55, but below this a slight excess of females. There is no evidence of a time trend. There is marginal evidence for between-district heterogeneity from the SMR's (p=0.086 for pooled; p=0.110 for males; and p=0.097 for females). In particular, Omagh has a raised pooled SMR (p=0.03 – Table II) and Derry has a raised male SMR (p=0.05). As expected the smoothed RR's show far more variability than the shrunk RR's. This is particularly obvious for males.

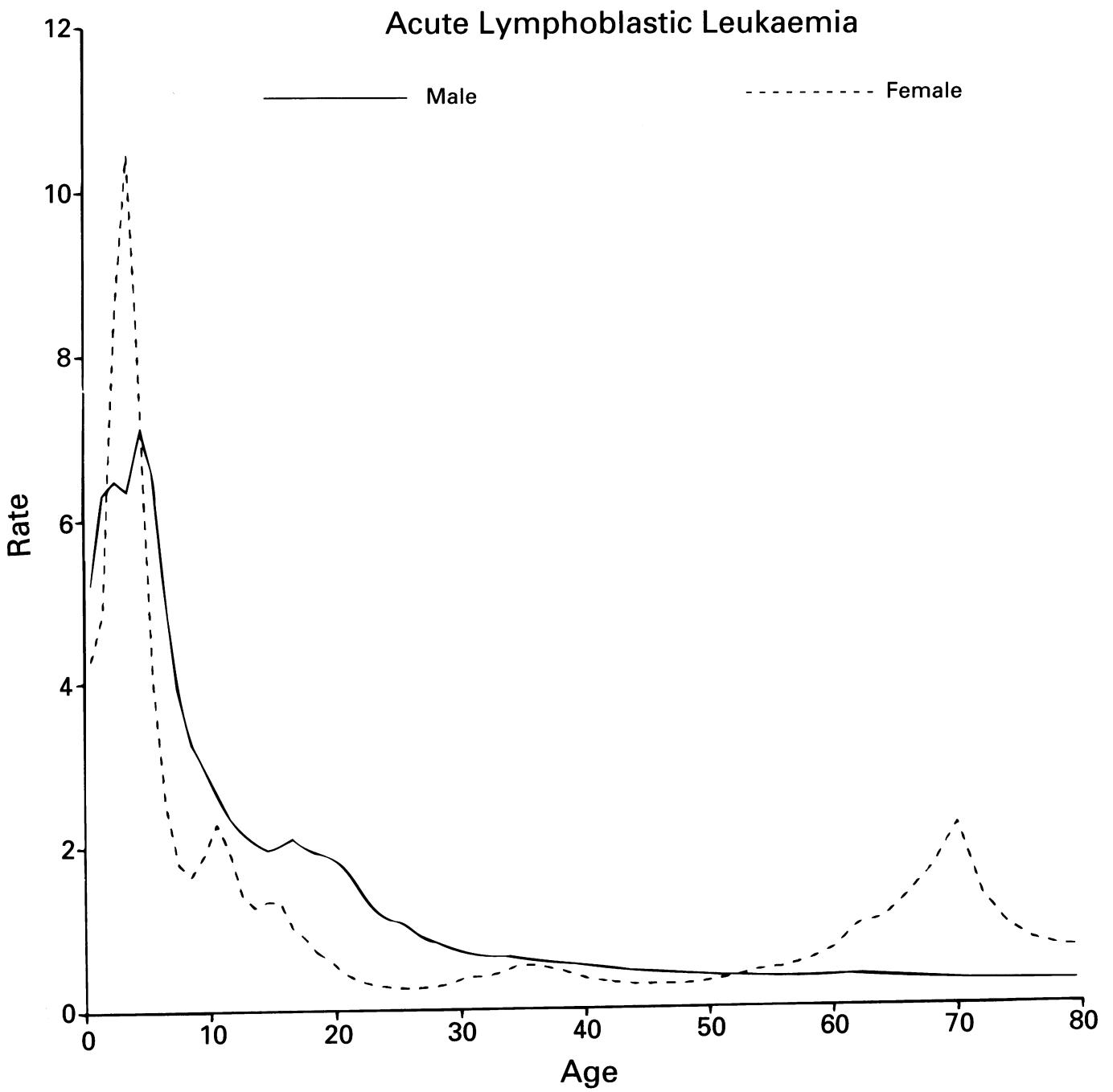


Fig 1. Age – specific incidence rates/100,000 population

There is a strong tendency for the highest rates to occur in the west of the province and the area comprising Belfast and the Ards/Strangford region. Lowest rates are observed in the North East and South East of Northern Ireland.

ACUTE LYMPHOBLASTIC LEUKAEMIA

There were 117 cases. The age-specific incidence rates show peaks in the first age quinquennium (Figure 1 and Table I). Subsequently there is a slight male excess in the under 50's and a female excess in the over 50's with a female peak around 70. There is no evidence of an increase with time.

There is a significant statistical interaction between sex and geographical distribution at district level (p=0.007). This indicates that the sex ratio of rates varies geographically. There is also marginal evidence for a statistical interaction between age and geographical distribution at district level (p=0.062). There is no evidence for between-district heterogeneity from either the pooled or female SMR's. However, there is strong variability between districts for males (p=0.011).

Fermanagh and North Down both have raised male SMR's (p=0.0007 and 0.020 respectively). Fermanagh has a raised pooled SMR (p=0.005), due to the excess of male cases (Table II).

Since there is a significant statistical interaction between sex and geographical distribution at district level, the maps of pooled rates may not be meaningful. Also, because there may be an interaction between age and geographical distribution, the male and female maps have to be treated with caution. (Accordingly, we only illustrate maps of male rates). These maps of male rates are illustrated (Maps 1 & 2) and show highest rates in the South West, particularly in County Fermanagh, and south of Lough Neagh, but also around Belfast Lough. Lowest rates are seen in the North and West of the province.

NON-HODGKIN'S LYMPHOMA

The study reports on 611 cases. Incidence is low in children but the incidence rates rise steeply from early adult life (Table I). There is a suggestion of an adolescent peak in males. There is a male excess at most ages. There is no evidence of an increase over time. Surprisingly, in view of English data suggesting the reverse (McNally et al – unpublished observations) there is some suggestion of a male decrease (p=0.036) over time.

There is no evidence for between-district heterogeneity in the SMR's (Table II). However, Belfast appears to have a raised SMR for males (p=0.048). Neither the shrunk RR's nor the female or pooled smoothed RR's show much variability. The male smoothed RR's show greater variability, the highest being observed in Belfast.

HODGKIN'S DISEASE

There were 133 cases of this condition. The age specific incidence curve shows a peak in young adults (Table I). After the modal values, which are similar in both sexes, there is a marked male predominance in older persons up to age 75. For the age group 75-79, there is a female excess. There is no evidence for a time trend.

There is no evidence for between-district heterogeneity in the SMR's (Table II). However, Ballymoney appears to have a raised SMR for females (p=0.04). There is not much variability in

TABLE III

MULTIPLE MYELOMA

Temporal variations (%) in standardised incidence rates

	MALE	*FEMALE*	*POOLED*
Year	*Rate (%)*	*Rate (%)*	*Rate (%)*
1989	5.4 (91.1)	3.8 (92.5)	4.4 (90.1)
1990	5.6 (95.0)	5.1 (124.3)	5.3 (109.7)
1991	5.7 (95.6)	4.8 (116.1)	5.2 (107.6)
1992	6.2 (104.4)	2.9 (70.1)	4.2 (86.5)
1993	6.8 (114.1)	4.0 (97.1)	5.2 (106.0)
Test for linear trend:	p=0.0141	p=0.5812	p=0.8374

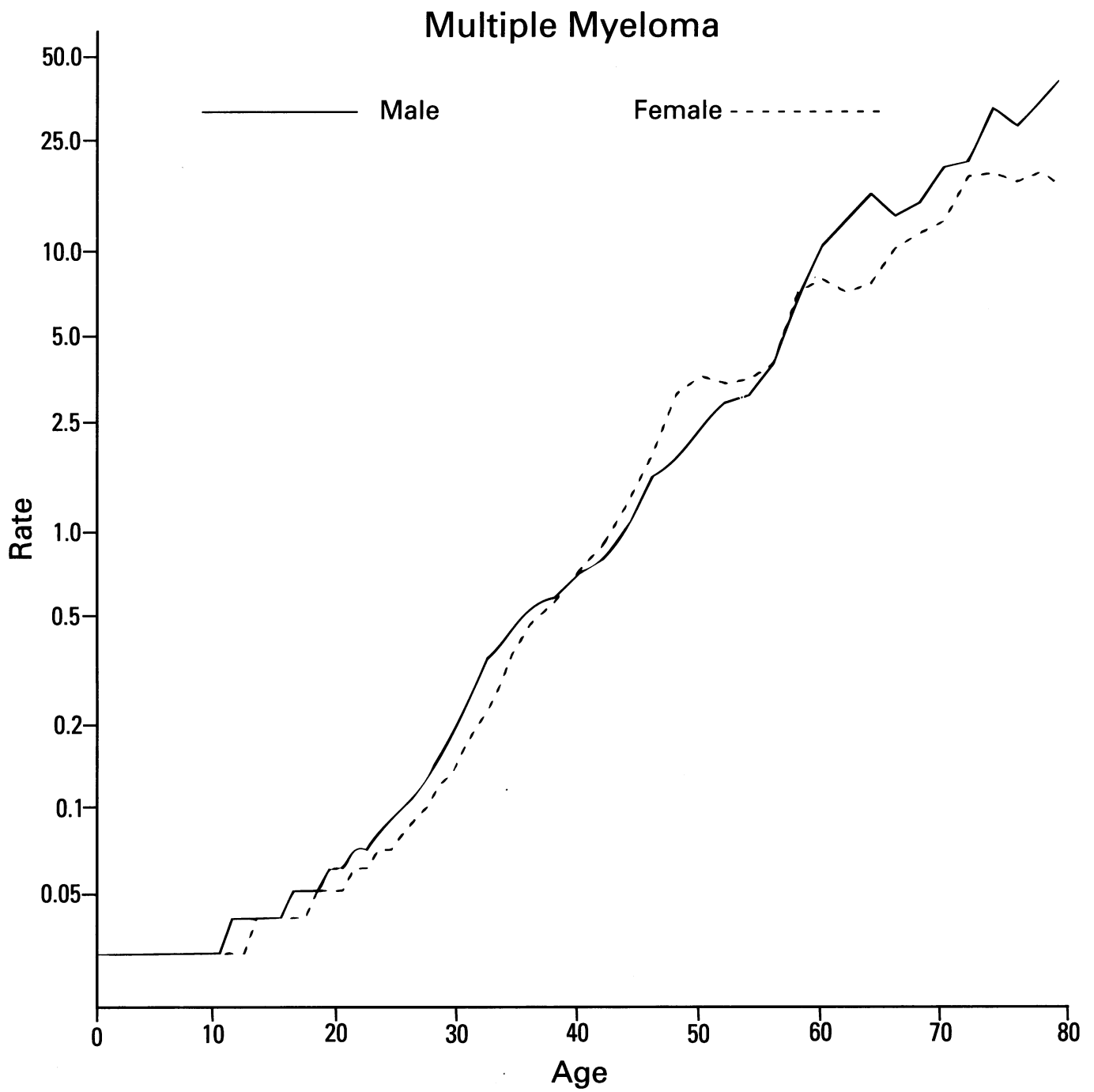
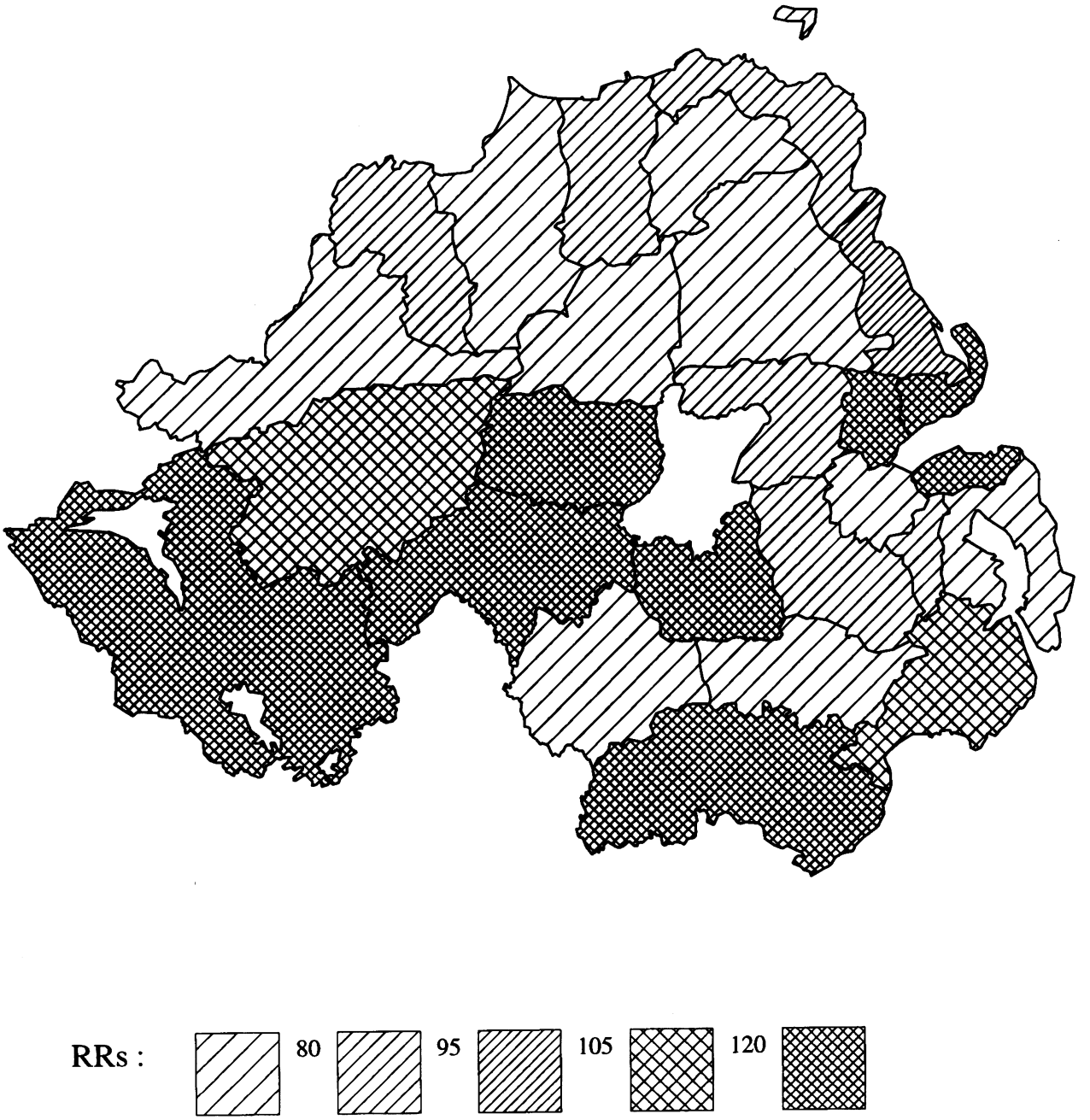


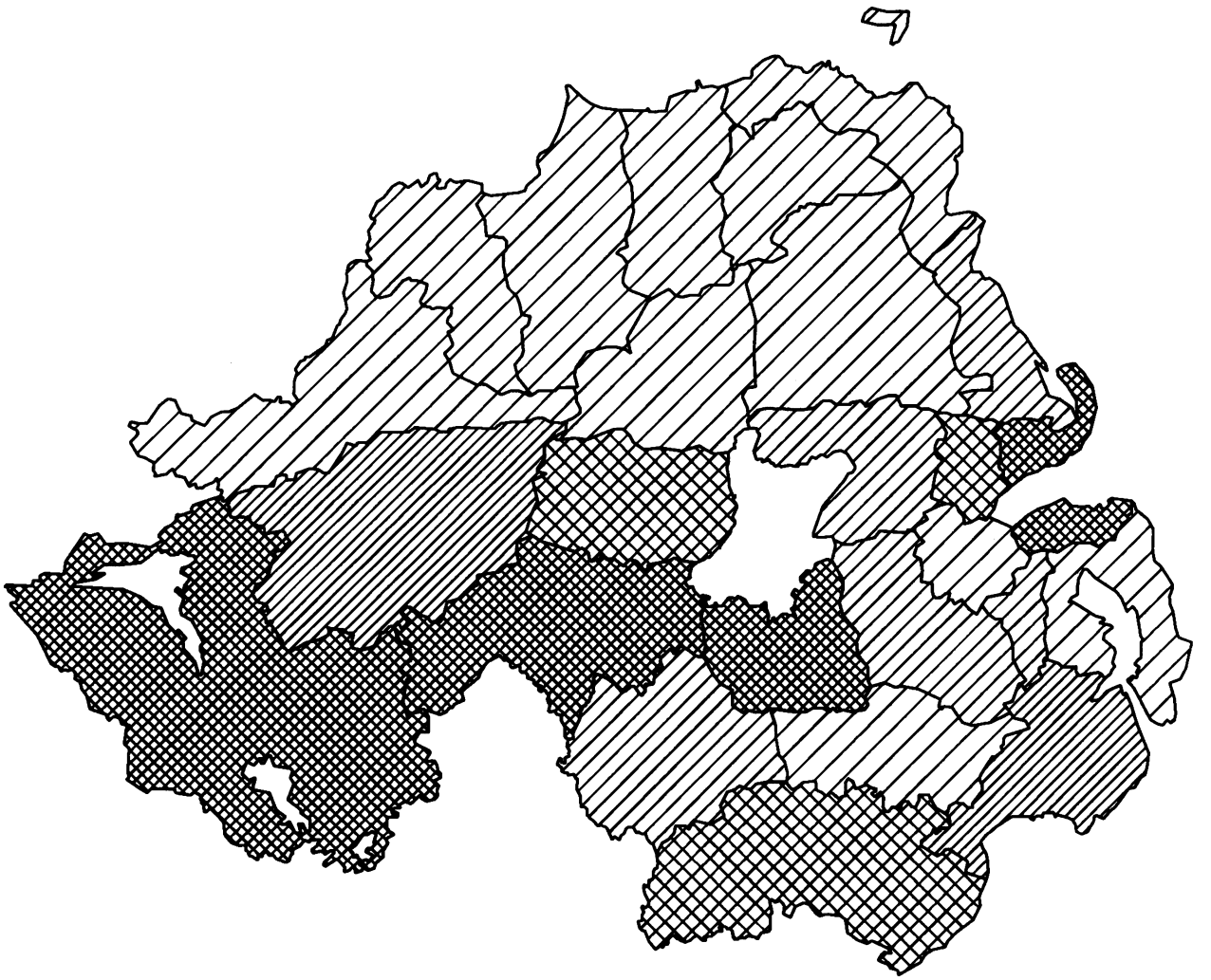
Fig. 2 Age – specific incidence rates/100,000 population

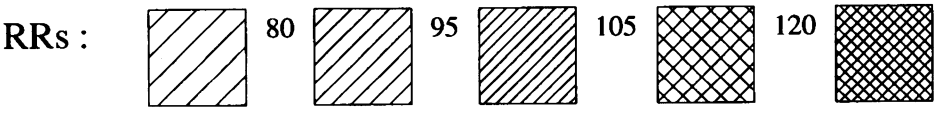
Map 1 ACUTE LYMPHOBLASTIC LEUKAEMIA
Incidence of disease (shrunk RRs) by district of residence. (Male)



NORTHERN IRELAND Local Government Districts.

Map 2 ACUTE LYMPHOBLASTIC LEUKAEMIA
Incidence of disease (smoothed RRs) by district of residence. (Male)

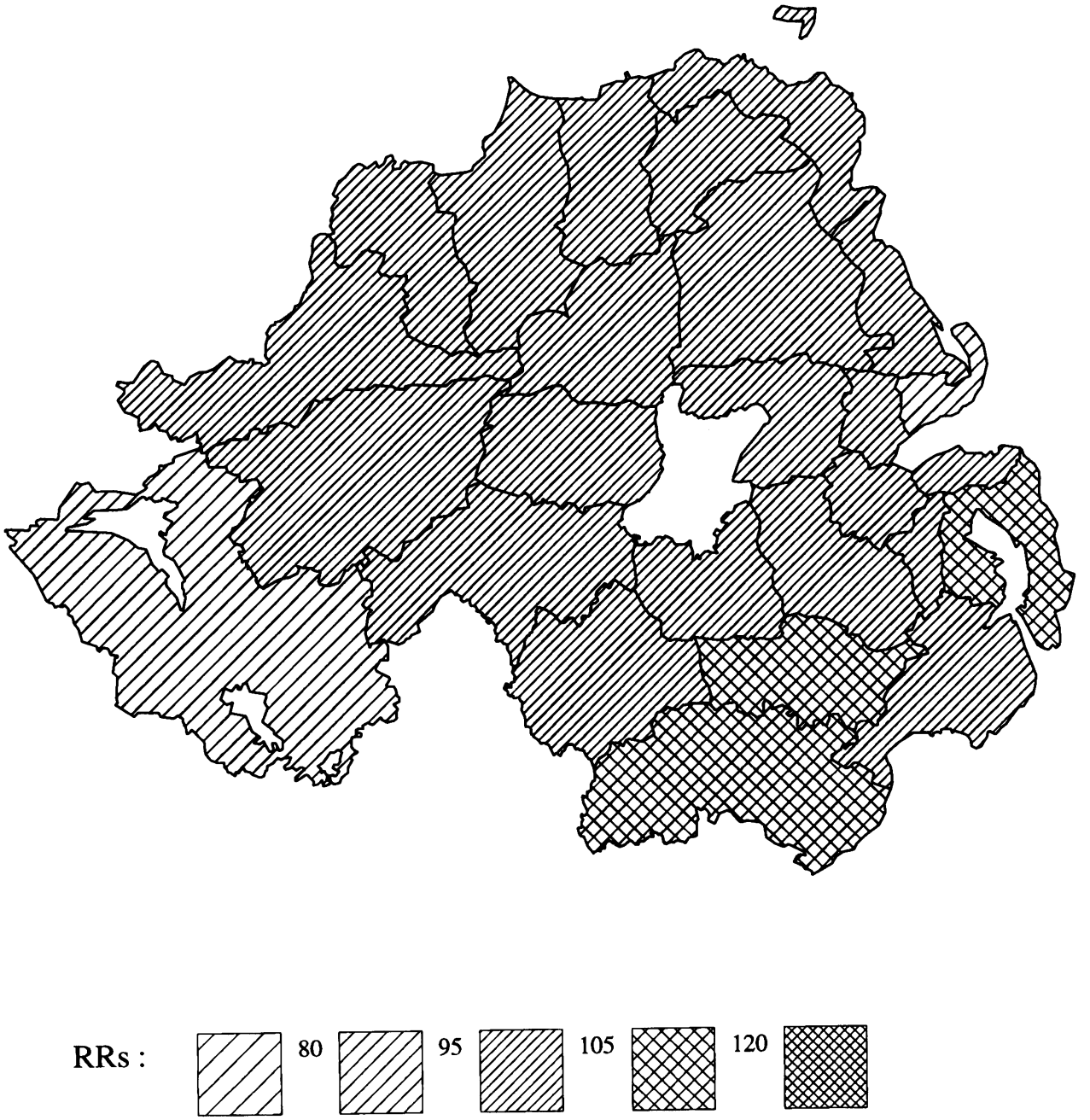




NORTHERN IRELAND Local Government Districts.

Map 3 MULTIPLE MYELOMA

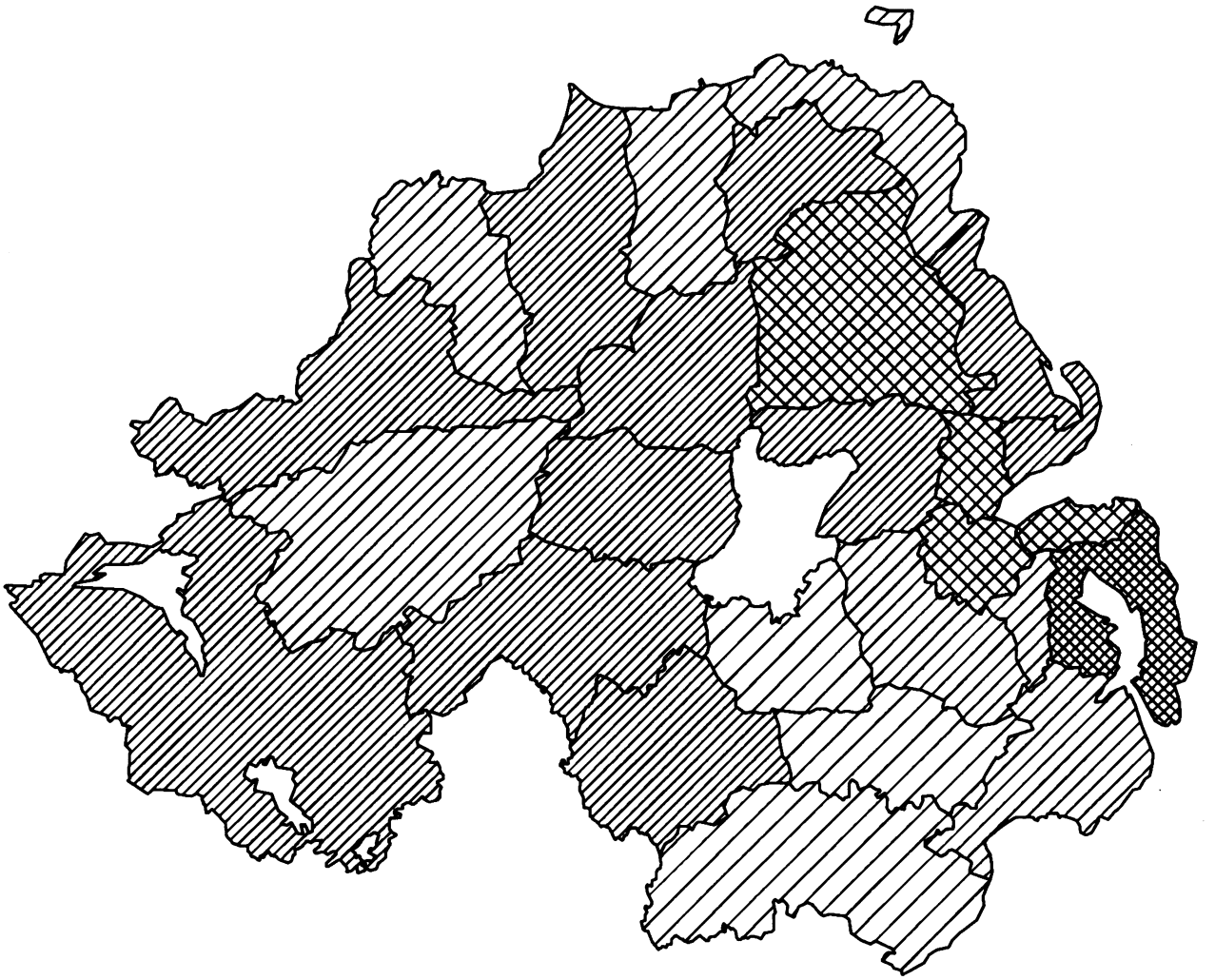
Incidence of disease (smoothed RRs) by district of residence. (Male)

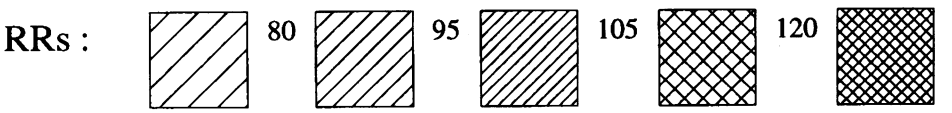


NORTHERN IRELAND Local Government Districts.

Map 4 MULTIPLE MYELOMA

Incidence of disease (shrunk RRs) by district of residence. (Female)





NORTHERN IRELAND Local Government Districts.

the shrunk RR's. No clear pattern emerges from the smoothed RR's. The highest female rates are in the North West and Mourne area. The highest male rates are in Castlereagh, Carrickfergus and Coleraine.

MULTIPLE MYELOMA

There were 224 cases. The disease is absent in children and young adults, but from the age of 30 onwards there is a steep rise with a marked excess in males over 60 (Figure 2 and Table I). There is evidence for an increase in the male rates (p=0.01), but the female rates were stable over the 5 year period (Table III).

There is a problem with under-registration of multiple myeloma, and so incidence rates are likely to be underestimates of the true rates.

There is no evidence for between-district heterogeneity from either the pooled or male SMR's. However, there is some evidence (p=0.083) of heterogeneity amongst the female SMR's. Ards has a raised pooled SMR (p=0.01 – Table II). The highest shrunk RR's occurred in the Belfast and Ards/Strangford areas. High smoothed RR's for males are observed in the Ards/Strangford area, and the Mourne district (Map 3). There were very low female smoothed RR's in the Armagh/South Down area (Map 4).

CONCLUSIONS

The authors regard this study as an important but initial step towards a careful and considered understanding of rates of disease in Northern Ireland. These early results will be supplemented by further work but they do not show unusual rates nor generate any major cause for concern. Indeed the results are quite similar to those from England and Wales.[1] The rates for the leukaemias except for ALL are slightly lower than in England and Wales whilst NHL rates are higher.

Possible under-enumeration in the census would affect district SMR's much more than overall province-wide age-specific incidence rates. This would have the consequence of artefactually raising SMR's in under-enumerated districts, and raising age-specific incidence rates in under-enumerated age groups. In particular the analysis of 35 cases of CML must be treated with caution. The most striking observation is the raised rates for ALL for males in County Fermanagh. This requires further investigation and explanation. The Podar report[2] examined the hypothesis that leukaemia incidence and mortality rates were higher in coastal than in inland areas of Northern Ireland. No significant coastal excesses were found.

The benefits of the data collection exercise are two-fold. For the first time, reasonably reliable estimates of the incidence of the leukaemias and lymphomas are available for Northern Ireland by age-group and local government district. These may be used in the planning of health services and may also be very useful in detecting any future excess occurrences of particular types of leukaemia and lymphoma.

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We wish to record that material in this publication has been produced using data relating to digitized boundary information which remains the property and copyright of the Crown. The 1991 Census data are Crown copyright, from the ESRC purchase.

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Audit of surgical delay in relationship to outcome after proximal femoral fracture

T R O Beringer, V L S Crawford, J G Brown

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SUMMARY

To ascertain the influence of surgical delay on outcome after proximal femoral fracture in elderly females, a cohort study of patients presenting in 1987 was compared to 1989/90. Organisational changes in the intervening period were introduced to reduce delay to surgical intervention. Two hundred and eighty females aged 65 years and over presenting from the local catchment area of an acute inner-city teaching hospital were enrolled in the study. Seventy-nine patients received surgery in 1987 and 186 in 1989/90. The one year mortality was 34% and 26% respectively. The proportion receiving surgery within 24 hours rose from 34% in 1987 to 57% in 1989/90. The relative hazard of the group receiving surgery on day 2 in comparison to day 1 was 1.7 (95% CI 1.0 to 2.9) when adjusted for co-variance of age and mental score. Medically fit elderly patients presenting with proximal femoral fracture have improved survival with early surgery within 24 hours of admission. Improvements in the organisation of hospital care will result in important benefits for the increasing number of elderly females presenting with proximal femoral fracture.

INTRODUCTION

Proximal femoral fracture in the elderly is a common condition occupying 25% of orthopaedic beds and has an attendant high mortality and morbidity. The influence of delay prior to surgical treatment in relation to outcome has been reported as both important[1-8] and unimportant.[9-11] The intention to reduce surgical delay allowed the study of outcome to be undertaken before and after measures were introduced to effect such a change. This study was, therefore, undertaken to seek to clarify in a proximal femoral fracture population the influence of surgical delay with respect to outcome.

METHODS

All females aged 65 and over admitted to the Fracture Unit in the Royal Victoria Hospital from a defined geographical area were entered in the study. The admissions in 1987 were compared with the admissions in 1989 and 1990. During the intervening period of one year (in 1988) considerable organisational efforts were made to reduce delay to surgical intervention following admission, in particular by improving theatre availability. Surgical and anaesthetic procedures were not altered. The type of fracture and time of surgery were noted, with patients being categorised according to time to surgery following admission into 4 groups – (1) within first 24 hours (day 1), (2) 24 - 48 hours (day 2), (3) more than 48 hours (day 3+) and (4) no operative intervention. Additional information was gathered on a weekly ward round and included pre-admission drug therapy, social circumstances, mental score,[12] type of dwelling and level of independence. The data were updated at each weekly review, place and date of discharge were recorded, and survival documented from general practitioner or hospital records as previously described.[1] Patients were deemed to require long term care if they remained in hospital for more than 180 days.

Department of Health Care for the Elderly, Royal Victoria Hospital, Belfast BT12 6BA.

T R O Beringer, MD, FRCP, FRCPI, Consultant Physician.

Department of Geriatric Medicine, Queen's University, Belfast BT9 7BL.

V L S Crawford, BSc, MSc, CBiol, MIBiol, Lecturer.

Department of Orthopaedic Surgery, Royal Victoria Hospital, Belfast BT12 6BA.

J G Brown, MD, FRCS, Consultant Orthopaedic Surgeon.

Statistical analysis was conducted using SPSS. Data were examined with Kaplan-Meier for survival curves and Cox's Proportional Hazards regression analysis was performed to investigate the influence of delay, age and mental score on survival.

RESULTS

A total of 280 females with femoral neck fracture were studied with the first cohort of 89 patients admitted in 1987 and the second cohort of 191 in 1989 and 1990. Surgery was not undertaken if the patient had a painless stable impacted sub-capital fracture or remained medically unfit for surgery and anaesthesia. There were 15 such patients, (ten in 1987, five in 1989/90) of whom 12 were unfit for anaesthesia and three had stable impacted sub-capital fractures. In addition to delays due to theatre and anaesthetic availability, patients were also delayed if deemed unfit for surgery and requiring medical stabilisation. This occurred in 18 out of 186 patients in 1989/90, with medical treatment required for respiratory tract infection in eight cases and stabilisation of diabetes mellitus in two cases. Other conditions which resulted in delay before surgery was undertaken included management of acute cerebrovascular accident, cardiac failure, renal failure, bronchiectasis, chronic obstructive airways disease, obstructive jaundice, aortic stenosis and declined consent.

The patient details are listed in Tables I and II and the outcome according to surgical delay in Table III. In 1987 the mean total delay to surgery was 2.6 days in comparison to 2.3 days in 1989/90 with 66% in 1987 receiving surgery within 48 hours of admission increasing to 81% in 1989/90 (Table IV).

Figure 1 illustrates the Kaplan-Meier survival curves for the surgically managed patients, indicating after 1 year 66% survival of the 1987 cohort and 74% survival of the 1989/90 cohort, falling after 2 years to 59% and 64% survival respectively.

Analysis of the survival at up to 2 years of operative cases by cohort using the Cox's Proportional Hazard model indicates a relative hazard of 0.82 (95% CI 0.51 to 1.32, $p = 0.37$) for the 1989/90 cohort in comparison to the 1987 cohort adjusted for the covariance of age and mental score. When adjusted for the additional covariance of surgical delay the relative hazard rose to 1.03 (95% CI 0.67 to 1.59, $p = 0.89$).

The relationship of surgical delay with respect to the outcome measures of length of hospital stay and survival of all patients (1987 and 1989/90 combined) are listed in Table III and Figure 2. There is a clear trend of increased survival with

TABLE I

Details of patients admitted in 1987 and 1989/90 with proximal femoral fracture

	1987	*1989/90*
Number	**89**	**191**
Mean Mental Score (SD)	6.85 (3.5)	6.43 (3.1)
Mean Age in years (range)	83.0 (65-94)	82.0 (66-98)
Mean LOS in days (range)	39.3 (1-180)	44.8 (1-180)
Median LOS in days	29	29
Number (%) treated surgically	79 (88.8%)	186 (97.4%)
Number (%) transferred for rehabilitation	38 (43%)	88 (46%)
Number (%) died in hospital	16 (18%)	27 (14%)
Number deaths (%) at 1 year	33 (37%)	54 (28%)
Number deaths (%) at 2 years	38 (43%)	72 (38%)
Number (%) discharged to own home	54 (61%)	126 (66%)
Number (%) discharged to long term care	5 (6%)	18 (9%)

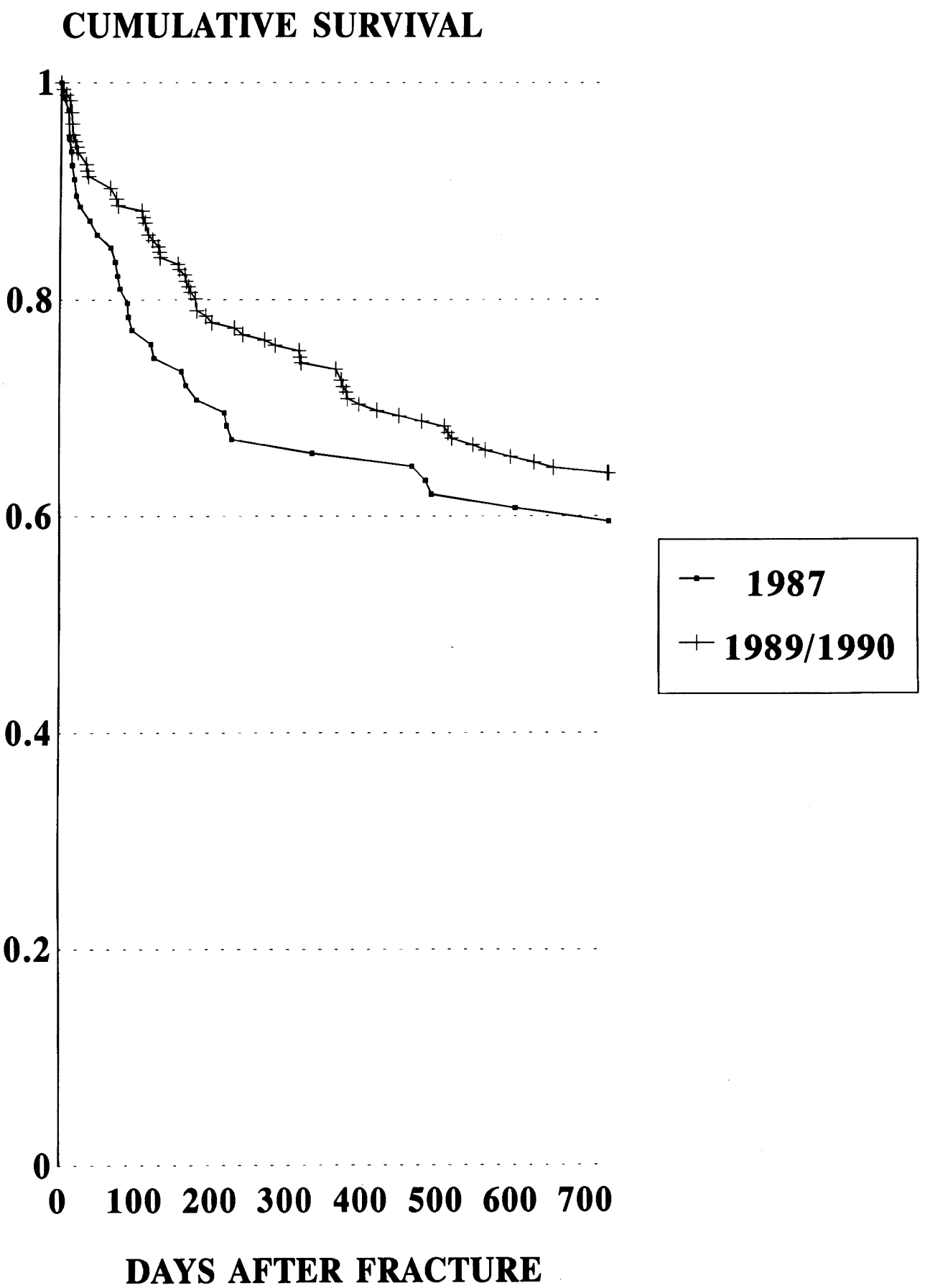

Fig 1 Outcome following surgical management (1987 vs 1989/90)

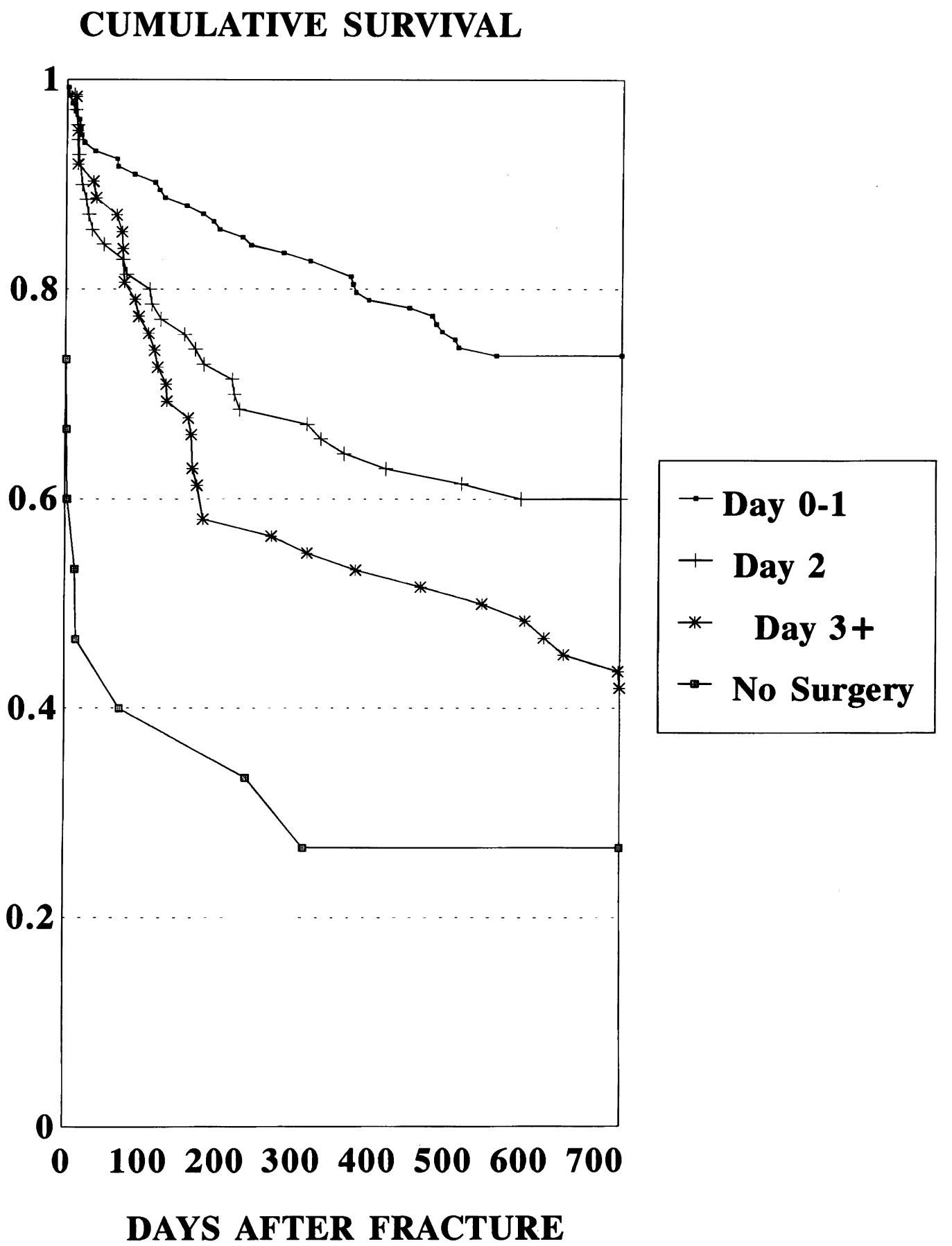

Fig 2 Operative delay and survival (1987, 1989/90 combined)

TABLE II

Details of surgically treated patients admitted in 1987 and 1989/90 with proximal femoral fracture

	1987	*1989/90*
Number	**79**	**186**
Mean age years (range)	82.7 (65-94)	81.9 (66-98)
Mean LOS in days (range)	41.9 (2-180)	44.6 (3-180)
Median LOS in days	31	29
Mean delay in days (range)	2.6 (1-14)	2.3 (1-17)
Median delay in days	2	1
Number (%) deaths at 1 year	27 (34%)	49 (26%)
Number (%) deaths at 2 years	32 (41%)	67 (36%)

TABLE III

Outcome with respect to time of surgery for proximal femoral fracture (1987 and 1989/90)

	Surgery			
	0-1 Days	*2 Days*	*3+ Days*	*No Surgery*
Number of patients	133	70	62	15
Mean age years	81.0	82.9	83.5	86.4
Total LOS in days (range)	34.3 (2-180)	52.5	54.2	29.7
Median LOS in days	21	35	36	13
Number (%) alive at 2 years	98 (74%)	42 (60%)	26 (42%)	4 (27%)
Hazard (CI) of death relative to surgery 0-1 days	—	1.7 (1.1-2.8)	2.7 (1.7-4.3)	6.0 (3.1-11.9)
Hazard (CI) of death relative to surgery 0-1 days adjusted for age	—	1.6 (1.0-2.7)	2.6 (1.6-4.1)	4.9 (2.5-9.8)
Hazard (CI) of death relative to surgery 0-1 days adjusted for mental score	—	1.6 (0.9-2.9)	2.7 (1.5-4.8)	1.8 (0.7-4.8)
Hazard (CI) of death relative to surgery 0-1 days adjusted for age and mental score	—	1.7 (1.0-2.9)	2.7 (1.5-4.8)	1.7 (0.6-4.6)

TABLE IV

Comparison of surgical delay in 1987 vs 1989/90

	1987	*1989/90*
Number (%) patients with delay 0-1 days	27 (34%)	106 (57%)
Number (%) patients with delay 2 days	25 (32%)	45 (24%)
Number (%) patients with delay 3+ days	27 (34%)	35 (19%)
Total Number	79	186

shorter time to surgery with 74% survival at 2 years amongst those receiving surgery within 1 day, 60% if receiving surgery on day 2 and falling to 42% survival in those with surgery after 3 or more days. The non-operative group had a 2-year survival of 27%. The relative hazard of the group receiving surgery on day 2 in comparison to day 1 was 1.67 (95% CI 0.95 to 2.93, p = 0.07) when adjusted for the covariance of age and mental score (Table III). The relative hazard of the group receiving surgery on day 3+ in comparison to day 1 was 2.68 (95% CI 1.5 to 4.76, p = 0.0007) when adjusted for the covariance of age and mental score.

DISCUSSION

This study reveals clinically important differences in survival between the two cohorts, with 34% mortality at one year in 1987 and 26% mortality at one year in 1989/90. Although this large difference between the cohorts did not achieve statistical significance, possibly due to inadequate study numbers, the principal variable factor contributing to the differences was surgical delay. Analysis of the 2 cohorts combined revealed a significantly worse mortality with delayed surgery on day 2 in comparison to day 1. It is important to consider the possible confounding influence that surgery may be delayed for medical care to allow time to stabilise the patient before proceeding to surgery. Analysis revealed that where surgery was delayed for medical reasons (18 out of 186 surgically treated patients in 1989/90) this resulted in a delay of 72 hours or more. The comparison of patients receiving surgery within 24 hours or 24-48 hours is not thus confounded by medical conditions and fitness for surgery. The differences in survival between those receiving surgery within 24 hours compared to 24-48 hours commence early in the hospital stay, supporting the role of early surgical intervention rather than other aspects of medical care being of importance. However, association does not imply cause and effect, and other important factors related to early surgery may remain to be identified.

It has previously been reported[13] that surgery delay for 72 hours in patients with acute medical illness in addition to the fracture was accompanied by lower mortality than early surgery. A similar pattern of care occurred in this study and provided sufficient time to enable medical care to improve fitness for anaesthesia in subjects deemed initially unfit.

While some studies have not demonstrated survival benefits of early surgery[8-11] other studies demonstrate improvements in mortality,[3, 7] morbidity,[5] pressure sore rates,[4] improved chances of returning home,[2] quality of bony union[14] and reduced stay in hospital.[6] In this study the improved number of survivors in 1989/90 was not associated with poorer outcome or increased dependency, as 66% were fit to return home compared with 61% in 1987.

The extent of surgical delay in this study with 57% receiving surgery within 24 hours may be contrasted with 83%[14] in Budapest, 78% in Glasgow[15] and 55% in England.[16] The proportion of 9.7% in whom surgery was delayed due to poor initial medical condition compares with 11.8% in Peterborough[4] with similar proportions 5.4% vs 5.8% treated conservatively. While considerable scope remains for a higher proportion of medically fit subjects to receive surgery within 24 hours in Belfast, many other centres in the UK are experiencing similar or greater delays, and the opportunity for improvement is considerable.

In addition to surgical delay and medical condition of the patient, other factors including age, sex, place of domicile and pre-fracture social function[17] strongly influence outcome after hip fracture. It is thus difficult to compare directly outcome between centres if such factors are not also allowed for. The wide range of post-operative one year mortality

rates may be demonstrated by the figures reported from Southampton of 42%,[18] Stirling of 33%,[19] 30% in Aalborg[20] and 14.8% in Ohio[3] in addition to the 26% reported in this study, and are likely to reflect in part differences in the populations presenting with hip fracture.

In conclusion this study indicates the ability to improve speed of operative fixation with attention to theatre availability and anaesthetic provision. There appear to be important benefits in terms of improved survival after hip fracture if elderly patients who are medically stable receive operative treatment within 24 hours, as recommended by the Royal College of Physicians.[21] Surgery may be delayed in 10% of cases for 72 hours or longer in acutely ill elderly patients to allow sufficient time to stabilise the patient before proceeding to surgery, and conservative management may be employed in 5-6% of cases.

Using these criteria it is likely that in excess of 80% of elderly patients presenting with hip fracture should be medically fit to benefit from planned and scheduled surgery within 24 hours of admission with resultant improvement in survival and the ability to return home. At present approximately 55% of hip fractures receive surgery within 24 hours in England.[16] There are thus considerable opportunities for improved outcome for elderly people with hip fracture with the use of such criteria in purchasing contracts for health care.

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The provision of adult intensive care in Northern Ireland with reference to the role of high dependency care

B C Morrow, G G Lavery, B M Blackwood, I M Ball, H N McLeod and J P H Fee

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Summary

In 1991 an audit of Intensive Care Services was carried out by the Northern Ireland Intensive Care Group. In conjunction with this regional overview, all patients in the Regional Intensive Care Unit, (RICU) in the Royal Victoria Hospital were assessed daily, over a 10 month period in 1990-91 and classified as conforming to either intensive care or high dependency status. These data were then used to compare adult intensive care service in Northern Ireland with recent national and international recommendations on intensive care.

Ten units in Northern Ireland were surveyed. In regard to national or international guidelines, all ten were deficient to some degree. Four units had significant deficiencies; small patient numbers, lack of 'dedicated' 24hr medical cover and or deficiencies in the provision of appropriate monitoring and or equipment. There was a large diversity in casemix among the ten units surveyed which suggested differing admission criteria.

The bed occupancy of RICU was 100%. Refused admissions constituted a further 13% of unresourced workload. The lack of physically separate, dedicated high dependency unit facilities meant that 26% of bed days were devoted to HDU care (usually for "improved" intensive care unit patients not yet ready for discharge to a general ward).

Achieving nationally recommended intensive care standards (on a regional basis) is probably only possible if a number of the smaller intensive care units are redesignated as high dependency units, and patients requiring intensive care are concentrated in a smaller number of larger ICUs. This will increase the frequency of interhospital transfer of critically ill patients.

INTRODUCTION

During the last decade there has been a significant increase in the numbers of patients admitted to the Intensive Care Unit (ICU). Unfortunately, there has not been an equivalent increase in ICU beds. Coupled with this, technical advances, willingness by surgeons to perform radical surgery in an increasingly elderly population, and public expectation have all served to further increase ICU workload. However, as well as pressing for extra resources it is also important that those already available are used appropriately and efficiently.[1-2] Recommendations on ICU provision and operational policy have been drawn up both by national bodies such as the Royal College of Anaesthetists[3], the Association of Anaesthetists[4]

Regional Intensive Care Unit, Royal Hospitals Trust, Belfast BT12 6BA.

B C Morrow, FFARCSI, Senior Registrar Anaesthetics.

G G Lavery, MD, FFARCSI, Consultant in Anaesthetics and Intensive Care.

B M Blackwood, RGN, Research Nurse.

J P H Fee, MD, PhD, FFARCSI, Professor of Anaesthetics, The Queen's University, Belfast.

Antrim Area Hospital.

I M Bali, PhD, FFARCSI, Consultant Anaesthetist.

H N McLeod, FRCA, Consultant Anaesthetist.

Correspondence to Dr Lavery

and the Intensive Care Society (UK)[5, 6] and also by international bodies, the European Society of Intensive Care Medicine[7, 8] and the Society of Critical Care Medicine.[9] The Clinical Resource Efficiency Team (CREST)[10] has reviewed intensive care in Northern Ireland and made recommendations which have stimulated change within individual units but as yet have had little influence on the regional strategy for Intensive Care across the province.

This paper has been constructed in two sections;

(A) An audit of ICU provision and activity in Northern Ireland conducted in association with the Northern Ireland Intensive Care Group (NIICG).

(B) An analysis of the workload and case-mix in the largest ICU within Northern Ireland.

Since ICU care and high dependency unit (HDU) care may go on side by side within an ICU, and an HDU patient should need less clinical and financial resources than an ICU patient, it is necessary to define the respective patient populations.

DEFINITIONS:

Intensive Care Patient: An intensive care patient is one admitted for the treatment of impending or actual organ dysfunction which is potentially reversible.[5, 10, 11] An intensive care patient may also be defined as one for whom the facilities of an HDU are insufficient.[3, 4] We defined an ICU patient in terms of features which reflect various aspects of organ dysfunction (Table I).

High Dependency Patient: A HDU patient requires a level of care intermediate between that delivered in ICU and the best which could be provided on a standard ward.[5, 10] In this study we defined a HDU patient as one who did not conform any of the features in Table I but who occupied an ICU bed.

SECTION A.

Ten ICUs, designated by the code letters A-J (Table II) were surveyed by means of a postal questionnaire on aspects of clinical activity, staffing and equipment levels. The questionnaires were completed by a consultant in all cases, and telephone follow-up was used to elicit returns from non-responders, and to clarify ambiguous or incomplete responses. We compared the information received with previously published recommendations [3-5] (Table III).

RESULTS

Number of admissions

Three units (F, I and J) had fewer than 200 admissions per year (the minimum recommended) and in the other units admission rates ranged from 215 to 559 patients per year (Table II). In units I and J, mechanical ventilation was instituted in less than 5% of patients, three other units (F, G and H) ventilated less than 30% of admissions and only three units (A, B and C) instituted mechanical ventilation in more than 50% of patients requiring mechanical ventilation (figure 1). This (and other less specific information) revealed that the admission criteria varied considerably from unit to unit.

Number of beds

One unit (J) had less than 4 beds (minimum recommended) and all other units had some beds which were closed due to lack of funding for nursing staff.

Consultant sessions

Only unit A had enough sessional allocation to have 24-hour dedicated consultant cover. Unit C had 10 consultant sessions allocated – allowing daytime cover during the standard working week. Emergency cover in this unit was by the consultant on call for anaesthesia who usually did not have daytime ICU sessions. The remaining units had between two and eight week-day consultant sessions with the remainder of 24 hour cover being provided by consultants who were also on-call for other areas e.g. day time theatre duties, obstetric cover or anaesthesia on-call.

Administration

All units had a named consultant in administrative charge.

Junior medical staff

Units A and C had dedicated 24-hour resident cover by non-consultant medical staff. In both cases these were anaesthetists-in-training. Two units (I & J) had no resident cover i.e. there were no trainee anaesthetists resident in the hospital. The non-consultant staffing of the other units was variable with anaesthetic trainees providing an ICU commitment which was combined with commitments elsewhere in the hospital.

Illness severity scoring and Audit

Only three units (30%) frequently used illness severity scoring. All three used the Acute

TABLE I

Criteria for ICU classification (any one of the following)

Patients requiring positive pressure ventilation
Intubated patients requiring use of continuous positive pressure breathing circuit (CPAP)
Patients requiring management using a pulmonary artery flotation catheter
Patients requiring intra-cranial pressure monitoring
Patients in acute renal failure requiring haemodialysis with at least one other organ system failure
Patients exhibiting cardio-respiratory instability requiring ongoing resuscitation

TABLE II

Key points describing ICUs in Northern Ireland compared with international guidelines

ICU	*Beds*	*Admissions* *Total*	*%HDU*	*Dedicated Consultant (24 hr/full daytime/ other)*	*24 hr Junior Medical cover*	*Illness scoring*
A	8	559	16%	24 Hrs	Y	Y
B	4	279	37%	Others	variable	N
C	6	387	29%	daytime	Y	Y
D	5	269	61%	Other	variable	N
E	4	228	53%	Other	variable	Y
F	4	67	58%	Other	variable	N
G	4	215	65%	Other	variable	N
H	4	265	58%	Other	variable	N
I	7	199	95%	Other	None	N
J	3	137	94%	Other	None	N
Guide -lines	>4	>200	<50%	24 hrs	Y	Y

Physiology and Chronic Health Evaluation (APACHE II) system.[12] There was no information on clinical audit requested in the questionnaire.

Equipment and Facilities

Table III summarises the criteria drawn up by the European Society of Intensive Care Medicine [8] for ICU bed-side equipment and unit facilities. These would suggest that there are deficiencies in the provision of almost every category of equipment in every ICU in the province. Overall the larger ICUs were better equipped with the exception of the provision of pulse oximetry devices which was at best one device per two beds in the two busiest ICUs. The authors felt that a minimum of three infusion control devices (volumetric pump/syringe driver) per bed should be available – four units (A, F, I and J) did not fulfil this requirement.

SECTION B

Introduction

The Regional Intensive Care Unit, Royal Victoria Hospital (RICU) is an 11 bedded unit possessing

TABLE III

Equipment levels in ICUs in Northern Ireland (ESICM guidelines require all answers to be Y and ratio of no/total beds to be 1/1).

	Intensive Care Units									
Equipment	*A*	*B*	*C*	*D*	*E*	*F*	*G*	*H*	*I*	*J*
Pulse Oximeter no/total beds	4/8	2/4	2/6	1/5	2/4	1/4	2/4	1/4	7/7	2/3
ECG	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
Intra-arterial pressure monitoring	Y	Y	Y	Y	Y	N	Y	Y	N	N
Mechanicalventilator no/total beds	Y	Y	Y	Y	Y	N	Y	Y	N	N
Non-invasive blood pressure	N	N	N	N	N	N	N	N	Y	N
Bedside blood gas measurement	Y	Y	Y	Y	Y	Y	N	N	N	Y
24 hr Technical support	Y	Y	Y	N	Y	Y	N	N	N	N
>3 infusion devices per bed	N	Y	Y	Y	Y	N	Y	Y	N	N

TABLE IV

Mean APACHE II and TISS scores by month over a 4 month period.

			APACHE II	*TISS*
Month 1	category	– ICU	14	39
		– HDU	8	17
Month 2	category	– ICU	13	40
		– HDU	7	24
Month 3	category	– ICU	15	36
		– HDU	12	23
Month 4	category	– ICU	15	34
		– HDU	12	24
Mean (SD) [Range]		– ICU	14.3 (0.96) [13-15]	37.3 (2.75) [34-40]
		– HDU	9.75 (2.63) [8-12]	22 (3.37) [17-24]

(at the time of this study) staff and funding for eight beds. It provides general intensive care services for adult patients in the Royal Group of Hospitals and for other hospitals which do not have an ICU. It also provides a province-wide service in conjunction with numerous regional specialties which are located within the hospital. In addition, when beds are available it accepts patients from other ICUs when such a transfer is felt appropriate by the referring staff. RICU has no associated high dependency unit (HDU) and so patients requiring HDU care receive this either in ICU or go to a standard ward where the ability to deliver a level of care approaching that of an HDU is variable.

The workload of RICU was investigated over a ten month period.[13] Each day the ICU consultant and registrar designated each patient in the unit as either an ICU case or an HDU case, using the criteria in Table I thereby constituting an ICU or HDU 'patient-day'. The data were also used to calculate bed occupancy in the unit based on the eight staffed beds. Patients who were refused admission to RICU due to lack of nursing staff or beds were documented. For four consecutive months within the 10 month study, every patient had daily APACHE II)Acute Physiological and Chronic Health Evaluation) and Therapeutic Intervention Scoring System (TISS) scores calculated.[14] With both scoring systems higher scores suggest more severe illness.

Results

During the study period, with 8 ICU beds functioning, there were 2432 patient days available. Three hundred and seventy-six patients utilised 2451 patient days – 101% of the days available. This occurred because patients were sometimes admitted to beds which were officially unstaffed. This was not unit policy but arose simply due to over-riding clinical indications for ICU care which could not be provided elsewhere. During the study there were 49 refusals to admit for reasons of lack of staff or beds. This represents an additional workload of 13% (assuming an average length of stay of 6.3 days) which could not be accommodated and is almost certainly an underestimate given the voluntary nature of the reporting and the fact that, when RICU was known to be full, further requests for admission may not have been made. Over a twelve month period in Belfast City Hospital ICU, there were 40 recorded refusals to admit.

During the study, 628 patient-days (26%) were devoted to HDU care. Four hundred and sixty-one (73%) of the HDU patient-days were required for patients formerly designated as ICU cases whose condition had improved but who were still not suitable for standard ward care.

With regard to ICU/HDU status, we found APACHE II scoring was not particularly helpful in differentiating ICU and HDU patients. There was a continuous spread of APACHE II scores although most ICU patients had scores >12 and most HDU patients had scores <12 (Table IV). TISS scores <24 were associated with HDU status and scores >34 with ICU status. This loose association is not surprising, since the criteria used to define ICU status were like TISS, based mainly on therapeutic interventions.

Discussion

This paper is the first to attempt to assess the adequacy of ICU provision in Northern Ireland against national and international standards. Although the information was collected four years ago, little has changed in the interim with respect to total number of ICU beds available or number of units delivering ICU/HDU care.

One of the difficulties facing all hospitals is the provision of a continuum of care, as dictated by the patient's condition, ranging from intensive care, through high dependency care, to general ward care and rehabilitation. In a United Kingdom survey only 23% of acute hospitals had both ICU and HDU facilities.[4] In some units surveyed the HDU proportion of workload exceeds 50%.[4,11] In order to maintain local ICU expertise it is recommended that at least 50% of the patients conform to ICU rather than HDU status.[3] The data summarised in Table II would suggest that units A, B and C are correctly described as ICUs whereas units I and J appear to be functioning as HDUs. Units D, E, F, G and H have a dual ICU/HDU role although in many the HDU role is predominant.

High Dependency Units differ from intensive care units primarily in the lower nurse staffing ratio per patient and in the lower level of provision of monitoring and other equipment. The recommended nurse: patient ratio in an ICU is 1:[14,10] compared with 1:2 for an HDU.[10] In terms of nursing whole time equivalents (WTEs) an ICU bed requires 6-7 WTEs and an HDU bed approximately 3-5 WTEs for 24 hour cover 365

TABLE V

Consequences of using over-extended ICU facilities for HDU care

Postponement at short notice of major elective surgery
Inability to admit ICU patients from own or other hospitals
Management of ICU patients in non-regional ICUs/Recovery rooms
Inter-hospital transfer of regional ICU patients to non-regional ICUs
Pressure to discharge early/high re-admission rate
Inability to provide training/teaching
Inability to provide for emergency situations
Stress related problems for staff/high staff turnover rate

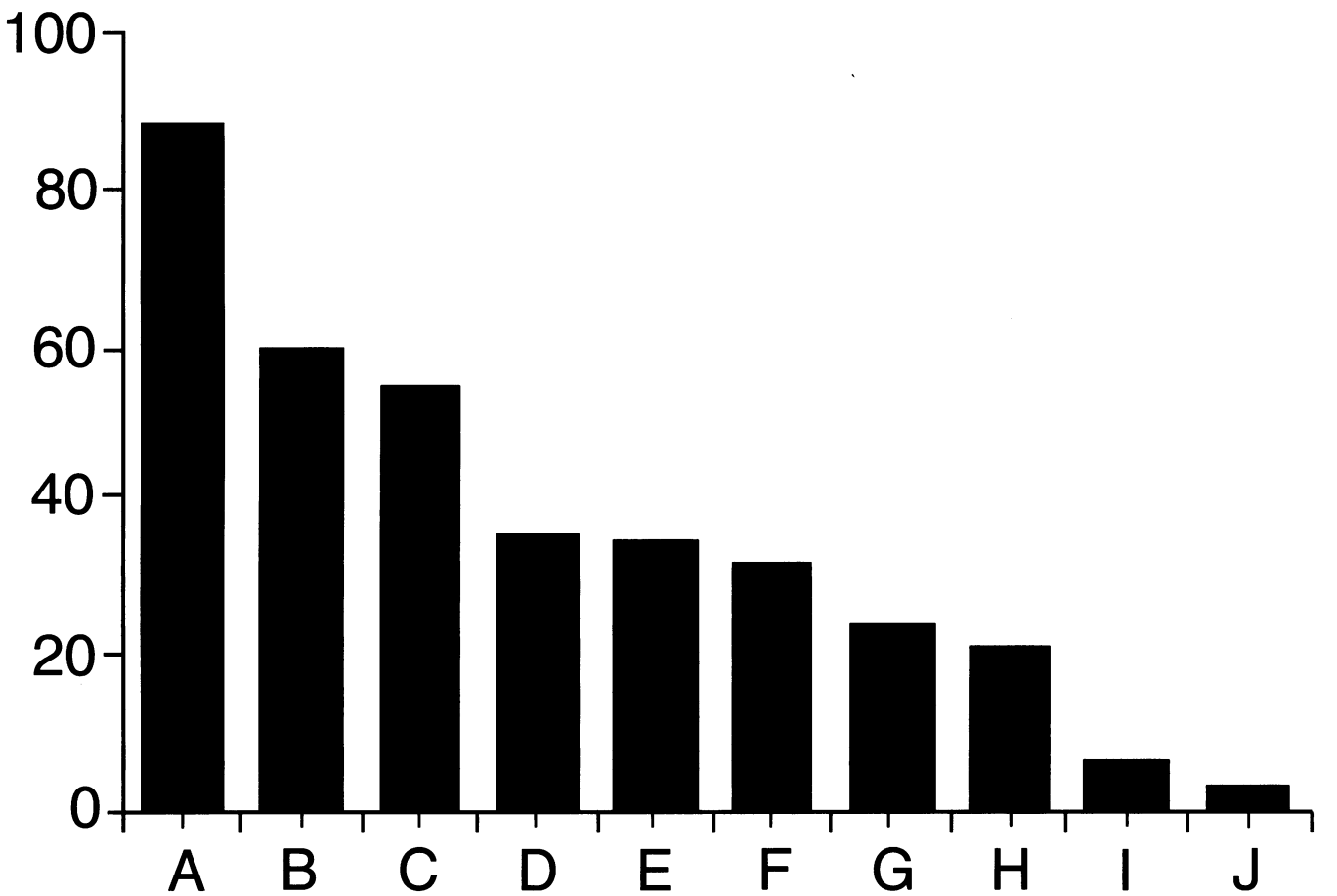

Figure Percentage of total admissions receiving mechanical ventilation by unit (designated A-J)

days per year. It is inefficient to look after high dependency patients in an ICU setting because the staffing and equipment advantages are lost. In addition, such a situation reduces the pool of ICU beds available for the treatment of the most seriously ill patients. Thus the absence of HDU facilities, due to a knock-on effect, reduces the capability to provide an ICU service at a time when it appears that there is a shortfall in ICU beds.

It is recommended that an ICU operates at 70% bed occupancy rate to allow for emergency admissions.[4, 10] An overextended ICU may face some of the problems outlined in Table V and these may be offset by the availability of an HDU to cater for patients not conforming to intensive care status but who are not yet well enough for general ward care. As a significant component of HDU workload is derived from ex-ICU patients[13] it is appropriate that a HDU should be situated adjacent to an ICU.[5]

It would appear from the above that some ICUs surveyed do not comply with the recommendations set out above[3-10] or European Intensive Care Society recommendations regarding equipment[8] (Table IV). Some have an insufficient number of admissions and others apply admission criteria which are based on local factors, but which would not normally be appropriate for intensive care. Technological advances in the investigation, treatment and monitoring of intensive care patients may place this type of advanced care beyond the range of some units. ICUs failing to meet previously mentioned guidelines provide insufficient clinical exposure and training opportunities for staff and are invariably inefficient.[4]

In order to address some of the problems outlined above, ICU care in Northern Ireland would need to be more centralised which may mean more frequent inter-hospital (IH) transfer. IH transfer may be associated with a deterioration in the patient's condition if the process is not properly conducted.[15, 16] Therefore it is of vital importance that the patients are adequately resuscitated and stabilised before transfer, monitored appropriately and accompanied by sufficiently experienced personnel.[17] This has staffing and equipment implications for both the referring and receiving hospitals. Clearly some small hospitals may be left without anaesthetic cover during transfer of critically ill patients[18] or they may be tempted to use inexperienced junior staff for this purpose. In some United Kingdom centres the receiving ICU retrieves the patient with a purpose-built and appropriately staffed mobile ICU thus overcoming the aforementioned staffing problems in the transferring hospital.[17]

It can be seen from the high number of refused ICU admissions that lack of available ICU beds appears to be a significant problem, at least in Belfast. The number of ICU beds, as a proportion of total acute beds, has been recommended as 1-2% [3, 10, 19] although, elsewhere for example in Germany the proportion may be as high as 10% in a University teaching hospital with regional specialties.[7] Greater emphasis on day surgery and shorter length of stay after operation will decrease the total number of acute hospital beds, and so ICU beds as a percentage of total hospital beds should actually be increasing. The number of ICU beds required within Northern Ireland is linked to (i) the provision for HDU care (ii) the appropriate use of ICU beds using accepted admission criteria and (iii) an accepted maximum bed occupancy for ICU which allows the capacity to respond to peaks in demand and provide scope for in-service training for staff. Thus it is impossible to give figures for ICU bed requirements in Northern Ireland. What is needed is an increase in the number of ICU beds, with proper audit to ensure that they are providing an ICU and not an HDU service. Where these extra beds should be provided is also difficult although it would appear prudent to provide the busiest units with more capacity and to provide more ICU capacity within Belfast which appears to have a significant mismatch between referrals and resources.

In conclusion, it would appear that, in Northern Ireland, of the 49 beds designated for "general adult intensive care" around 50-60% function as ICU beds while the remainder provide an HDU service. The beds providing the ICU service are under significant and constant pressure and are failing to meet the clinical demand.

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Home Ventilation in Northern Ireland

A M Nugent, J D M Lyons, I C Gleadhill, J MacMahon

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SUMMARY

Thirteen patients were identified as receiving assisted ventilation at home in Northern Ireland in 1994. Two patients have since died. An increasing number of patients are starting home ventilation,, especially by nasal mask. Recognition of the needs of these patients and provision of care require further consideration.

INTRODUCTION

Long-term home mechanical ventilation was introduced over 50 years ago with the iron lung'. This was a life-saving treatment during poliomyelitis epidemics and provided ventilatory support by means of a negative pressure cuirass. In recent years there have been considerable advances in the development of portable ventilators to deliver intermittent positive pressure ventilation, especially by non-invasive means such as nasal mask. Patients with ventilatory failure from various causes such as central hypoventilation, muscular dystrophies and scoliosis, may benefit greatly from assisted ventilation at home. It is therefore important to develop a service for provision of home ventilation in Northern Ireland. The aim of this study was to identify the patients currently receiving assisted ventilation at home in Northern Ireland and to make an assessment of their needs and quality of life.

METHODS

As there is no central unit in Northern Ireland for initiating home ventilation, an attempt was made to identify patients by contacting consultants in the Belfast area and large district general hospitals who were most likely to care for patients requiring assisted ventilation at home ie. respiratory physicians, anaesthetists and neurologists. Some names were also obtained from the distributor of the NIPPY ventilator which is a portable ventilator for intermittent positive pressure ventilation (Medical Therapeutics Ltd. for Thomas Respiratory Systems, London). Case records were then checked to obtain information on the reason for ventilation and the type of ventilation system used. Only patients receiving intermittent positive pressure ventilation were selected; those patients receiving continuous positive pressure ventilation, referred to as CPAP, used to treat obstructive sleep apnoea, were excluded. There were no patients using negative pressure support systems. A total of 13 patients were identified during 1994. A questionnaire was sent to each patient to obtain information regarding ventilator use and quality of life. There were 12 questions regarding the practical use of the ventilator; space was left for further comments. Patients were asked to score quality of life on a visual analogue scale (1 to 7) and were asked specifically about their level of activity.

RESULTS

Details of the 13 patients are shown in the Table. All patients were initiated on the current mode of ventilation except patient 7 who initially used a nasal mask, but this became ineffective and he had a tracheostomy 2 years later. All but three patients had ventilation initiated in Northern Ireland. Aftercare, including maintenance of the ventilator, is varied and provided by the initiating

Department of Respiratory Medicine, Belfast City Hospital, Belfast BT9 7AB.

A M Nugent, MD, MRCP, Senior Registrar.

I C Gleadhill, MB, FRCPEd, Consultant Physician.

J MacMahon, MB, FRCPEd, FRCP, DCH, Consultant Physician.

Department of Anaesthetics, Craigavon Area Hospital, Craigavon, BT63 5QQ.

J D M Lyons, MB, FFARCSI, Registrar.

Correspondence to Dr Nugent.

TABLE

Demographic details of patients using home ventilation including the mode of delivery of ventilation, the date of starting long term ventilation and the site of initiation of ventilation.

Patient	*Age (years)*	*Sex*	*Diagnosis*	*Mode**	*Start date*	*Site***
1	37	F	Old poliomyelitis	T	Dec 1980	RICU
2	50	M	Acid maltase deficiency	T	June 1983	RICU
3	22	F	Minicore myopathy	T	Aug 1986	RBHSC
4	52	F	Mitochondrial myopathy	T	Oct 1987	RICU
5	19	M	Minicore myopathy	N	July 1990	RBHSC
6	13	M	Congenital muscular dystrophy	N	May 1991	RBHSC
7	40	M	Myotonic dystrophy	T	Nov 1991	Papworth
8	26	M	Central hypoventilation	T	Jan 1992	Papworth
9	39	M	Congenital kyphoscoliosis	N	Mar 1992	Papworth
10	40	F	Congenital kyphoscoliosis	T	May 1993	BCH ICU
11	32	F	Klippel-Feil syndrome	N	Sept 1993	BCH Resp.
12	33	F	Congenital kyphoscoliosis	T	Oct 1993	BCH ICU
13	67	M	Old thoracoplasty	N	Aug 1994	BCH Resp.

*T tracheostomy; N nasal mask.

**RICU Royal Victoria Hospital Intensive Care Unit, Belfast.

RBHSC Royal Belfast Hospital for Sick Children Intensive Care Unit, Belfast.

Papworth Respiratory Support Centre, Papworth Hospital, Cambridge.

BCH ICU Belfast City Hospital Intensive Care Unit.

BCH Resp. Belfast City Hospital Department of Respiratory Medicine.

units, the patient's local hospital and Medical Therapeutics Ltd. Questionnaires were received from all 13 patients. In response to practical questions, nine patients used the ventilator at night only, and three for part of the day as well as at night. One patient used the ventilator continuously. All patients found the ventilator easy to use and had someone at home to help. All patients had a telephone at home. Of 13 patients, six reported that the ventilator broke down on at least one occasion. This only occurred with patients who had been using the ventilator for more than two years. The machine was repaired within 24 hours in all cases, except for one patient who required hospital admission for several days until the repairs were done. Of 13 patients, eight felt that they could get advice 24 hours a day. One patient, who did not feel advice was readily available, suggested a 24 hour 'helpline' . Particular problems highlighted by patients included:

1. Nasal discomfort due to the mask.
2. Lack of regular servicing of the ventilator.
3. Difficulty in obtaining replacement parts eg. humidifier, tubing, filters.
4. Lack of battery power in the event of an electricity power failure.

Quality of life was measured on a scale of 1-7, with 1 = poor and 7 = excellent. Two patients felt that this was poor (score 1-2), seven patients felt this was reasonable (score 3-S) and four patients felt they had a very good quality of life (score 6-7). The lowest score (1) was given by patient 3 who used the ventilator continuously. The three

patients (7, 8 and 10) who used the ventilator for part of the day as well as at night all gave a score of 4. In terms of activity, 11/13 patients were up all day; one patient was up for half the day and another for short periods. No patient was confined to bed. The figure shows the types of activities patients were able to do. Of note, three patients were able to go to work. Two patients have since died during 1995: patient 11 died from worsening respiratory failure and patient 13 from a combination of renal failure, cardiac failure and respiratory failure.

DISCUSSION

Home mechanical ventilation is indicated for certain patients with chronic hypercapnic respiratory failure. It is particularly effective in those with neuromuscular diseases and chest-wall deformities.[1] Benefits can include an improvement in arterial blood gases, quality of sleep, exercise tolerance [2] and overall prognosis.[3] Home ventilation may be used in patients with chronic obstructive lung disease but the long term benefit is inconclusive at present.[4] Patients currently receiving home ventilation in Northern Ireland have neuromuscular diseases which are only slowly or non-progressive, chest wall deformities or central hypoventilation. There has been an exponential increase in patient numbers over the past 15 years, with 9 of the 13 patients having started home ventilation since 1990. Also, two-thirds of these patients were initially treated using a nasal mask. The increase in numbers probably reflects the advances in development of portable ventilators and the nasal mask for non-invasive delivery of ventilation. However, we have no record of patients who may have been using assisted ventilation at home but died prior to the start of this study. It is also important to note that, because of the lack of a central register, we may not have included all patients receiving home ventilation. Problems highlighted in the study included the lack of advice 24 hours per day, lack of regular servicing for some of the ventilators, and difficulty in obtaining disposable items such as tubing.

Use of home ventilation should be to improve quality of life as well as possibly prolonging life.[5] Quality of life was assessed in this study using a short unvalidated questionnaire. The results are not of any statistical significance, but give an overall impression of the quality of life for these patients as well as an assessment of their activity. A prospective study using a standardised questionnaire would be required to look at the effect of home ventilation on quality of life. The patients in this study are relatively young (mean

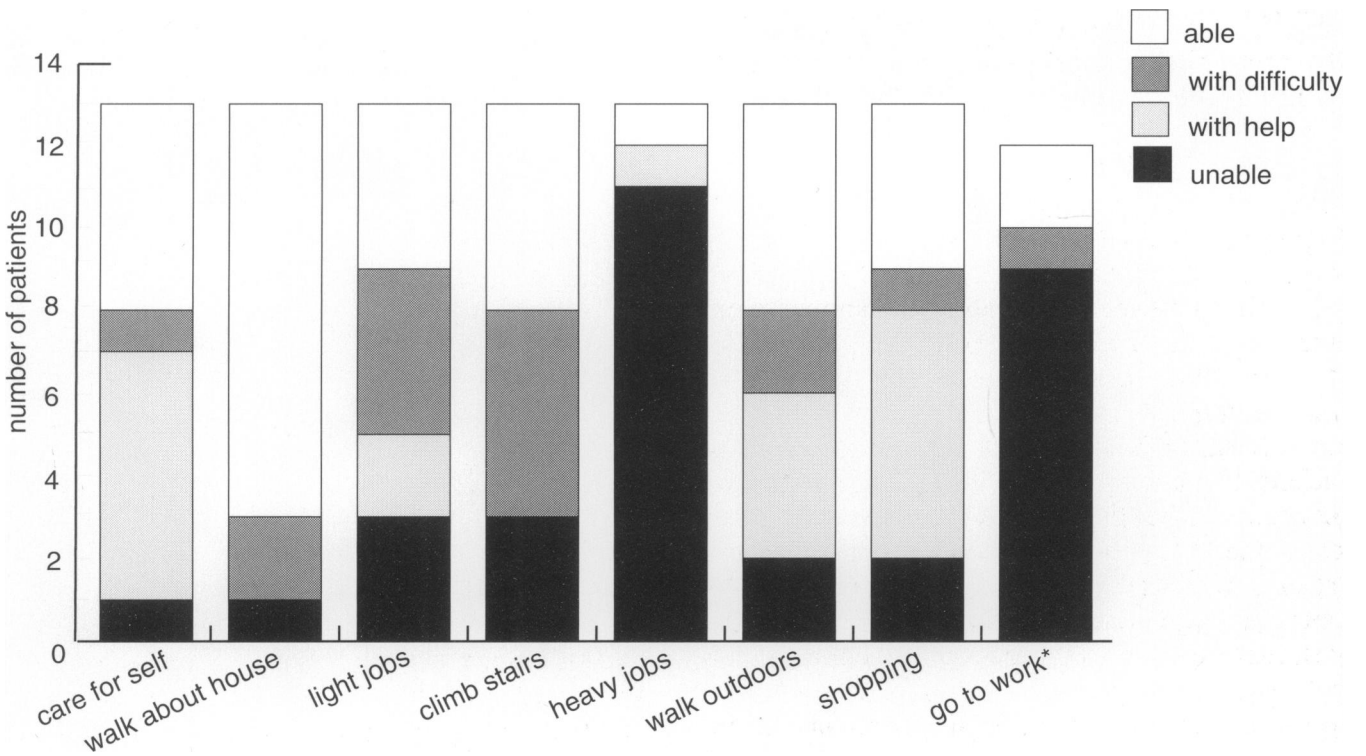

Fig Graph showing the ability of patients to perform certain tasks. *Patient 6 was excluded because of age (13 years).

age 36.2 years, range 13-67 years). Only 2 out of 13 patients felt that their quality of life was poor. Most were able to walk about the house and do light jobs; three patients even went out to work. An issue which is not addressed directly in this study is that of funding. With the lack of a central unit for commencing ventilation, there is no central funding mechanism. At present some ventilators are purchased with NHS funds, others are rented from Medical Therapeutics Ltd. Some funding is provided from the site of initiation of ventilation and some from the health board in the area where the patient resides. This issue requires further discussion and development of a comprehensive policy.

At present the number of patients in Northern Ireland receiving home ventilation is small but the number is steadily growing. In France, which has a well developed home care service, there are more than 5,000 people receiving home mechanical ventilation.[4,6] In the United Kingdom the number of patients requiring assisted ventilation at home is not known, but is currently estimated at around 2-3 per 100,000 population and expected to increase. The British Thoracic Society is currently setting up a register of patients receiving home ventilation in order to assess patient requirements nationally. In Northern Ireland, with a population of around 1.6 million, it may be conservatively estimated that around 40 patients require home ventilation. Options for managing these patients need to be considered, including the development of a specialist unit, either independently or within an existing department. The service provided should include assessment of patients with chronic respiratory failure and initiation of the appropriate mode of ventilation. There should also be adequate education and support for the patient and carers, including provision of a regular maintenance service for equipment and immediate advice should problems arise.

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A comparison of the effect of intramuscular dicofenac, ketorolac or piroxicam on postoperative pain following laparoscopy

J J O'Hanlon, H Beers, B K D Huss, K R Milligan

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SUMMARY

Sixty patients presenting for in-patient gynaecological laparoscopic surgery were randomly allocated to receive either diclofenac 75mg (n=20), ketorolac 30mg (n=20) or piroxicam 20mg (n=20) as an intra-muscular injection immediately after induction of anaesthesia. Postoperative visual analogue scores over the first 24 hours, using a 10cm scale, ranged from 3.2–0.5 in the diclofenac group, 2.7–0.85 in the ketorolac group and 2.8–0.5 in the piroxicam group. The scores did not differ significantly between the three groups (p>0.05). Mean time (SD) to first analgesia was 27(94) minutes in the piroxicam group, 16 (30) minutes in the diclofenac group and 62 (120) minutes in the piroxicam group. Six out of twenty patients in the diclofenac group required further analgesia compared to nine out of twenty in the other two drug groups. This difference was not significant. There were no reports of increased bleeding, bronchoconstriction, bleeding from the upper gastrointestinal tract, renal impairment or pain from the intra-muscular injection site in any of the groups. The administration of a non-steroidal anti-inflammatory drug to patients presenting for laparoscopic surgery reduces postoperative pain. There were no obvious differences between the agents used.

INTRODUCTION

Non-steroidal anti-inflammatory drugs [NSAIDS] are useful adjuncts to opioids for postoperative analgesia.[1] NSAIDS can provide similar analgesia to the opioids,[2] but avoid the sedation, respiratory depression, nausea and vomiting caused by them. Many workers have shown that both diclofenac and ketorolac can reduce opioid requirements following major gynaecological and upper abdominal surgery.[3,4,5] Diclofenac can provide similar analgesia to fentanyl following knee arthroscopy.[6] Unfortunately intramuscularly administered diclofenac has been associated with muscle damage,[7] and due to increased reporting of severe bleeding and renal impairment, especially in the elderly[8] the recommended dose of ketorolac has been reduced to a maximum daily dosage of 30mg.

We compared the analgesic efficacy and incidence of side-effects of diclofenac, ketorolac and piroxicam, given intramuscularly after induction of anaesthesia, in patients undergoing inpatient gynaecological laparoscopic surgery.

METHODS

The study protocol was approved by the Regional Medical Ethics Committee and written informed consent was obtained from 60 ASA 1-2 (ie patients who are healthy or have a mild systemic illness) female patients scheduled for either in-patient diagnostic laparoscopy or laparoscopic sterilisation. Patients with a history of upper gastrointestinal symptoms, known hypersensitivity to the study

Department of Anaesthesia, Lagan Valley Hospital, Hillsborough Road, Lisburn, BT28 1JP.

J J O'Hanlon, BSc, FFARCSI, Registrar.

H Beers, MD, FFARCSI, Consultant.

B K D Huss, MB, FRCA, Consultant.

Department of Anaesthetics, Belfast City Hospital, Lisburn Road, Belfast BT9.

K R Milligan, MD, FFARCSI, Consultant.

Correspondence to Dr J O'Hanlon, Anaesthetic Senior Registrar, Department of Clinical Anaesthesia, Royal Group of Hospitals, Grosvenor Road, Belfast BT12 6BA.

drugs, impaired renal function, asthma or on medication likely to interfere with the study results were excluded. We explained the use of the visual analogue scale (VAS) 0-10 at the preoperative visit. (The VAS was 10cm in length with 0 at the left end, representing "no pain" and 10 at the right end scoring "the worst pain imaginable").

Patients were premedicated with lorazepam 2mg by mouth 2 hours before surgery. Anaesthesia was induced with propofol 2mg/kg and fentanyl lmcg/kg. Atracurium 0.5mg/kg was given to facilitate tracheal intubation and intraoperative ventilation. Anaesthesia was maintained with 1–1.5% isoflurane in 65% nitrous oxide in oxygen. At the end of the procedure neuromuscular blockade was reversed with neostigmine 2.5mg and glycopyrrolate 0.5mg.

Following induction the patients were randomly allocated to receive a 3ml deep intra-muscular injection in the lateral compartment of the right thigh of either diclofenac 75mg (group D), ketorolac 30mg (group K) or piroxicam 20mg (group P).

The patients' age, height, and weight were recorded, and the interval from the end of surgery until the first request for analgesia was noted. Postoperative analgesia was prescribed in the form of either paracetamol lg or intra-muscular 'Cyclimorph 10' 0.01 ml/kg. This was administered to the patient by the recovery ward nurses who were unaware of the study drug given. Oral analgesia was administered if the patient's pain score was 3 or greater and and cyclimorph was given if the pain score was 5 or greater. The dose and timing of any postoperative analgesia was noted. Patients completed their VAS scores for pain on movement at the following times: on admission to recovery ward, at 1 hour, 2 hours, 4 hours and 24 hours after completion of surgery. They were also asked about the presence of musculoskeletal pain and pain from the NSAID injection site.

For statistical analysis we used an independent samples Student's t-test for continuous variables, the Kruskal-Wallis test for VAS scores and Chi-square for categorical samples. A P value of < 0.05 was considered statistically significant.

RESULTS

Data were obtained from 60 patients and treatment groups were similar in respect of age, height, weight and nature of surgery. There was no difference in the dosages of propofol or fentanyl between the three groups (Table I).

The VAS pain scores (Table II) in the three different groups were not significantly different at any time in the 24 hour postoperative study period. Median (Interquartile range) VAS scores (Table II) in the study groups were diclofenac 2.1(2.6), ketorolac 2.1(2.7) and piroxicam 2.3(2.5). The mean (SD) intervals to first analgesia (Table II) were 27(93.7), 16.3(30.2) and 62(120) minutes in the diclofenac, ketorolac and piroxicam groups respectively ($p>0.05$), although the time to first analgesia seems longer in the piroxicam group the results were skewed by one patient who required cyclimorph 420 minutes after surgery. Six patients in the diclofenac group, nine in the ketorolac group and nine in the piroxicam group required further analgesia in the form of a single opioid intramuscular injection, but this difference was not statistically significant. Of the twenty four patients who received an intra-muscular opioid, six patients received co-codamol initially, but this did not provide sufficient analgesia.

DISCUSSION

The NSAIDS can reduce postoperative pain by central and peripheral cyclooxygenase inhibition.[9] This has led to their use as single analgesics[10] or in combination with opioids. Prostaglandins are present in menstrual fluid, and the NSAIDS can reduce the pain associated with menstruation.[11] Similarly they might be expected to reduce pain after surgical manipulation of the Fallopian tubes.[12]

Piroxicam is an oxicam and not related to acetylsalicylic acid. It has different characteristics from other NSAIDS such as a longer half-life (30 hours).[13] This is due to extensive protein binding allowing a once daily dosage which should provide longer duration analgesia compared to the other NSAIDS.[14] Previous studies have demonstrated that piroxicam, in oral and intramuscular formulations is superior to placebo and other widely used NSAIDS in providing analgesia. In dental patients oral piroxicam 20mg was shown to be superior to 50mg diclofenac, and in a similar group of patients there was no difference between 50 and 100mg of diclofenac.[15] In arthroscopy patients Morrow et al[16] showed 30mg of ketorolac to be clinically superior to 75mg diclofenac. When piroxicam was compared with other commonly used NSAIDS in patients with osteoarthritis it showed good clinical efficacy and as there were fewer reported side-effects it was thought generally more tolerable.[14, 17, 18]

TABLE I

Physical characteristics in the treatment groups shown. Values are mean. Standard deviation shown in brackets.

	Diclofenac (n=20)	*Ketorolac (n=20)*	*Piroxicam (n=20)*
Age: years	34 (7.7)	30 (6.1)	31 (7.88)
Height: cm	156 (7.2)	157 (7.2)	155 (6.8)
Weight: kg	68 (6.7)	62 (8.8)	61 (6.2)
Laparoscopic sterilization:	6	6	6
Diagnostic laparoscopy:	14	14	14
Propofol dose: mg	155 (30)	153 (30)	156 (26)
Fentanyl dose: mcg	74 (14)	70 (15)	74 (16)

TABLE II

Median (interquartile range) VAS scores over the first 24 hours after surgery and mean (SD) time to first analgesia.

	Diclofenac (n=20)	*Ketorolac (n=20)*	*Piroxicam (n=20)*
Median VAS scores	2.1 (2.6)	2.1 (2.7)	2.3 (2.5)
Time to first analgesia (minites)	27 (93.7)	16 (30.1)	62 (120)

However there was no difference in VAS scores between the three study groups postoperatively but there was a difference in the time to first analgesia in the ketorolac group compared to the diclofenac and piroxicam groups. In the latter two groups there were patients requesting analgesia 360–420 minutes after surgery as compared to 130 minutes in the ketorolac group. Although not statistically significant, due to the small number, it would suggest that diclofenac and piroxicam may have a longer effect than ketorolac. By giving the NSAID to gynaecological laparoscopy patients the number of patients requiring postoperative analgesia was reduced, and most patients reported adequate analgesia. Despite the longer half-life of piroxicam, all three drugs produced similar results, suggesting the reduction in postoperative pain occurred in the immediate perioperative period. Preoperative nerve blocks in patients undergoing inguinal hernia repair have been shown to provide better postoperative analgesia than postoperative nerve blockade.[19] The preoperative reduction of the inflammatory response by the NSAIDS provided the patient with good analgesia. However is immediately post induction the most beneficial time of administration of NSAIDS? More work is required to answer this question.

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Antineutrophil cytoplasmic antibodies in myelodysplasia

D R Hull, S A McMillan, I Maeve Rea, Noleen Boyd, Mary F McMullin

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SUMMARY

Antibodies to neutrophil cytoplasmic antigens (ANCA) are good serological markers for patients with mainly vasculitic conditions. Two main types of ANCAs have been detected, the first termed cytoplasmic antineutrophil cytoplasmic antibody (cANCA) are mainly associated with patients with Wegener's granulomatosis, the other termed perinuclear antineutrophil cytoplasmic antibody (pANCA) are mainly associated with patients with renal vasculitis, rheumatic and collagen disorders. These antibodies are against various constituents of neutrophil granules. In patients with myelodysplasia, defects in normal granulocyte development are seen. We report a series of twelve patients with myelodysplasia of whom at least four showed a low titre and one a high titre of pANCA. Two of these patients also had demonstrable activity against myeloperoxidase (MPO). None of these patients had any evidence of systemic or cutaneous vasculitis or of any autoimmune disorder. There was no pANCA positivity in an age matched control group.

INTRODUCTION

The myelodysplastic conditions are a heterogenous group of haematological disorders characterised by refractory cytopenias. They include quantitative and qualitative abnormalities of the myeloid cell lineage resulting in reduced chemotaxis, phagocytosis and enzyme content.[1,2] In the 1980s autoantibodies directed against the cytoplasmic constituents of neutrophils (ANCA) were discovered. Many of the antigens were found to be enzymes normally contained within the neutrophil granules, these include myeloperoxidase, proteinage 3, elastase, lactoferrin and cathepsin G.[3]

At least two types of ANCAs can be distinguished by indirect immunofluorescence on ethanol fixed neutrophils: cytoplasmic (cANCA) and perinuclear (pANCA). Associations have been shown to exist between the occurrence of these antibodies and various vasculitic disorders such as cANCA with Wegener's granulomatosis and microscopic polyarteritis, and pANCA with renal vasculitis as well as various rheumatic and collagen vascular disorders.[4]

This study was undertaken to look into the occurrence of antineutrophil cytoplasmic antibody activity in myelodysplasia.

SUBJECTS AND METHODS

Twelve patients with an established diagnosis of myelodysplasia according to the French - American - British (FAB) classification,[5] had their sera tested for ANCA by indirect immunofluorescence according to the method described by Wiik[6] at the 1st International Workshop on ANCA as did twelve healthy controls. Briefly, serum samples were screened for ANCA at dilutions of 1 in 10 and 1 in 20, and if positive titrated until endpoint. 80µl of appropriate dilution was incubated at room temperature for 30 minutes on ethanol fixed neutrophil cytospins and dryed before use. After washing in PBS (Phosphate Buffered Saline) antihuman globulin conjugate (Dako UK, Ltd.) was added and incubated for a further 30 minutes

Department of Haematology, Royal Victoria Hospital, Grosvenor Road, Belfast BT12 6BA.

D R Hull, MRCP, DipRCPath, Registrar.

Regional Immunology Laboratory, Belfast City Hospital, BT9 7AB.

S A McMillan, PhD, Consultant Clinical Scientist.

Noleen Boyd, MB, DipRCPath, Senior Registrar.

Department of Geriatric Medicine, Whitla Medical Building, Belfast City Hospital, BT9 7AB.

I. Maeve Rea, BSc, MD, FRCP, Consultant Physician.

Department of Haematology, Queen's University of Belfast, Institute of Pathology, Grosvenor Road, Belfast BT12 6BL.

Mary F. McMullin, MD, MRCP, MRCPath, Senior Lecturer.

Correspondence to Dr Hull.

TABLE

Details of patient group

Case	*Diagnosis*	*Age in years*	*pANCA*[1]	*MPO*[1]	*pANCA*[2]	*MPO*[2]
1.	RA	83	–	<15%	–	20%
2.	RA	90	20	<15%	10	<15%
3.	RAEB	81	20	<15%	20	<15%
4.	RAEB	72	–	<15%	–	<15%
5.	RAEB	78	–	<15%	20	<15%
6.	RAEB	79	–	<15%	–	<15%
7.	RAEB	78	20	16%	10	16%
8.	RA	71	160	<15%	NOT AVAILABLE	
9.	RAEB	78	20	<15%	20	<15%
10.	RAEB	70	–	<15%	10	<15%
11.	RA	54	–	<15%	–	<15%
12.	RARS	64	–	<15%	–	<15%

ABBREVIATIONS:

RA	Refractory anaemia
RAEB	Refractory anaemia with excess blasts
RARS	Refractory anaemia with ring sideroblasts

at room temperature. If required reincubation was performed with antihuman IgG and IgM (Dako UK, Ltd.) to determine immunoglobulin class specificity. The slides were then washed in PBS, mounted and viewed using a fluorescence microscope.

Serum containing pANCA was recognised as a non-granular perinuclear or nuclear staining of the neutrophils. A cANCA pattern was recognised by a granular cytoplasmic staining. If positive for either p or cANCA the serum was titrated until an end point was obtained. Sera from patients with antinuclear antibody (ANA) also exhibit a pANCA pattern therefore all positive sera were tested for ANA by indirect immunofluorescence. All serum samples were also tested for the presence of antimyeloperoxidase antibodies (MPO) by ELISA (Biodiagnostics Ltd England), Positivity was taken as greater than 15% of positive standard, and for the presence of anti-nucleolar, anti-mitochondrial, anti-smooth muscle and anti-gastric parietal cell antibodies by the indirect immunofluorescence technique.

Patients were retested after an interval of 2-6 months where possible.

A control group of healthy people from a similar age group was also tested.

RESULTS

Sera from 5 out of the 12 patients studied showed titres for pANCA on initial testing; a further patient negative on initial testing was positive on repeat testing. No patients showed positivity for cANCA, antinuclear antibody or other autoantibodies. One patient had borderline activity against myeloperoxidase initially, two patients were positive on repeat testing. The details are given in the table. In the control group no cases showed positivity for pANCA though two had demonstrable cANCA activity; all were negative for antimyeloperoxidase activity.

DISCUSSION

We have shown positive titres for pANCA in at least 5 out of 12 patients with myelodysplasia and

none in a control group of similair age. There is a strong association between ANCA in high titre (80 or greater) and many vasculitic diseases. There have been a few reports of an association between myelodysplasia and various vasculitides,[7,8] but none of our patients showed any clinical or laboratory evidence of systemic or cutaneous vasculitis or of any autoimmune disorder.

The pathophysiological significance of ANCA, especially in low titre, is uncertain. A recent study has shown that a wide range of conditions can be associated with low ANCA titre, especially pANCA. Many of these cases did not show any evidence of vasculitis.[9] Certain experimental data suggest that ANCAs do play a role in the pathogenesis of vasculitis.[10] Stimulated neutrophils express a number of molecules, including neutrophil granule enzymes at their surface. It has been suggested that ANCAs react with these surface enzymes to further activate neutrophils into producing reactive oxygen species with the further release of lysosomal enzymes leading to vasculitis.

Patients with myelodysplasia have reduced numbers of abnormal neutrophils and are at an increased tendency to infection.[11] In short term culture granulocyte-macrophage colony forming units (CFU-GM) are reduced and abnormal,[12] so indicating that there is a defect in neutrophil development. We have discovered that in this group low titres of pANCA are present, this in contrast with the control group where pANCA was not detected.

We postulate that the abnormal neutrophils in myelodysplasia may lead to exposure of abnormal constituents to the host immune system thereby stimulating antibody formation.

Acknowledgment.

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Coccygodynia

M Zayer

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SUMMARY

Ten coccygectomies were performed. Patients were all females (aged 26-74, average 46). All patients expressed satisfaction after the operation (one was deceased at the time of follow up). The material is too small for definitive conclusions, but it shows clearly that carefully selected cases with traumatic or idiopathic coccygodynia could benefit from coccygectomy.

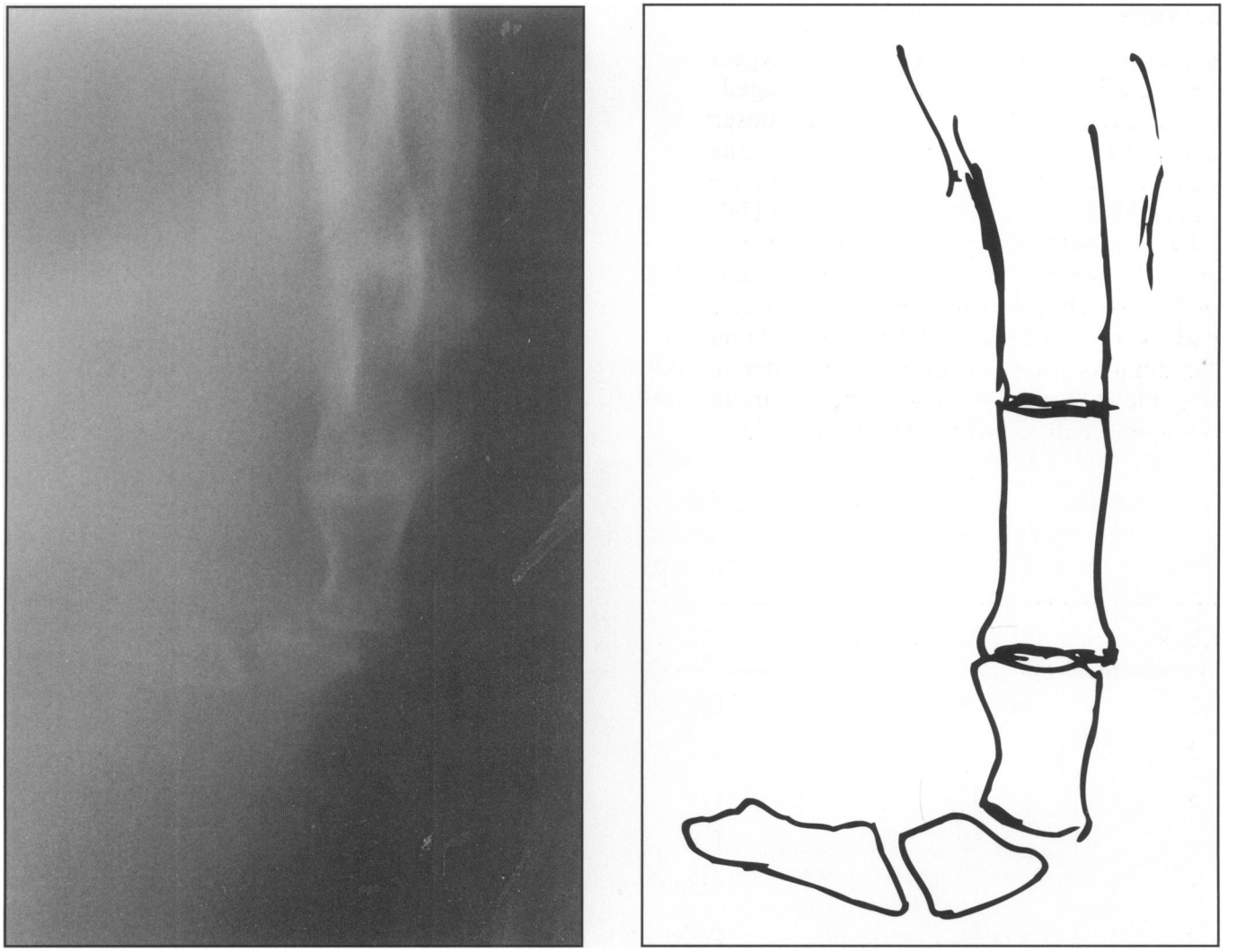

Figure X-ray showing severe forward deviation of the coccyx. (Case 5)

Department of Orthopaedics, Ängelholm Hospital, 262 81 Ängelholm, Sweden.
Mohammed Zayer, MD.

INTRODUCTION

The word coccyx is derived from the Greek word for cuckoo because of the resemblance to the beak of this bird. The conception of the painful coccyx (coccygodynia) was proposed by Simpson in 1859.[1] It is a symptom rather than a disease and may be caused by congenital deformity, fracture, infection, sprain, arthritis or tumours (chordoma, teratoma, chondro – or osteosarcoma); often there is no identifiable cause.

A variety of treatments includes hot baths, rubber ring cushions, plaster jackets, suppositories, physiotherapy, sacral rhizotomy, manipulation, epidural injections, local injections and finally coccygectomy (Wray et al 1991).[2]

MATERIAL AND METHOD

In the period from 1978 to 1993, 10 coccygectomies were performed. All were females (aged 26-74 years, average 46) who had tried conservative treatment such as rubber ring cushion, physiotherapy, local steroid injections, transcutaneous nerve stimulation (TNS) and NSAID. All had persisting symptoms after conservative treatment for one year or more. Five of the patients gave a history of a fall; in two cases coccygodynia started with parturition; in one case the symptom started immediately after an anal operation and in two cases no history of trauma was obtained. X-ray showed severe forward deviation of the coccyx in nine cases (figure). The incision was longitudinal with total resection of the coccyx, the patients lying prone under general anaesthesia; no drainage was used. The mean age of the patients was 31.7 years at the time of trauma, 43.3 years at operation and 48.4 at the last presentation (Table).

The symptoms usually started after the trauma, but increased in intensity the year before operation. In the two cases without trauma the duration of the symptom had lasted several years (case 2), and one year respectively (case 5), while in case 10 the symptoms had started immediately after extirpation of a perianal tumour which was performed two years prior to coccygectomy. Seven of the ten patients were operated on by the author.

RESULTS

Nine of the ten patients were alive at the time of assessment. The deceased patient had suffered from colonic diverticulosis, spondylolisthesis at L4-L5 and referred pain to the coccyx and anal region. She had a sigmoidectomy at age 72, and coccygectomy at age 74 with no relief of symptoms until she died at the age of 77. Patient 7 developed a postoperative staphylococcal infection which was treated with antibiotics. All patients were asked by telephone whether they could participate in a routine clinical and radiological follow up examination, but all refused because they all were symptomless, very satisfied and therefore believed that there was no need for such an examination.

TABLE
(age in Years)

Case	*Age at onset*	*Aetiology*	*Age at operation*	*Age at follow up*
1	14	fall	26	41
2	–	unknown	74	77 (died)
3	43	fall	59	69
4	42	fall	53	59
5	–	unknown	49	54
6	31	parturition	42	46
7	42	fall	46	49
8	12, 14	fall	31	33
9	19	parturition	42	43
10	40	anal surgery	42	42.5

DISCUSSION

The aetiology of coccygodynia is still debatable. Bremer (1896)[3] believed that such patients were suffering from anxiety, neurosis or even hysteria and so strongly denounced coccygectomy. This view is entirely rejected by others who do not consider these patients to be neurotic. Their symptoms have only not been understood (Wilson 1976,[4] Wray et al 1991). Many authors have thought coccygodynia to be referred pain from a lumbosacral disc prolapse (Richards 1954[5]) uralgic state due to irritation of the sacral nerves (Bohm and Franksson 1958,[6] Wright 1971[7]). Patients with lumbosacral disc prolapse failed to improve after coccygectomy and later underwent lumbar disc excision with relief of symptoms (Wray and Templeton[8] 1982; Bayne et al 1984[9]), and therefore the theory of referred pain from a lumbar disc prolapse seems to be supported in some cases.

It is thus very important to select the suitable case for operation, and exclude cases with symptoms not related to the coccyx, and to try conservative treatment first.

Our material is too small for definitive conclusions, but it shows clearly that carefully selected cases with traumatic or idiopathic coccygodynia could benefit from treatment by coccygectomy.

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The Clinician Scientist – An endangered species?

Annual Oration – Royal Victoria Hospital – 5th October 1995

Ingrid V Allen

I am grateful to my fellow members of staff for doing me the honour of asking me to give this, the 168th, annual oration, but honour and pleasure of course are not synonymous, and this occasion for me, while a great honour, is a qualified pleasure – probably for the audience too, so our sympathies are mutual. There is however one aspect which is pleasurable, and that is to be introduced *as a lady*. Since my appointment to the staff of this hospital I have been described by various epithets, all justified but not all entirely complimentary; it is therefore a singular honour to be described not only as a lady but as "the first lady".

In a way it shows how far medicine has come from those early days, for example here in Belfast, when to quote from J C Beckett and Theodore Moody's History of Queen's:-[1] "In April 1891, nine women medical students and twenty three men –(medical students were always intelligent), petitioned President Hamilton thus:- *We, the undersigned, beg to draw attention to the following facts with regard to the position of women studying at Queen's College: Women, though allowed to attend the lectures at the aforesaid College, do not hold the legal status of students. They may enter for examinations, but are not eligible for any of the prizes or scholarships. As this position is clearly an anomalous one, we think that in the interests of justice some change should be made. We therefore humbly petition you to take such steps as shall seem to you advisable to obtain for women studying at Queen's College a position equal to that which they now hold in the Royal University, in which all degrees, honours exhibitions, scholarships and prizes are open to students of either sex."*

Beckett and Moody go on to say in the patrician style of the professional historian:- "Hamilton not only supported this, but to allay any doubts about the ability of women to profit by higher education he quoted the opinion of Professor Redfern: *'The continued successes of females in the intermediate and various university examinations for some years past forbid any further speculations as to their chances in intellectual competitions with men. No one would dare at present to suggest that they will not be able to hold their own in intellectual struggles on any subject, if they have equal advantages with men"* – and the rest of course is history.

The first woman to graduate in medicine at Queen's, Dr Elizabeth Bell, did so in 1893, and today I look across at our student body, a total reflection of the gender composition of the young adult population. You will notice my use of the politically correct word 'gender' rather than 'sex' – I wonder whether today Sir William Osler would get away with his light-hearted quip that in medicine there are not just two sexes but three – men, women and women physicians. I would add a fourth, male surgeons, and say "long live humour and sex, two very important components of life". The serious point is that today, at last, the gifts of men and women are fully used in the cause of medicine.

This of course is our students' day and our Chairman has already welcomed you and given you a flavour of the culture and philosophy of this great hospital and it is as an extension of those ideas that I have chosen, as the subject of my Oration, The Clinician Scientist – an Endangered Species? In defining clinical science and the role of the clinician scientist, the cardinal issue is our acceptance that medicine is a science in its own right. That is not to say that the practice of medicine for the majority demands the establishment of new facts or principles, but rather that in the practice of medicine the opportunity exists to advance knowledge, and

Department of Neuropathology, Royal Victoria Hospital, Belfast BT12 6BA.

Ingrid V Allen DSc, MD, FRCPath, Professor of Neuropathology.

this opportunity can only be exploited fully by the application of basic science to the more applied science of clinical practice. In accepting this fact we should not think too narrowly as to what the relevant basic sciences are – they cover a wide spectrum, from the most fundamental and structural, for example physics and chemistry, through to cognitive psychology, social science, engineering and economics.

Thus it has been stated that "Medical History involves social and economic, as well as biological content, and presents one of the central themes in human experiences".[2]

In all cultures, although the practice of medicine has involved elements of the religious and the intuitive, the overwhelming element has been and is scientific.

If primitive man could use medicinal plants for their specific antifebrile, laxative, emetic, antispasmodic, diuretic, analgesic, sedative, stimulatory and hallucinatory effects (Lyons, History of Medicine),[3] with what greater certainty can we in this age affirm the Hippocratic view of medicine as a science in its own right, and with Hippocrates say "there is no science which has no basis in fact".[4]

We too would endorse the view of Flexner (1910),[5] expressed over 2000 years after Hippocrates, but not deviating from the Hippocratic logic. In Flexner's ideal medical education, two principles operate – first that the basic sciences, (that is chemistry, physics and biology) provide the intellectual foundation of modern medicine, and secondly that the scientific method should be applied to the practice of medicine as well as to research. "It makes no difference to science", said Flexner, "whether usable data be obtained from a slide beneath a microscope or from a sick man stretched out on a bed".

Flexner's seminal report was based on the nineteenth century successes of European, including British medicine, and laid the framework for twentieth century successes in biomedical research in the United States.

If therefore we accept medicine as a science, and scientific endeavour the basis of advance, then the medical scientist as an individual is of enormous importance. A clinician certainly, but one whose major role is to establish new facts, new principles and new methods. Of course, throughout history such individuals have existed. Among the most famous for example is Joseph Lister, who used and acknowledged the work of Pasteur in his studies of wound sepis. This illustration indicates precisely the role of the clinician scientist, as do many less famous but nevertheless important local examples.

I will quote one – the late Dr Lewis Hurwitz,[6] when working here in Belfast with Professor Molly McGeown in the very early days of renal transplantation, used an interdisciplinary approach involving clinical neurology, biochemistry, transplantation technology and neurophysiology to show the beneficial effect of renal transplantation upon the peripheral neuropathy of chronic renal failure.

The achievements of the scientific approach are legion, and the need for dedicated clinician scientists has become increasingly great as the biological revolution has taken off and its translation into clinical practice becomes a realistic goal. It is the clinical investigator who serves this function and is the vital bridge between basic science and improvements in health care. It is therefore paradoxical, that many now consider the species of clinician scientist to be endangered. The most extreme and pessimistic view was expressed by Professor Gordon Gill at the University of California at San Diego, in his essay on 'The End of the Physician Scientist'.[7] He describes how from the 1960s to the 1980s biomedical research enterprise in the United States passed largely out of the realm of clinicians and into the realm of non-medically qualified postdoctoral scientists. He states that similar changes occurred in Europe, including the United Kingdom, in the 1990s. "Like it or not" he concludes "the separation of Physicians and Scientists is well advanced" – "partial attention to either science or medicine is no longer enough".

Many disagree with this view and I hold myself among them. I would emphasise the diversity of medical research, and recognise that some will be done by medically qualified scientists and some by other scientists, and that these two are complementary. Molecular biology will enrich clinical medicine enormously, but it is only the starting point to an understanding of phenotype, and epidemiology will continue to hold the key to preventive medicine.

The particular difficulty for the clinician scientist is in gaining sufficient knowledge of the relevant basic sciences, while retaining and developing

essential clinical skills. Many would agree with Judah Folkman who has recently succinctly described the negative attitudes that are likely to surround the budding clinical investigator of today when he states that: "The individual who attempts to combine investigation with a clinical career travels the toughest road, however fruitful it may be in the end. His counterpart in basic science thinks he is a dilettante researcher, his clinical colleagues think he is unsafe, and his mother-in-law says, – He's 35 years old and still working on rats. When will he be a real doctor?"[8]

However in contemplating the potential adverse factors influencing the clinician scientist, I would like to quote from John Gardner and would agree that in fact "we are faced with a series of great opportunities brilliantly disguised as insoluble problems".[9]

No one wants clinical science to fail and it is therefore essential that the necessary changes in medical training, in the practice of medicine, and in the allocation of resources are managed correctly. Several factors operate including the exponential growth in science, greater specialisation in science and medicine, competition for resources and the perhaps timely death of the renaissance amateur clinician scientist.

Medicine faces some specific and indeed unique challenges, in that the emerging biological principles and the associated technology apply to the whole of medicine, while medicine itself is still held in the stranglehold of a systematised anatomical framework. These intellectual and logistical challenges are only now being considered by medical schools and teaching hospitals throughout the world, and as yet no pattern of planning has emerged which gives us confidence in looking to the future.

At the same time as we face these issues, we are reorganising, again world wide, the medical curriculum, postgraduate medical training and health care delivery, the latter dictated by market forces, while underlying ethical dilemmas remain.

At times like this we would endorse the words of Gaius Petronius, Arbiter, Proconsul at Bithynia in AD 65:-[10] *"We trained hard but it seemed that every time we were beginning to form teams we would be reorganized. I was to learn later in life that we tend to meet every situation in life by reorganizing, and a wonderful method it can be for creating the illusion of progress while producing confusion, inefficiency and demoralization".*

So let us consider how the clinician scientist may be affected by all of these changes. First of all in the training of tomorrow's doctors. The curriculum has to be a compromise, balancing the pursuit of knowledge for its own sake with the requisition of practical skills essential for safe practice. The solution put forward by the General Medical Council is a reasonable compromise, and allows each medical school to put its own distinctive 'stamp' on its training.

The emphasis is on a core curriculum of factual teaching supplemented by and with equal emphasis on special study modules:- *"The greatest educational opportunities will be afforded by that part of the course which goes beyond the limits of the core, that allows students to study in depth in areas of particular interest to them, that provides them with insights into scientific method and the discipline of research and that engenders an approach to medicine that is constantly questioning and self-critical".*[11]

However, without being cynical, one wonders if all the members of the General Medical Council really mean what they say. The Council goes on to enumerate attitudinal objectives which a training in medicine should achieve. There are twelve in all, each worthy, but that relating to the acceptance of the responsibility to contribute to the advancement of medical knowledge is listed last – let us hope that heavenly influences operate here and the last indeed shall be first.

Our limited academic resources, however, present us with a challenge and the new curriculum is a potential threat to clinical research. For the best of educational reasons it is labour-intensive for the teachers, yet it is unreasonable and educationally unsound to assume that all the teaching will be done by the non-research-active, and indeed the strongest case can be made for sufficient critical teaching mass so that the most active researchers have the time and the support to impart their knowledge and enthusiasm to the next generation. This requires careful planning so that limited academic resources are used to the full and, where possible, future doctors, dentists and nurses are taught together and National Health Service doctors have sufficient time to honour their teaching obligations. Equally, the importance of non-medical scientists cannot be over-

emphasised. Whether working in the Health Service or in the University, their career structure and security of tenure should be such that they can contribute fully to the teaching programme and to medical research and health care delivery. This latter group is particularly important in intercalated BSc degrees and in combined MB/PhD programmes where the medically qualified obtain the fundamentals of other branches of science which they can then apply in their future career. These intercalated degrees have been shown in several studies to be the key elements in the future careers of many leaders of academic medicine and of clinical researchers. The undergraduate curriculum therefore cannot be looked at in isolation but forms a continuum with postgraduate medical training and impinges on the training of other professionals involved in health care delivery. It must be emphasised that all medical practitioners should have the capability to play their part in the sciences of clinical audit, research on outcomes, and use of information systems.

Some of these skills will be attained in the undergraduate curriculum, but it will be necessary to continue at a postgraduate level, perhaps with the attainment of a Master's degree in research methodology.

For the few, aspiring to be academic leaders and clinician scientists, a more flexible training programme is essential, with three/four years set aside to learn laboratory or statistical and epidemiological skills. It is the need for this carefully planned programme which poses one of the major threats to the survival of the clinician scientist. The difficulties of planning such a programme, taking into account the Calman recommendations for postgraduate medical training, and the even greater difficulty of funding such a programme in the present atmosphere of uncertainty, both academic and NHS, present us with a major challenge. The Medical Committee of the Higher Education & Funding Councils has noted a fall in the number of applicants for academic posts and the House of Lords Select Committee on Science and Technology in its recent report "Supporting Research and Development in the NHS", alerts us further to this danger.

Lord Walton and his committee state:- "The evidence that an increasing number of doctors are choosing a career in clinical practice rather than academic medicine is very powerful''.[12] The Committee go on to ask that the government should give urgent priority to this problem so that the issue can be analysed and appropriate remedies implemented. What about other resources essential to clinical science? The NHS has been described as the largest and potentially the best human biology laboratory in the world. This is probably true, but as with all large organisations, the prioritisation for the use of resources and the measurement of effectiveness of that use is difficult, and several general points have to be made. First, it is government that determines research expenditure and for all governments expenditure in biomedical research is in competition with expenditure on other branches of science, some of which may have more political or economic short-term benefit. Most governments have in the last few decades maintained absolute levels of expenditure for medical research but have not managed to maintain relative values; for example, only recently have defence research budgets been cut, and moreover many politicians seem unaware of the financial benefits which have resulted from medical research.

Would that the public, who are perhaps more intelligent than some of our politicians, know for example that to take some statistics from the United States:-[13]

- The introduction of lithium for the treatment of Manic Depression has saved 145 billion dollars in hospitalisation costs in 25 years.
- Potassium citrate treatment for preventing kidney stone recurrence saves an estimated 400-870 million dollars per year.
- The haemophilus influenza B vaccine for meningitis a further 350-450 million dollars annually.
- The disputed and expensive Interferon therapy recently on trial for multiple sclerosis has reduced hospitalisation by 25%.

In addition new rational therapies are on the horizon for Alzheimer's disease which will give not only many millions a new lease of life, but unfortunately may mean that certain world statesmen will be in office even longer!

How sad then, that funding for research is proving increasingly more difficult to obtain and that only 25% of National Institutes of Health and 20% of Medical Research Council's alpha-rated

projects receive funding. This is particularly detrimental at a time when these funds have to be spread even more thinly, including not only traditional clinical science, but Health Services research. It is therefore imperative that in welcoming and implementing the Culyer report on research in the Health Service,[14] the government recognises that while the principles enunciated by Culyer are rational, the resource required for proper implementation is probably greater than that presently available. Let us hope that these issues are of sufficient importance to the enfranchised of this country that they are addressed in the various party political manifestoes before the next general election.

But what of Northern Ireland with its medical school and teaching hospitals? Much has changed in my view to modify the opinion expressed by Sir Peter Froggatt and Professor Barry Bridges in their history of the first 150 years of the Belfast Medical School,[15] when they state that research, while not wanting, was never a prominent feature of this medical school.

Sir Peter and Professor Bridges emphasise that their views are largely based on achievements before 1948, and that the advent of the National Health Service and the development of full-time academic units have had a significant beneficial effect on research output. Our distinctive cultural characteristics, summarised as a social cohesion despite political differences, with pragmatism and sound clinical orientation, together with our pride in learning, give us a firm basis, building on the developments of the last 50 years, to become a major medical research centre.

I would like to consider these opportunities under three headings – Regional planning, Regional collaborations and Critical research mass. First of all let us consider regional planning. It is encouraging that in Northern Ireland as in other parts of the United Kingdom some framework for research has been laid down. The Universities, stimulated in part by the funding council's Research Assessment Exercise, have formulated their individual research strategies, and the Department of Health has more recently begun to define its research priorities. Nationally, efforts are being made to maximise on resource and to prevent the divergence of medical school and Health Service priorities. How much more important that we, in a small region of 1.6 million people should achieve this objective. It is therefore encouraging that at last there appears to be some movement on the appointment of a Regional Director for research and development. Given the advantage that we can learn from others' mistakes, let us hope that we can formulate a structure which embraces biomedical research for the province and thus enables all players to achieve maximum output.

We expect and indeed hope that the Culyer report will be implemented in Northern Ireland and it is therefore important that this Hospital defines its core research facilities and is ready to benefit from the national competition. How encouraging therefore that the Trust Board has decided to increase further our research profile by advertising for a Clinical Research Fellow at consultant level.

Secondly what of the very fruitful collaborations we can develop to further our research? These clearly range from the local to the national and international, and again should be focused, strengthening our mainstreams of research but not stifling individual curiosity. Indeed it is this very process of focusing, by which a research culture is achieved, which stimulates the individual and leads to a response with new and original ideas. Many schemes for collaboration exist but I would like to mention the potential for industrial collaboration. The Northern Ireland Industrial Research and Technology Unit (IRTU), linked to the National Office of Science and Technology, has long been concerned that biomedical research has not developed overall to a significant degree in Northern Ireland, though in some branches major success has been achieved: the reasons for this are various and beyond my capability of analysis. Certainly if we attempt to develop genetic biotechnology, we have many highly successful competitors, frequently based adjacent to the great graduate institutes of the world, such as Cambridge, England, and Cambridge, Massachussetts. How much better that we consider some other enterprise; for example could this Hospital, working together with the medical school's new Department of Telemedicine, and through the good offices of IRTU, find an appropriate industrial partner to exploit these new developments in medicine? I would hope these and other worthy examples should get serious attention.

Finally, our achievement of critical research mass, and here we have particularly interesting

opportunities. Perhaps, uniquely in Europe, we have an intellectual continuum, within a few square miles, of basic science, all clinical specialties at secondary and tertiary level, incorporating Queen's University and its medical school and the major Belfast teaching hospitals: this in a region of 1.6 million people, with a strong primary care and community base. We have an excellent infrastructure and our objective must be to become the leading medical centre in Ireland, with a planned use of resources including basic science, community, and acute hospital facilities. The latter of course must be the hub of the biological research wheel, while the dispersed community services are essential for epidemiological research. Almost certainly we have not achieved optimum planning in these respects and will only do so if several principles are adhered to. First and foremost the decisions must be based on science and on need, and not on political objectives. We must request and encourage our politicians to absolve themselves from their parochial responsibilities, and instead to join with us in meeting the greater challenge of an acute hospital plan for Northern Ireland, a Regional Specialty plan, and a research and development plan.

I therefore have sympathy with the constraints placed upon the McKenna Committee and I certainly hope that the McKenna report,[16] which will undoubtedly be a stimulus for discussion, will not necessarily be the final word on a framework for specialty rationalisation. If we continue to use a King Solomon approach to the baby of acute medicine in Belfast, then we will certainly lose that baby. Much more thought needs to go into the development of the City and Royal Hospitals sites, perhaps not in a complementary style, but rather in a unified style, from primary through to tertiary care. Such an approach will take much time and further debate, but if we use the guiding principles of service needs and of the fully-costed needs of teaching and research, then the rewards will benefit us all. So back to you students. Your opportunities too are enormous and you can look to a most rewarding future. You can imagine it is January 1st, 2004. You may well be working in this hospital, getting your wake-up call, a bit groggy because last night it was a good party, but encouraged by your surroundings in the luxury of the new Royal, and further encouraged by the dulcet tones of your Chief Executive reminding you that it's 6.30 am, and please remember the Mission Statement. It's New Year's day, but in this, the 21st century, all the wards and operating theatres are open 365 days a year, so you dash off, perhaps to the Gene Therapy Clinic or the Cognitive Therapy Workshop. Perhaps you look at patients, not just from Northern Ireland but from further afield, for world medicine will have to maximise use of expensive resources.

So to all medical students I would say, take heart, you will have a wonderful time in medicine. Do not be too concerned about health care reforms – they are predictable and happen about every 20 years; do not worry about curriculum reforms – the intelligent teach themselves; honour your teachers – they may have many deficiencies but they are probably doing their best; and above all – honour your patients – because they are your scientific partners.

Finally, I would direct your attention to something attributed to that great internationalist and Christian humanist, Erasmus, born to an unmarried mother and orphaned when both his parents died of the plague when he was 13. "Live as if you are to die tomorrow, study as if you were to live forever".

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A history of prehospital coronary care

J F Pantridge, C Wilson

Allan Burns in 1809 in his book "Observations on Diseases of the Heart" wrote "where however the cessation of vital action is very complete and continues long we ought to pass electric shocks through the chest: the practitioner ought never . . . to despair of success till he has unequivocal signs of real death".

One hundred and fifty seven years were to elapse before Burns' instructions were initiated successfully outside hospital. Several events led to the report of the first pre-hospital resuscitation by Pantridge and Geddes in 1967.[1] Beck in 1947 successfully defibrillated a human heart[2] and in 1956 reported the successful open chest correction of ventricular fibrillation complicating a coronary attack.[3] Zoll showed that transthoracic defibrillation was possible in the clinical situation.[4] Kouwenhoven in 1960 demonstrated that blood flow to vital organs might be maintained simply by compressing the lower end of the sternum;[5] thus he initiated cardiopulmonary resuscitation (CPR).

The possibility of CPR and defibrillation led to the introduction of hospital coronary care units in 1963 by Day in Kansas City[6] and Brown in Toronto.[7] However in the same year Bainton and Peterson in Seattle found that among deaths from coronary heart disease in people 50 years and younger 63% of the deaths occurred within one hour of the onset of symptoms.[8] Since the average delay to hospital admission in Belfast was of the order of eight hours[9] the majority of deaths occurred outside hospital. Hospital coronary care units were therefore of limited value. Indeed if (as claimed) they reduced the hospital mortality from 30% to 20% the impact on the community mortality from the heart attack could not be greater than 4.5%.[10] In the mid 60s experience of hospital coronary care units supported the proposition that the majority of deaths occurred from ventricular fibrillation, and that ventricular fibrillation could be corrected. Since these deaths usually occurred outside hospital there was a wide gap between what was being done and what might be possible. One of us (JFP) has commented that the predicament of the coronary victims was somewhat similar to that of battle casualties in the eighteenth century. In 1792 Larrey, a young French army surgeon, noted the plight of the wounded. French army regulations at that time dictated that the medical personnel should remain one league (2.42 miles) behind the battle area. The wounded reached the surgical depots usually after a delay of some 24 hours and were frequently moribund or dead. Larrey devised a light vehicle that transported the surgeons and their equipment to the front line and thus revolutionised military surgery. One hundred and seventy-four years later a mobile unit to deal with coronary casualties was initiated in Belfast.

Towards the end of 1965 it was decided that an attack should be made on the problem of pre-hospital coronary deaths. The available defibrillators manufactured for hospital use were mains powered. However, with the able assistance of a technician, Alfred Mawhinney, a so-called portable defibrillator was constructed from a mains operated machine charged by two 12-volt car batteries through a static invertor. A discarded ambulance was recommissioned. A grant of £2000 from the British Heart Foundation paid the salary of the senior house officer Dr John Geddes, and that of an ambulance driver. The system was activated by the attending general practitioner telephoning a direct line to the nursing station of the coronary care unit where an adjacent red telephone was linked to the ambulance depot so that the cardiac ambulance could be summoned immediately. In addition to the senior house officer and driver the ambulance was staffed by a

Queen's University Belfast.

J F Pantridge, CBE, MC, DSc(Hon), D Univ(Open)(Hon), MD, FRCP, FRCPI(Hon), Honorary Professor.

Antrim Area Hospital.

C Wilson, FRCP, FACC, Consultant Cardiologist.

coronary care trained nurse. The senior house officer and nurse did not in fact have official authority to operate outside hospital. However the Belfast Coronary Care Scheme, or Cardiac Ambulance service began on January 1st 1966.[11]

When the grant was exhausted, funding from the Northern Ireland Hospitals Authority was requested. One of us (JFP) was summoned to a meeting of the Hospitals Authority's members. Their attitude towards the scheme was entirely negative until it was pointed out that they might be held responsible for the deaths of coronary victims who perished because the unit was not available. This somewhat far fetched argument convinced the members. The unit was reprieved.

The world's first pre-hospital coronary care unit still operates virtually unchanged thirty years after its initiation. In the report of the operation of the scheme over its first 15 months[1] it was stated that "it has been shown, perhaps for the first time, that the correction of cardiac arrest outside hospital is a practical proposition". However this was not so. In 1775 Abildgaad, a Danish veterinary surgeon, had "shocked a single chicken into lifelessness and upon repeating the shock the bird took off and eluded further experimentation".[12] The report in 1967 of the initial results of the operation of the Belfast unit generated much interest in the USA. On September 1st 1967 Time Magazine ran a feature article stating that "most heart attacks occurred at home. It usually takes hours to get the patient to the equipment, though the first few minutes and hours after a heart attack are the most critical. Top US government officials believe that in the case of at least one patient with a heart attack history, namely Lyndon Johnson, the equipment should be installed in his home – the White House. Since that is not practicable for every man the alternative is to rush the equipment to the patient."[13] The article went on to describe the pre-hospital scheme in "Northern Ireland's dour capital city of Belfast". The Belfast unit got further US media attention, including a front page article in the New York Times, when shortly before the end of his presidency Lyndon Johnson had a second coronary attack while on a visit to his daughter in Virginia. He was managed by a unit based on the Belfast plan.

One of the important dividends from the operation of a mobile unit was the study of the very early phase of acute myocardial infarction. Observation of patients within an estimated 30 minutes of symptoms showed a high incidence of abnormalities of heart rate and blood pressure resulting from autonomic disturbance with over-action of the sympathetic or parasympathetic components, or both.[14] It was also shown that early correction of the autonomic disturbance was associated with a marked reduction in the mortality from cardiogenic shock and pump failure.[15] Since cardiogenic shock is invariably associated with massive myocardial damage it was possible to predict that the early initiation of coronary care with correction of vagal over-activity by atropine and of sympathetic over-activity by beta-blockers would result in limitation of the size of the myocardial infarction.[10] The supposition that following coronary occlusion the magnitude of the resulting area of infarction might be limited has led to extensive research.

The principle of pre-hospital coronary care was rapidly accepted in the USA, Australia,[16, 17] and many other parts of the world, but R J Kernohan in Ballymena's Waveney Hospital was the first to follow the lead of Pantridge and Geddes, establishing a similar mobile unit in 1966 with equally impressive results.[18] Over the next few years most other major hospitals in Northern Ireland followed suit. A novel pre-hospital coronary care system at the Ulster Hospital, Dundonald, used a small van to transport the cardiac team and equipment to the patient.[19] The first programme in the USA patterned on the Belfast plan was started in New York in 1968 by William Grace, Professor of Medicine at St. Vincent's Hospital.[20, 21, 22] Grace had spent 10 days in Belfast observing the Belfast unit. Grace's unit was staffed by medical personnel but many others including Miami,[23] Seattle,[24,25] Portland (Oregon);[26] Los Angeles,[27] Columbus (Ohio)[28] and Nassau County (New York),[29] used paramedical personnel. Nagel in Miami used radio telemetry which enabled the paramedical personnel to transmit the cardiac rhythm of the collapsed patient to the hospital and receive instructions from the physician in the coronary care unit.[23] It was hoped that with medical supervision paramedical intervention might be regarded as legal. The Lancet article recording the initial results of the Belfast scheme was a catalyst for the Seattle pre-hospital coronary care programme initiated by Cobb. In 1968 Cobb received a grant of $450,000 from the Washington Regional Medical Programme. A two tier system was initiated in Seattle in 1970. One of the many

first aid units from the Seattle Fire Department would be first to reach the collapsed heart attack victim. Cardiopulmonary Resuscitation (CPR) was started. The hospital based mobile coronary care unit was despatched simultaneously with the first aid unit and when it arrived provided definitive treatment such as defibrillation. Since the sooner resuscitation is started the more likely the chance of survival, a programme of citizen training in CPR was initiated in 1972.[25] Eventually over 600,000 people in Seattle had training in CPR. The Seattle programme made US national news on the CBS "Sixty Minutes" TV show. Many Americans considered the pre-hospital coronary care schemes a remarkable advance in patient care. Before their initiation 50% of the country's ambulance services were provided by 12,000 funeral undertakers. The morticians possessed the vehicles which could carry a patient on a stretcher. The initial pre-hospital coronary care schemes in the United States were funded from the Federal Regional Medical Programmes. Within a decade of the Belfast initiative every major city in the USA had a pre-hospital coronary care scheme. The impact of these schemes varied. An individual who collapsed in Seattle from a coronary attack complicated by ventricular fibrillation had a 30% chance of survival, while those collapsing in New York or Chicago had much less chance. One of us (JFP) emphasised that the widespread implementation of effective pre-hospital coronary care depended on the availability of small light and cheap portable (and ideally pocket) defibrillators. However a major obstacle to this availability appeared in the mid seventies. L. A. Geddes and his colleagues at Purdue University purported to show from data acquired from animal experiments that the patient's weight was an important determinant of the energy required for ventricular defibrillation.[30] They indicated that the maximum energy available from most defibrillators, 400 watt secs., would be inadequate for many patients. The production of massive machines storing 1000 watt. sec. was contemplated. This was particularly disturbing since a step towards a pocket defibrillator, a small instrument weighing 7lb., the "Pantridge Portable", had just appeared.[31]

A study was immediately initiated to investigate the Purdue proposition. This showed that low energy shocks, 165 watt. sec. were successful in removing 95% of episodes of primary ventricular fibrillation.[32] The battle over the energy requirements for defibrillation and therefore the battle for the portable defibrillator was won. The Belfast findings in relation to energy levels required for defibrillation were later confirmed.[33, 34, 35]

The Seattle programme of a tiered response was undoubtedly effective. During the first year of its operation 61 patients were defibrillated of whom 31 survived to leave hospital. However the programme depended on initial CPR by either citizens or first aid teams. Those involved in emergency medicine know that there is an inverse relationship between the duration of ventricular fibrillation and long term survival.

One of us (JFP) therefore suggested that if small cheap defibrillators had a fail-safe mechanism like the safety catch on a pistol the layman might defibrillate. It was reasonable to assume that anyone capable of doing CPR could use a fail-safe defibrillator. The possibility of the development of such an instrument certainly existed since Mirowski had described an automatic defibrillator.[36] The implantable defibrillator depended on picking up the cardiac rhythm from the tip of a catheter in the right ventricle. When ventricular fibrillation appeared the apparatus automatically delivered a defibrillating shock. One of us (JFP) discussed with Mirowski the possibility of using his circuit to pick up the rhythm from the chest surface so that a defibrillator might be produced which would deliver a shock only when VF was present. Mirowski was adamant that it was impossible. Artefact he thought would be the problem. JFP was unconvinced about the impossibility of a fail-safe defibrillator and after a prolonged discussion with Cobb (Seattle) he suggested a Foundation for immediate resuscitation (FIR). Cobb agreed to contact the defibrillator manufacturers. Thus the automatic external defibrillator was born.

Although after 1967 there was a rapid spread of pre-hospital coronary care units throughout the world the idea was not supported by the DHSS in Britain. This apathy may have precipitated the decision of the Royal College of Physicians, London, and the British Cardiac Society to set up a Joint Working Party on the care of the coronary patient. The Chairman was Lawson McDonald, Senior Cardiologist at the National Heart Hospital. The members included the President of the Royal College, Sir Cyril Clarke, the Registrar of the

College, Sir Kenneth Robson, and four physicians with special experience of coronary care. The Working Party reported in 1975 and recommended that the DHSS should actively encourage the development of mobile coronary care.[37] The DHSS on the advice of its standing medical advisory committee (SMAC) refused to accept the recommendations of the Working Party. However in 1982 SMAC reversed its view.

Despite the obvious logic of mobile coronary care and the reported success of such schemes it had not been shown that the community mortality from myocardial infarction could be reduced. This definitive evidence was provided by a study of two similar communities in Northern Ireland (Omagh and Ballymena) only one of which had a mobile coronary care unit.[38] This study showed that the availability of mobile coronary care in Ballymena was associated with a 21% reduction in overall community mortality and 38% reduction among patients aged less than 65. Thus the addition of mobile coronary care to conventional hospital coronary care facilities might save 30,000 lives (20,000 aged less than 65) per year in the United Kingdom. An additional important finding was that only 5% of lives saved could be attributed to resuscitations from cardiac arrest. Most of the benefit was probably due to the prevention of arrhythmic death, and limitation of infarct size by earlier therapeutic intervention. This conclusion was similar to that of a community study by Crampton.[39] It was not surprising that on completion of the Omagh/Ballymena study a mobile coronary care unit was immediately established in Omagh. All areas of Northern Ireland are now served by medically-manned mobile units.

The extension of pre-hospital coronary care to include general practitioners carrying defibrillators[40] and cardiac trained emergency ambulance staff equipped with monitor/defibrillators[41] was reported from Ballymena. The best results may be achieved by utilising the skills of all three disciplines, the general practitioner, paramedic and mobile coronary care unit, in an integrated system providing rapid resuscitation and medical treatment, including thrombolytic therapy when indicated.

On 31st July 1990 Kenneth Clarke, then Secretary of State for Health, announced that 3.8 million pounds sterling was to be made available to equip 2,350 front line ambulances with defibrillators. Clarke's action was more than 24 years after the first ambulance was equipped with a defibrillator in Belfast. Thus approaching half a million unnecessary premature deaths in the United Kingdom may have resulted from the 24 year's delay. The negative attitude of the DHSS arose in part from the Nottingham study.[42] That study purported to show that mobile units were unnecessary. Indeed it reported that it is doubtful whether there would be any significant benefit from training ambulance crews. The Nottingham Study was financed by the DHSS and was presumably contract research. The results indicate the great dangers of such types of research. Nevertheless the equipping of ambulances was an important step towards acceptance of the need for pre-hospital coronary care and undoubtedly has led to an increase in successful resuscitations in the community. However, it does not address the fact that only a small percentage of the lives saved by pre-hospital coronary care can be attributed to resuscitation from cardiac arrest. Only by providing much more complete medical care can the full benefit be realised. The advent of thrombolytic therapy in acute myocardial infarction has further focused attention on the desirability of earlier medical treatment before transfer to hospital.[43,44,45] This provision can best be achieved by a medically-manned mobile unit. As a result of the Belfast initiative 30 years ago Northern Ireland is the best prepared country in the world to take full advantage of this and any future therapeutic innovation in early treatment of myocardial infarction.

The American Heart Association has appointed a special task force focused on automatic external defibrillation, and potential for public access to inexpensive fail-safe devices. Conservative estimates by the American Heart Association suggest that as many as 100,000 American lives might be saved each year if there were greater public access to automatic external defibrillators (AEDs).

Soon such instruments may be as ubiquitous as fire extinguishers. The American president's plane is no longer the only aircraft to carry a defibrillator; successful defibrillation on a commercial flight has now been reported to us. (O'Rourke, personal communication).

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36 Years of Renal Services at the Belfast City Hospital: Looking back

Mary G McGeown

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The renal services for Northern Ireland came to be centred in the Belfast City Hospital for a number of reasons. Let me tell you how this came about.

The artificial kidney was first used successfully by Dr Wilhem Kolff in the Netherlands, during the Second World War. At the end of the War he published his results,[1] and gave three of his machines to centres abroad. One was given to Hammersmith Hospital in London, leading to great interest in kidney diseases there. Dr Graham Bull (later Sir Graham) one of the group of young men working there, with his colleagues developed a very useful method of treatment of kidney failure, based on control of fluid intake, a special diet providing calories for nutrition with minimum production of waste products, and isolation of the patient to prevent infection. This "conservative treatment", that is without the use of the artificial kidney, is adequate for patients with less serious temporary renal failure. In 1952 Graham Bull came to Belfast as our first full-time Professor of Medicine. He introduced here the use of the by then famous Bull-Borst diet for treatment of patients with kidney failure.

In 1958 a boy about 11 years old was badly injured in a road traffic accident, developed kidney failure, and was treated by the Bull-Borst method in the Royal Belfast Hospital for Sick Children. He was transferred to Hammersmith Hospital when "conservative treatment" seemed to be insufficient. Ironically his own kidneys began to recover as soon as he arrived there and he did not need artificial kidney treatment after all.

This case attracted much public attention and the question was raised in Stormont as to whether Northern Ireland needed to have its own artificial kidney. The late Mr John Megaw, a pioneer urological surgeon, saw this as an opportunity to enhance the standing of the Belfast City Hospital. He approached Professor Bull with the suggestion that an artificial kidney service should be set up at the Belfast City Hospital. Professor Bull agreed. In due course I was appointed to set up the service.

Early in 1959 I went with Mr Megaw and Mr Fred Storey, then head of the firm which supplied equipment for the hospitals of the Province, to visit Leeds General Infirmary and the RAF Renal Unit at Halton, to decide on the equipment needed. The trip included a memorable evening when the two gentlemen took me to see a light-hearted musical called "Irma La Douce".

Part of Ward 9 in the main block of the Belfast City Hospital was to be converted to provide a suite of three rooms for the new renal unit, and two cystoscopy theatres for Mr Megaw. Eventually the twin coil type artificial kidney we had chosen arrived. In the meantime it was kept in a small storeroom in Ward 15, where I unpacked it, and read the available literature. Early in June, 1959, I set it up as a demonstration for a general practice refresher course being given by Mr Megaw. Remember that I had never seen an artificial kidney in use. I had been appointed because of experience of the conservative treatment of acute renal failure, higher qualifications in medicine and biochemistry, and research experience related to kidney diseases in Professor Bull's laboratory. I was appointed at the low grade of Junior Hospital Medical Officer, as money was short, "to see how it would go." However this offered a permanent post and I wanted to return to clinical medicine. Two years

Belfast City Hospital Association: 15 June, 1995, Hillsborough Castle.

Department of Medicine, University Floor, Tower, Belfast City Hospital, Belfast BT9 7AB.

Present appointment: Professorial Fellow, The Queen's University of Belfast.

later the post was re-advertised at the grade of Senior Hospital Medical Officer, and finally in 1962 as a Consultant post.

To return to 1958, a young Israeli, Dr Eliahou, working in Professor Bull's laboratory, was due to return home. He was very keen to see the artificial kidney in use, so we had persuaded Mr Richard Welbourn (later Professor Welbourn) of the Department of Surgery to make a dog uraemic by tying the ureters. A few days later the artificial kidney was taken to the Department of Surgery laboratory and we set up dialysis on the dog, of course under anaesthesia. Repeated blood tests demonstrated that the treatment successfully reduced the blood urea. A few days later Dr Eliahou returned to Israel, later to become head of Israel's first Renal Unit in Tel Aviv. I made arrangements to go to Halton to see the RAF treat a few patients with dialysis. However before I could depart an eighty year old man was admitted under Mr Megaw suffering from very severe kidney failure and near to death. I was reluctant to treat him by dialysis, never having seen it used on a patient, but Mr Megaw insisted that I could not let the patient die without trying to save him. We took the equipment to his operating theatre in Ava 2 and there, on 22 June, 1959, carried out the first artificial kidney treatment in Northern Ireland. Mr Megaw inserted tapered plastic cannulae in the artery and vein at the patient's wrist. Eileen Martin, the research technician who worked with me in Professor Bull's lab, weighed out appropriate quantities of the simple chemicals needed to make up repeated batches of dialysis fluid. Over the six hours of treatment the biochemistry laboratory carried out frequent blood urea and dialysis fluid tests, long after normal hours, my son John Freeland acting as courier. I inadvertently allowed one batch of fluid siphon out of the 100 litre tank, and had to send an SOS to Eileen to weigh out another set of chemicals before she went home. Apart from this all went smoothly, the blood urea fell very satisfactorily, and the patient seemed to improve and began to regain consciousness. However he did not recover and he died a few days later from a cerebral haemorrhage.

My next attempt to go to Halton was thwarted by the appearance of another patient. A woman in her early thirties with kidney failure following a post-partum haemorrhage was admitted under Professor Bull in the Royal Victoria Hospital. The artificial kidney was transported to the class-room between wards 2 & 3, electric plugs were changed and make-shift plumbing devised. The patient received repeated dialysis treatments over 35 days of almost complete absence of urine production and went on to full recovery of kidney function. She returned to her job as a school-teacher and had a normal pregnancy two years later. I had the pleasure of seeing her almost 20 years later when she was again admitted to Ward 3, this time with thyroid trouble. She had indeed made a complete and lasting recovery from acute severe renal failure.

I never paid that visit to Halton to see how the twin coil kidney ought to be used. A succession of patients with acute kidney failure continued to arrive. These were treated in the ward theatre most convenient to the patient, in the Belfast City Hospital, the Royal Victoria Hospital, or the Royal Belfast Hospital for Sick Children. Many of the patients survived, but some died. I recruited a technician from the biochemistry laboratory, Maurice Bingham, who weighed out the chemicals, prepared and tested the dialysis fluid, and looked after the equipment. Each treatment required about two hours of work to set up, over six hours for the treatment and changes of dialysis fluid, and nearly another two hours to clear up and ensure that all was well with the patient, a long and stressful day.

Things became simpler when my own unit was ready in the spring of 1960, although Maurice Bingham had emigrated to Canada for a greatly increased salary and I had to look for another technician. This time I recruited Jack Lyness, still in post now as chief of a team of 11 technicians.

The service for treatment of acute renal failure at the Belfast City Hospital led to referral of patients with other forms of kidney disease including some with advanced chronic renal failure. At each dialysis an artery and a vein were used up, so that only a few treatments were possible. The plight of these chronic patients was a constant stimulus to work out ways to extend treatment. We found that repeated infusion of heparin often allowed the cannulae to be used several times, giving a short extension of the time during which kidney function could be replaced. This of course was not helpful for patients with irreversible chronic kidney failure. In 1961 Dr Beilding Scribner, a research fellow in Hammersmith, found that cannulae made of teflon inhibited

blood clotting.[2] He described his experience with the long term use of teflon cannulae at an international meeting in 1963, which led to vigorous controversy about the ethics of keeping patients alive by dependence on a machine.[3]

By this time the first dedicated nurses had been appointed, the late Kay Maguire in 1963, later joined by Maureen McKinney who has just retired. Between them they were responsible over the years for the huge development of the role of nurses in renal services. At the 1995 Congress of the European Dialysis Nurses' Association held in Athens on 11-14 June, 1995, it was decided to institute a medal to be awarded annually in memory of Kay Maguire, a fitting tribute to her work.

With the help of Mr Will Hanna, then senior registrar with Mr Megaw, we used Scribner's arteno-veuous shunt for the first time in early January, 1964. Over the next few years young surgeons training with Mr Megaw had the task of surgically inserting the cannulae for each patient, after I had spent hours tailoring them to fit the contours of the individual's wrist. Mr Joseph Kennedy, Mr William Graham, and Mr James Blundell amongst others helped in this way. But bear in mind that we had only the one artificial kidney intended for use on patients with acute reversible kidney failure, who of course took priority. However, from early January, 1965, we provided regular treatment *during the night* twice weekly for one, then two patients. A loan of two flat plate artificial kidneys, cheaper in use and which did not require several units of blood for priming, was arranged. The patients were treated during the night in one of Mr Megaw's urology theatres. The dirty "kidneys" with their membranes were carried through Ward 9 to be scrubbed in the female patients' bath. We did not know of the risk of hepatitis B!

Jack Lyness played an important part in the expanding service. Each patient needed 400 litres of dialysis fluid per treatment, but at first we had only the 100 litre tank belonging to the twin coil kidney. Jack spent two nights each week on a couch in the surgeons' changing room, being awakened by the nurse each time a new batch of fluid had to be prepared and tested. Next day he worked the usual hours. After about six months we obtained a huge plastic fish tank in which Jack prepared big batches of dialysis fluid. He used an oar for stirring the fluid and had to get into the tank to scrub it. There were numerous other problems. Patients developed episodes of fever, on one occasion eventually traced to the water storage tank which had become contaminated with pigeon droppings. The dialysis tank overflowed from time to time, fluid pouring down into the accident and emergency department below.

I was continuously on-call. We were young together, and though hard it was a wonderfully inspiring project! Team and patients trusted each other completely.

In the early 1960s kidney transplantation began to seem possible. In 1954 the first successful human organ transplant was carried out in Boston between identical twins.[4] Attempts to transplant kidneys between siblings, parent to child, even between non-identical twins, all failed rapidly from rejection. It was found that rejection could be prevented by prior whole-body irradiation, but the patients invariably died from overwhelming infection. Attempts to use drugs to prevent rejection had failed until 1961 when Mr Roy Calne, (now Sir Roy) working in Boston, used azathioprine for renal transplantation, first in dogs, then in 1962 in a human patient.[5] At last rejection could be prevented without killing the patient. Moreover, the kidney had been taken from a cadaver.

From 1962 onwards my whole endeavour was directed towards providing kidney transplantation, backed up with an efficient maintenance dialysis service, for patients whose own kidneys had irreversibly failed.

Kidney transplantation had been attempted from 1960 onwards at Hammersmith Hospital and Edinburgh Royal Infirmary, when the rare situation had occurred of kidney failure in one of a pair of identical twins. They began to use azathioprine, later combined with huge doses of cortisone, for prevention of rejection of grafts taken from closely related donors. These centres agreed to take my patients when I could find a close relative willing to give a kidney. Three such early attempts all failed.

However the patient being maintained by regular night-time dialysis from January, 1965, was transferred to St Mary's Hospital, London, in April of that year. A few days later she was given a cadaver transplant which functioned well for over seven years. A second of our patients was

given a transplant there in August 1965. His graft continues to function perfectly over 30 years later, now being recognised as the longest surviving cadaver kidney transplant in the world. These patients, and those which followed during the period when I functioned as a sort of transplant broker, gave me opportunity to develop necessary skills in the use of immunosuppressive drugs. Meantime I campaigned vigorously for kidney transplantation to be set up here, and for expansion of the dialysis service.

In the summer of 1968 we commenced work in a new custom-built Renal Unit situated at the back of the Ava Hospital. The team was enlarged by two surgeons, Mr Stewart Clark (who emigrated in 1975), Mr Joseph Kennedy, a second nephrologist Dr Joseph McEvoy (who also emigrated in 1975), anaesthetists Dr John Alexander (just retired) and the late Dr John Cecil Hewitt, and Dr Sam Nelson who set up the Tissue Typing Service (now in charge of the Craigavon Area Laboratory). Over the years many others joined the greatly increased staff which now includes six nephrologists, a rota of five surgeons, and the internationally renowned Tissue Typing Service led by Dr Derek Middleton. The service also makes big demands on all the other departments of the Hospital. Space prevents mention of all those who have made this possible, but the seminal role of the late John Megaw, followed by Joseph Kennedy, Gordon Loughridge, Sam Nelson and later Richard Donaldson must be gratefully acknowledged.

On 22 November, 1968, we carried out our own first kidney transplant. We planned to use cadaver grafts almost exclusively, although at that time most units were using living related donors. The first transplant was a cadaver graft which functioned well for a time, but after about three months severe rejection occurred leading to loss of the graft, and the patient resumed haemodialysis. The second graft was a very long-term success, and continued to function well until the patient died from coronary heart disease 24 years later. This was the beginning of a very successful renal transplant service,[6-8] which made its own unique contribution to immuno-suppression for transplanation.[9, 10]

Renal 1 as the new premises came to be called, provided for six patients to receive regular haemodialysis treatment. By the time it was ready for use, providing two haemodialysis stations, it had become clear that it was not big enough. At maximum we could treat six patients with chronic renal failure. Patients with acute renal failure and post-transplant patients were nursed in six individual rooms. The unit also contained a small operating theatre. Other renal units across the British Isles already had or were planning units containing ten dialysis stations. The need for more space for haemodialysis was already acknowledged and planning for a 10-bed extension, Renal 2, began almost as soon as Renal 1 was opened. This included two very large rooms for preparation and sterilisation of the flat plate dialysers then being used, and an area for servicing and maintenance of the automatic electronic proportioning systems used to dilute, check and heat the concentrated dialysis fluid (which had superseded the use of solid chemicals). More office space, kitchen, sluice, linen room, CSSD store were added to complete the L-shaped building in 1972.

At the beginning of 1969 a disastrous epidemic of hepatitis B occurred in several haemodialysis units in Great Britain. Haemodialysis patients suffer from severe anaemia, due both to depression of bone marrow by the chronic renal failure and regular small loss of blood occurring from haemodialysis treatment and blood sampling. Unlike other patients who receive transfusion they regularly return to the hospital in circumstances when others may come in contact with their blood. We too encountered hepatitis B, ironically within three months of the opening of the new and much larger dialysis facility of Renal 2. The unit was spacious with the recommended wide spaces between dialysis stations. The routine cross-infection precautions to prevent patient's blood contaminating staff or other patients were rigorously observed.[11] Mishaps such as needle sticks or significant spillage of blood had not occurred after the new premises were put into use. At this time testing of blood for transfusion for hepatitis B was not in general use, but had been introduced by Dr John Connolly of the Northern Ireland Virology Service for all blood to be given to our patients and all transfusions were traceable to source.[12] The new unit was gradually filling up with new regular dialysis patients, as we trained more nursing and technical staff to look after them.

A male patient developed hepatitis B jaundice six weeks after his admission to the Renal Unit. He had not received transfusion following admission,

but we later discovered that he had received a transfusion (untested for hepatitis B antigen) in the hospital from whence he was transferred, although this fact did not come to light until after he had developed jaundice. Dialysis in isolation was attempted in a cubicle off the main ward, but this was deemed insufficient by Dr Sheila Polakoff, who had collected data from all UK units where infection had developed. She advised that treatment of the infected patient should be carried out in entirely separate facilities from the main haemodialysis ward. This was provided with two beds in a mobile home adjacent to the unit, nurses volunteering to look after these patients. Additional precautions to avoid any possibility of contamination with blood were introduced, which were both time consuming and expensive. In spite of all the care, five other patients developed hepatitis B jaundice and the unit had to be closed to admission of new patients for six months, the incubation period after the diagnosis of the last case for hepatitis B. Only one of the six jaundiced patients survived to have a successful transplant. Worse, patients who would otherwise have been accepted for haemodialysis therapy died during the waiting period. Sister Maguire pricked herself with a needle which had been used on the first infected patient, causing all of us great anxiety, as medical and nursing staff had died in other renal units. Mercifully she developed only a minor illness, but hepatitis B antibody was detected in her blood, showing that she had been infected.

As early as 1963 I had experimented with the use of peritoneal dialysis for the treatment of acute renal failure but in general at that time it was inferior to haemodialysis. However it was in occasional use and necessity led to its introduction for regular treatment, 24 hours twice each week, for two or three patients with chronic renal failure, from 1967. This became possible because the Royal Victoria Hospital agreed to the use of a side-ward of Wards 3 and 4. This was suitably converted and two of their nurses were trained to carry out the treatment. This service enabled a small number of patients to be kept alive until a cadaver graft was found. One of these patients remains alive with a functioning graft more than 26 years later. Peritoneal dialysis for long-term replacement of kidney function became of major importance after Nolph developed continuous ambulatory peritoneal dialysis (CAPD) in 1978. When the technique was improved and simplified by Oreopoulos (who had received his training in nephrology in Belfast) it became increasingly widely used. CAPD has proved particularly suitable for the treatment of children and adolescents where the relative freedom of self treatment away from the hospital is a great advantage. It also facilitated treatment of the increasing numbers of older age patients and now makes a major contribution to renal replacement therapy.

Once the hepatitis mini-epidemic was declared over, the numbers of patients rapidly increased to comprise two cohorts of 10, each patient receiving two 14-hour treatments each week. Once these cohorts were full we were limited to treating those 20 patients, and new patients could be accepted only when a space occurred due to removal of an existing patient by renal transplant or death. Yet Renal 2 was closed on Wednesdays and at weekends. Lack of finance, leading to shortage of trained nursing staff, and shortfall of all facilities persisted in spite of innumerable requests for help. Over the years there were painfully slow increases in the provision of haemodialysis facilities, while the outpatients became thronged with increasingly sick patients hoping desperately that their turn would come in time. The load on the medical staff increased to breaking point time and again; only then was more money allocated for the unit and more staff provided. Figure 1 depicts the periodic increases in numbers of patients receiving regular dialysis therapy over the years 1968 to 1994, as new finance arrived. Ten dialysis stations were provided when Renal 2 opened in 1972. Two more stations were obtained in 1978 by replacing two beds with four reclining chairs. Wednesday/ Saturday shifts were opened in 1979, allowing treatment for 36 patients. Meantime more efficient dialysers were developed and shorter periods of dialysis became adequate, and between 1982 and 1984 it became possible to fit in an additional three or four patients in late afternoon/evening. Patients who had still a little kidney function remaining, or were small and light, could be treated for shorter time, again allowing a few extra sessions to be added. Progress in this direction eventually allowed for multiple shifts over the 24 hours to be instituted.

Dr Maurice Savage was appointed as Paediatric Nephrologist in 1982, facilitating acceptance of children below age 10 (older children had been treated by dialysis and transplantation from the

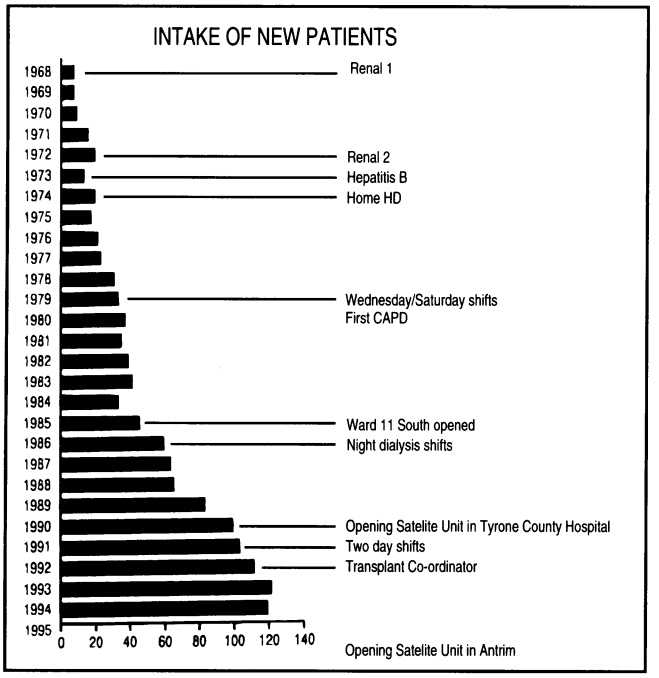

Fig 1. New patients accepted for dialysis by year.

mid-1970s). Figure 1 also shows that the number of new patients remained almost stationary in those years where new finance was not forthcoming, when the number of patients accepted was equal to the numbers diminishing either by death or by transplantation. The very success of the dialysis programme in the earlier years contributed to the problem, as most patients survived to require treatment in succeeding years.

Where did the increasing number of patients come from?[13] In the early 1970s patients were accepted for regular dialysis only up to the age of 50, later in the decade to 55 years. As the 1980s progressed occasional older patients in otherwise good general condition were accepted for dialysis and a few even received successful transplants. Patients whose renal failure was due to diabetes mellitus or other systemic disease were not accepted (here or elsewhere in the UK) until the late 1970s. At the present time about 11 % of our new patients suffer from diabetic renal failure.

The number of transplants also increased over the years, (Figure 2) providing spaces for new patients, but always severely limited by the number of suitable cadaver kidneys available. From the earliest days the Belfast Unit has been an integral part of the UK Transplant Service (UKTS) [I served on one or other management committees from when it was set up in 1972, being Chairman from 1983, until it became a Special Health Authority (UKTSSA) in 1990]. Successful transplantation requires good tissue matching, which is facilitated by exchange grafts through UKTS, as the search for an acceptable match can be extended throughout Europe. Yearly national statistics have shown that Northern Ireland is regularly amongst the top providers of cadaver organs, thanks to generosity of our public and the help of intensive care units, especially that of the Royal Victoria Hospital.

An important aim of the Northern Ireland Kidney Research Fund is public education about the need for kidney donors. This, as well as the success of the Transplant Games Team, has helped to encourage donation by demonstrating that a successful transplant can return a dialysis patient to a normal life-style, even allowing younger female patients to have successful normal pregnancies. A few patients have received renal grafts from a close relative, but this "Gift of Life" from a relative is only occasionally possible. The appointment of Eleanor Donaghy as Transplant Co-ordinator in 1992 greatly facilitated the transplant service, and has increased public awareness of the need to permit organs to be used after death. By the end of 1994 a total of 829 renal transplants (723 first, 94 second, 10 third and two fourth grafts) have been carried out, and 435 patients have surviving grafts. There are 111 patients on peritoneal dialysis, mainly on CAPD, and 207 receiving haemodialysis, including those in the satellite unit in the Tyrone County Hospital (1990), now under the care of Dr Peter Garrett.

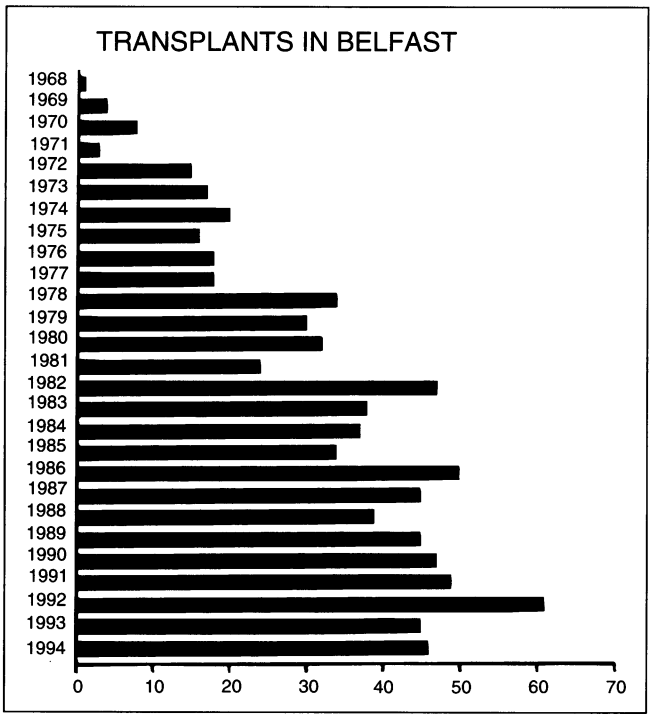

Fig 2. Renal transplants carried out in Belfast.

A second satellite unit has just been opened (1995) at the new Antrim Hospital headed by Dr Henry Brown.

The renal services might have developed differently. When Renal 1 was in the early planning stage it was suggested by the Chief Medical Officer of the Northern Ireland Hospitals Authority that the whole service would be better sited in the new A Block of the Royal Victoria Hospital, close to the Respiratory Intensive Care Unit. The very loyal support which the Belfast City Hospital Medical Staff had given to the nascent service made me unwilling to move, although the prospect of Dr Robert Gray's Respiratory Failure Unit as close neighbour was certainly attractive. From the beginning, the plans for the new City Hospital which evolved into the Tower included space for renal medicine. Later when it was clear that even with Renal 2 there was need for more space, a plan to put a second storey on the two Renal wards went almost to the stage of working drawings before I was persuaded that it would be preferable to settle for increased space on Floor 11 in the Tower Block. The Renal Unit remained single storey. The late Paddy Semple used much ingenuity to accommodate our new plan around the ducting system and lift shafts of the Tower. I had some regrets about this decision later, as the delays in building grew longer and longer, but it may have been the right one for the future of the service.

ACKNOWLEDGEMENTS

I gratefully acknowledge the contribution of innumerable people who have worked with me in one way or another over the years, some for many years, others for shorter periods but none the less making great contributions to the service. Some have been mentioned already and there are many who could join the list, including Sadat Metha and Khurshaed Anwar who carried out many kidney transplants and innumerable insertions of vascular and peritoneal cannulae in the theatre of Renal 1, and returned to India and Pakistan respectively. Many of the province's intensive care units have obtained organ donors, by far the biggest contributor being the Royal Victoria Hospital, in spite of the increase in workload this entails. I am grateful to Maureen McKinney for data on dialysis services, and to Peter McNamee and Colin Middleton for help with the statistical records.

I cannot close without paying tribute again to the Northern Ireland Kidney Research Fund, founded in 1971 by the late Mrs Josie Kerr MBE, her husband, Mr Walter Kerr, her family, and their many friends. And of course to my own constant support, my late husband Max Freeland.

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Case Report

MRI findings in a rare cause of bladder outlet obstruction

M A Hyland, J T Lawson, A O'Doherty, J Kennedy, D Biggart

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We report the magnetic resonance imaging (MRI) findings in an unusual case of bladder outlet obstruction.

CASE REPORT. A 30 year old woman presented with acute urinary retention. She had a 3 month history of increasing difficulty passing urine. There was no history of haematuria or dysuria. An intravenous urogram revealed a large mass causing elevation of the bladder base on the right side. There was no significant ureteric obstruction, though the right ureter was slightly full (fig. 1).

Ultrasound examination showed a hypoechoic slightly inhomogenous mass measuring 6 cm by 5 cm (fig. 2). It was unclear whether this arose from within or from below the bladder. The uterus was slightly bulky but not in continuity with the mass. Cystoscopy suggested extrinsic compression and no mucosal abnormality was seen. Fine needle aspiration revealed only a few degenerative cells and was insufficient for diagnosis.

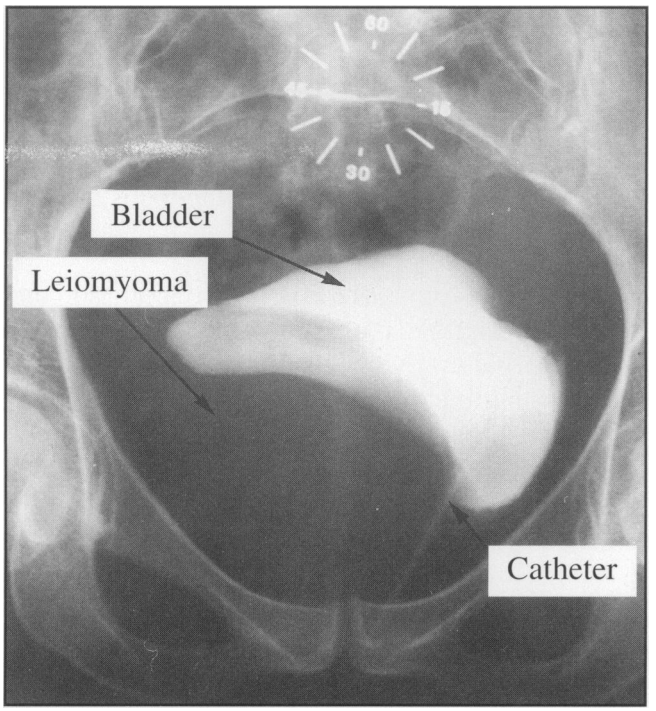

Fig 1. Intravenous Urogram – A mass can be seen arising from the right inferolateral margin of the bladder. A catheter is in situ.

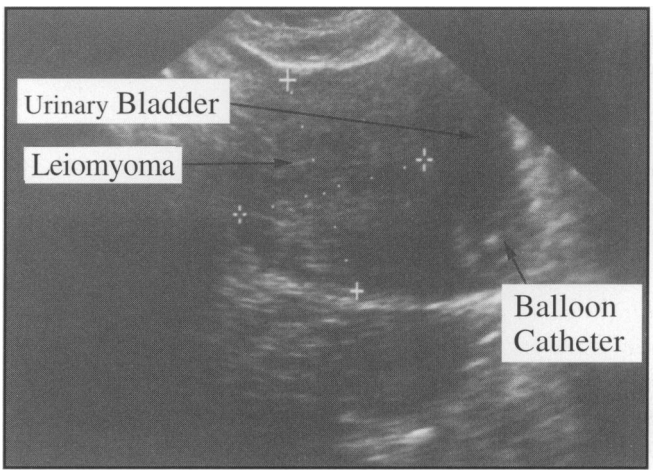

Fig 2. Ultrasound scan – Transverse scanning shows a mass of mixed echogenicity. It was unclear whether this was extrinsic or intrinsic. A catheter balloon can be seen lying on the left side of the bladder.

MRI of the abdomen was performed. Coronal T1 weighted (T1W) – (500/11/1) (repetition time/ echo time/excitations), axial multi-echo T2W – (2000/80-30), sagittal and coronal T2W Fast Spin Echo (FSE) – (4000/85/1) sequences were used. The lesion was clearly separate from the vagina, uterus and rectum. It arose from within the bladder

Belfast City Hospital, Department of Radiology.
M A Hyland, FRCR, Consultant Radiologist.
J T Lawson, MRCP, FRCR, Consultant Radiologist.
Belfast City Hospital, Department of Urology.
J Kennedy, FRCS, Consultant Urologist,
Belfast City Hospital, Department of Pathology,
D Biggart, FRC (Path.), Consultant Histopathologist.
Royal Victoria Hospital, Department of Radiology.
A. O'Doherty, MRCP, FRCR, Consultant Radiologist.
Correspondence to Dr Hyland.

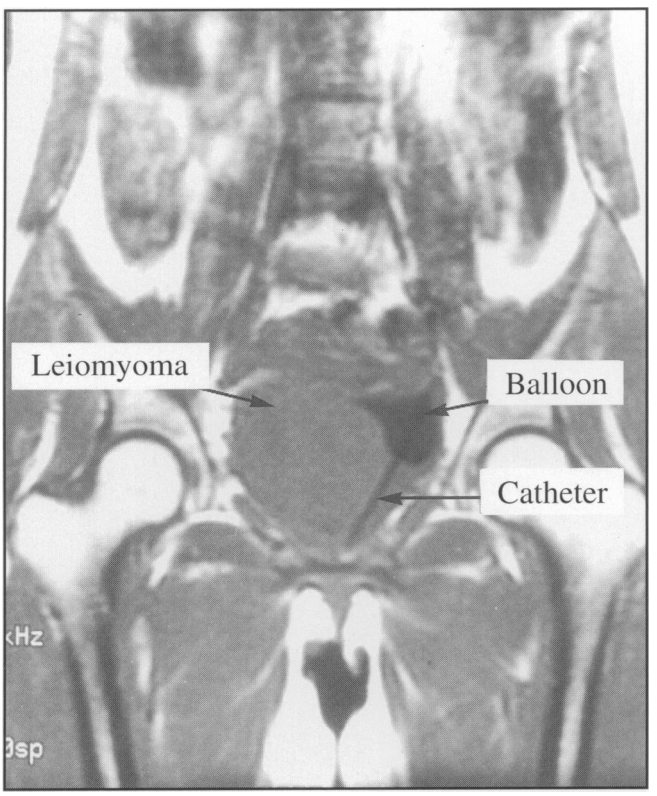

Fig 3. MRI Scan : Coronal (SE/TR500/TE11) – The mass shows a homogenous signal and appears to arise from within the bladder wall.

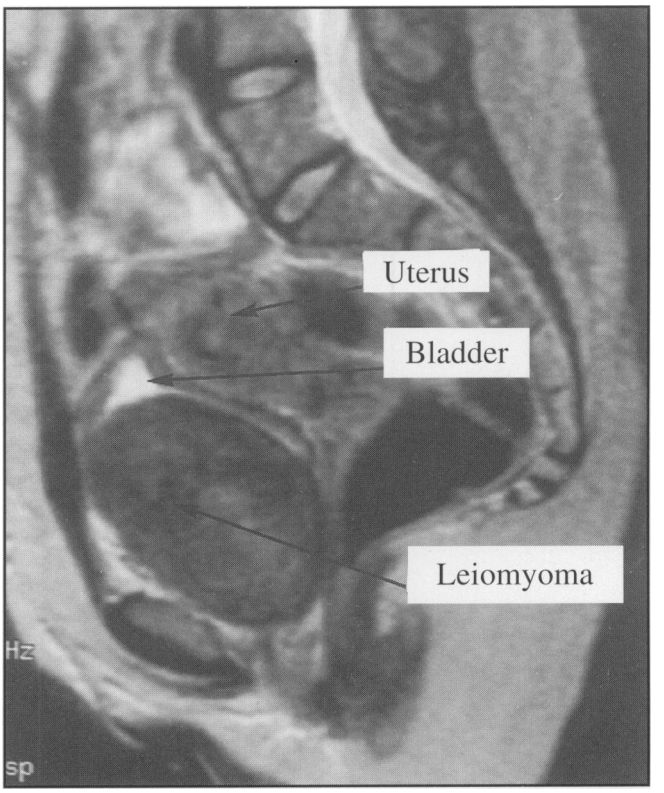

Fig 4. MRI Scan : Sagittal (FSE/TR4000/TE85) – The mass has an inhomogenous signal with a central region of diffuse high signal. The tumour has a well defined margin and is separate from the vagina and uterus. Small low signal foci can be seen.

wall. On T1W images the mass had a homogenous intermediate signal intensity similar to muscle. A well defined margin was noted. Around the edge of this region there were several small foci of low attenuation.

At operation a large well defined mass was removed from the bladder wall.

Pathological examination revealed a 175 gram encapsulated ovoid firm tumour mass with a greyish white whorled appearance after sectioning. Histological examination showed interweaving bundles of uniform smooth muscle fibres, separated in some areas by collagenous fibrous tissue. There was no evidence of mitotic activity and no nuclear pleomorphism or necrosis to suggest malignancy. The features were those of a benign leiomyomatous tumour.

DISCUSSION

There have been three previous reports of bladder leiomyoma demonstrated by MRI. Tomoe et al[1] describe the tumour as having an inhomogenous intensity on T1W (spin echo 400/20).In our case the tumour appeared quite homogenous on T1W. On T2W sequences Maya et al[3] noted patchy areas of high intensity. We found a more confluent central area of high intensity on similar sequences. Tomoe et al report small foci of low signal intensity on T2W. We could identify multiple small foci of low signal throughout the leiomyoma. These may correspond to the areas of collagenous fibrous tissue.

Uterine leiomyomas are much more common and normally described pathologically as degenerative or non-degenerative.[2] The former create a low intensity nodule with a smooth surface on T2W. The signal intensity is intermediate on T1W. Degenerative uterine leiomyomas histologically show hyalinization, oedema and calcification. This produces an inhomogenous pattern with areas of high and low signal on T2W.

Leiomyomas may arise in any tissue containing smooth muscle. 95% are found within the genital tract.[4] They have also been described in the skin, retroperitoneal region, gastrointestinal tract and urinary tract. In the latter they are most frequently seen in the bladder or renal capsule.

Only 1-5% of bladder tumours are benign. Of these 35% are leiomyomas. Approximately 170 cases of bladder leiomyoma have been described. These usually occur in women between the ages of 30 and 55; sixty per cent are endovesical. Intramural leiomyomas account for 30% and 10% are extravesical. Bladder leiomyomas are usually asymptomatic; endovesical lesions however may casue dysuria, urinary infections, irritative urinary symptoms, haematuria or obstruction.

Other causes of submucosal masses include hamartomas, nephrogenic adenomas and phaeochromocytomas. Only bladder phaeochromocytomas have been described on MR1. These show iso or hypo-intense signal on T1W and markedly increased signal on T2W. Bladder leiomyomas are benign and surgical removal is usually curative.

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Idiopathic spontaneous pneumoperitoneum – avoiding laparotomy – a case report

W D B Clements, B R Gunna, J A A Archbold, T G Parks

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The majority of patients presenting with spontaneous pneumoperitoneum (SP) undergo emergency surgery. It is virtually a conditioned reflex for surgeons, when presented with radiological evidence of free subdiaphragmatic air to proceed to a laparotomy. Laparotomy and general anaesthesia are associated with significant morbidity, therefore it is important to recognise SP and treat it appropriately. It is equally important to be aware of the spectrum of diseases which can present with SP.

We report a case of self-limiting massive idiopathic pneumoperitoneum and discuss the pathophysiology and appropriate techniques for its management.

CASE REPORT. A previously healthy 68 year old woman presented with a five day history of gradually increasing abdominal distension, right shoulder tip and epigastric pain. There were no associated gastrointestinal or systemic symptoms. She had been taking non-steroidal anti-inflammatory drugs for three weeks for a groin strain but was otherwise well.

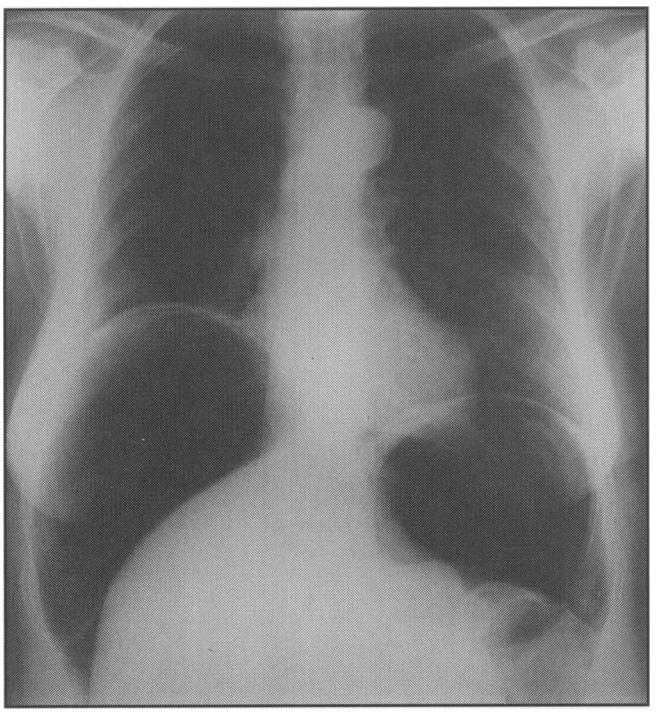

Fig 1. Plain erect abdominal X-ray demonstrating a massive pneumoperitoneum.

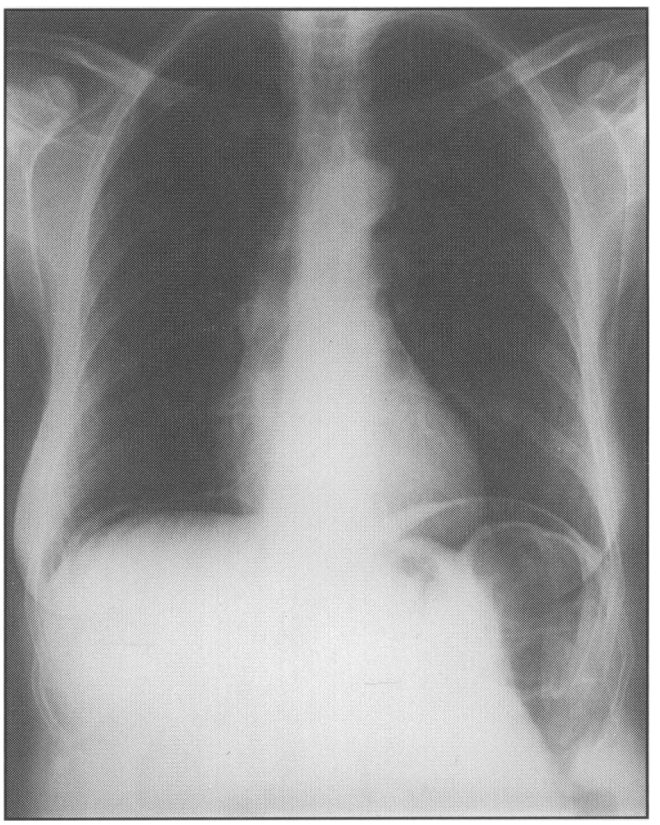

Fig 2. Plain X-ray 6 days later demonstrating spontaneous resorption of the pneumoperitoneum.

Belfast City Hospital, Lisburn Road, Belfast BT9 7AB.
W D B Clements, BSc, FRCS, Senior Registrar.
B R Gunna, FRCS, Registrar.
T G Parks, MCh, FRCS, Professor.

Downe Hospital, Downpatrick.
J A A Archbold, FRCS, Consultant Surgeon.
Correspondence to Mr Clements

On exanination her abdomen was markedly distended, tympanitic to percussion but not tender. There was no clinical evidence of intestinal obstruction. Plain radiographs of the chest and abdomen revealed a large pneumoperitoneum [Fig 1] and a diagnosis of gastrointestinal perforation was considered. However, in view of her wellbeing she was treated with intravenous fluids and nasogastric suction only. Blood picture and a biochemical screen were within normal limits. Water soluble contrast studies were performed on the upper and lower gastrointestinal tract, both of which were normal. Endoscopy was subsequently performed and this also showed a normal mucosal pattern. Plain x-rays of the abdomen were carried out on alternate days: they demonstrated spontaneous resorption of the intraperitoneal air [Fig 2]. The patient remained well and was discharged home after 10 days.

DISCUSSION

The radiological sign of pneumoperitoneum results from perforation of the gastrointestinal tract in more than 90% of cases.[1] The relevance of this sign was first described by Popper in 1915 and in the following year Dandy demonstrated an association between radiological pneumoperitoneum and a pathological disease state.[2] In 1925 Vaughan and Brams demonstrated free intraperitoneal air in 85% of 29 patients with perforated peptic ulcer disease.[3] Radiographic artefacts may mimic the appearance of free intraperitoneal air and it is important to exclude interposition of the colon between the diaphragm and the right lobe of liver[4] when considering the diagnosis of spontaneous pneumoperitoneum. Chandler et al. were the first to cast doubt on the relevance of this sign when they reported 11 of 29 patients having pneumoperitoneum in the absence of peritonitis.[5] Since then there have been sporadic reports in the literature highlighting various non-surgical conditions which predispose to SP, where laparotomy is unnecessary.[6] Non-surgical causes of SP may be classified according to the source of the gas. Three anatomical sites are recognised:- thoracic, abdominal and the female pelvis. Traumatic pneumothorax, cardiopulmonary resuscitation, mechanical ventilation, chronic obstructive airways disease, *pneumatosis cystoides intestinalis*, jejunal diverticulosis and emphysematous cholecystitis have all been described in association with SP.[7, 8]

In females the natural communication between the fallopian tubes and the peritoneal cavity may predispose to this clinical entity following gynaecological manipulation, pelvic sepsis with gas-forming organisms, post partum exercises or orogenital sexual activity.[9, 10] The condition has also been described following dental extractions and adenotonsillectomy, where no obvious explanation is apparent.[11, 12] Iatrogenic pneumoperitoneum is usually asymptomatic and frequently follows laparotomy. It may be detectable in thin people for up to three weeks following surgery but usually it resolves within 10 days.[13] It may occur after complicated endoscopic procedures and is used routinely in minimal access surgery. It is occasionally employed to distend the abdominal cavity prophylactically prior to repair of large incisional herniae so as to avoid respiratory embarrassment in the postoperative period.

Occasionally, as in this case, the diagnosis is never established and one may only speculate as to the underlying aetiology.[14, 15] A consistent finding of non-surgical pneumoperitoneum is the massive amount of free intraperitoneal gas and the paradoxical absence of other abdominal signs.

In the absence of peritonism or other overt clinical signs, careful observation, regular abdominal examination combined with peritoneal lavage and water soluble contrast studies of the gastrointestinal tract will reduce the incidence of negative laparotomy. Furthermore, a subgroup of patients with other remediable diseases may be identified who require specific investigations and therapeutic strategies.

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Case Report

Oral Phentolamine Mesylate in the treatment of Complex Regional Pain Syndrome

G J McCleane

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Complex Regional Pain Syndrome (previously known as reflex sympathetic dystrophy, RSD) is a condition presenting with burning, non-dermatomal pain associated with hyperhidrosis, intermittent oedema and discolouration and with evidence of mechanical and thermal allodynia. Conventional treatment is with sympathetic blockade produced by local anaesthetic injection around the appropriate sympathetic ganglia or by the use of agents depleting the sympathetic nerve endings of noradrenaline (eg intravenous regional sympathetic block with guanethidine). In a relatively small percentage of cases treatment is not effective. Phentolamine mesylate has been shown to be useful in diagnosing pains with a sympathetic component[1] but to date this has not been used for treatment by the oral route for this condition.

CASE REPORT A 32 year old male presented with a 2 month history of burning, non-dermatomal pain affecting the right lower leg following a soft tissue injury precipitated by a fall. In addition to pain he had intermittent oedema, blue discolouration, hyperhidrosis and mechanical and thermal allodynia. Radiographic examination failed to reveal any abnormality. Simple analgesics failed to control his pain but it was completely although temporarily relieved for 48 hours by an intravenous bolus of 15 mg phentolamine mesylate. A diagnosis of complex regional pain syndrome type 1 (at that time known as reflex sympathetic dystrophy) was made.

Subsequently a lumbar sympathectomy using phenol was performed under radiographic control. This relieved the discomfort for 6 weeks. When the pain returned it was not amenable to non-steroidal or simple analgesics and indeed repeat chemical lumbar sympathectomy produced no relief. This patient attended the clinic every 3 days and was given phentolamine mesylate 20 mg intravenously which relieved pain for 2 days.

After 10 months of intravenous therapy as described a dose of 20 mg phentolamine was given orally on a daily basis (the content of the ampoule was emptied into a glass of water). This gave consistent pain relief over a 24 hour period. The regime has been maintained for the three month period leading up to this report.

Despite its effect on peripheral alpha receptors, treatment with short acting alpha antagonist phentolamine mesylate is not associated with significant hypotension or reflex tachycardia.[2] Orally active alpha antagonists are available (for example phenoxybenzamine) but these seem to be less active against sympathetically maintained pain and have a greater hypotensive effect. Oral use of phentolamine is not appropriate as a routine treatment, but may be useful in the diagnosis and the treatment of the small group of patients in whom conventional treatment is unsuccessful but who are responsive to phentolamine. Phentolamine mesylate has been used orally in those with erectile impotence[3,4] but has not been described before for the treatment of those with complex regional pain syndrome.

Craigavon Area Hospital Group Trust, Department of Anaesthetics, 66 Lurgan Road, Portadown, BT63 5QQ.

G J McCleane, MD, FFARCSI, Consultant Anaesthetist.

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Case Report:

Necrotizing Fasciitis: two cases in a single family

R Gilliland, M Whiteside, S J Kirk, R J Moorehead

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Despite recent intense media coverage, necrotizing fasciitis has been a well recognised if uncommon clinical entity for many years.[1,2] A mother and son, both of whom have inflammatory bowel disease, presented to our unit within a three month period of each other.

Case 1 A 55-year-old woman presented with two or three week's history of increasing perianal pain. She had a long history of ulcerative colitis and ankylosing spondylitis and had been taking a prolonged course of steroids. The perineum was erythematous and an extensive area of cellulitis was present which included both labia majora and both groins.

A large area of necrotic skin and fat was excised. This procedure was complicated by the rapid onset of septic shock necessitating admission to the intensive care unit. Further debridement was necessary on the third post-operative day and pan-proctocolectomy was carried out on the following day. At laparotomy there was no evidence of perforation or abscess formation. Ventilation, inotropic support and antibiotic therapy were required for two weeks. Necrotic tissue from the perineum grew *Bacteroides* spp.

Case 2 A 29-year-old man, with a past history of sigmoid colectomy for a vesico-colic fistula secondary to Crohn's disease, presented with a 24-hour history of severe perianal discomfort which prevented him from walking. Despite medical management, including steroid therapy, he had ongoing symptoms of Crohn's disease and elective total colectomy was planned. Examination revealed erythema and tenderness in the right perianal region. He was taken to theatre within 12 hours and the ischio-rectal area incised. No pus was obtained. Twelve hours later he had developed an exquisitely tender spreading cellulitis in the right groin and he was taken back to theatre immediately. Skin was excised to fascial level and 1 centimetre beyond the boundaries of the cellulitis. Group C *haemolytic streptococci* and coliforms were cultured from the exudate. Histology confirmed the presence of necrosis and marked inflammation.

Both patients required skin grafting to cover the areas of skin loss. They made a steady uneventful recovery.

DISCUSSION

Necrotizing fasciitis is a life-threatening infection characterised by rapidly developing gangrene of the subcutaneous tissue with ensuing necrosis of the overlying skin.[3] It has similarities to the idiopathic scrotal gangrene described by Fournier which is confined to the skin of the male genitalia.[1]

Regardless of the family relationship between the two patients, no evidence exists that they or any of the other recent British cases can be linked.[4] The common denominator is more likely to be that both had chronic inflammatory disease which predisposed them to this condition. Furthermore, the immunosuppressive effect of steroid therapy may have made them more susceptible to fulminant infection.

These cases illustrate the main principles of management,[3,5] namely:

1. Prompt resuscitation with intravenous fluids, intravenous broad spectrum antibiotics and intensive care management.
2. Early and radical excision of all involved tissues.
3. Early wound inspection and further debridement as necessary.

General Surgical Unit, The Ulster, North Down and Ards Trust, Belfast, Northern Ireland.

R Gilliland, MB, FRCS, Senior Registrar.

M Whiteside, MB, FRCS, Senior Registrar.

S J Kirk, MD, FRCS, Consultant Surgeon.

R J Moorehead, MD, FRCS, Consultant Surgeon.

Correspondence to Mr Moorehead.

Organisms frequently isolated from operative specimens include coliforms, *Bacteroides* spp and *Streptococcus faecalis*.[3] Antibiotic therapy should not be delayed until sensitivities are obtained and the presence of anaerobes necessitates the use of metronidazole, usually in combination with cephalosporins and penicillin. Although more easily recognised, Fournier's gangrene is treated in much the same fashion.[6]

Mortality rates of 43-100 percent have been reported from necrotizing fasciitis.[3] However, early detection and aggressive surgical management can reduce mortality to 10 percent.[5]

ACKNOWLEDGEMENT

The authors thank Mr S T D McKelvey for permission to report case 2.

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Case Report

Transverse myelitis: a complication of systemic lupus erythematosus that is associated with the antiphospholipid syndrome

A E Smyth, I N Bruce, S A McMillan*, A L Bell

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We report a case of a patient with Systemic Lupus Erythematosus (SLE) complicated by the antiphospholipid syndrome and recurrent episodes of transverse myelitis. Transverse myelitis is a rare complication of SLE and most cases are associated with the presence of an antiphospholipid antibody (APA). The pathogenic mechanism of transverse myelitis in this condition may result from a vasculitic process. However, the association with an APA suggests a thrombotic causation, hence consideration should be given to anticoagulant therapy in addition to established immunosuppressive treatment. This case also illustrates the value of recently developed enzyme linked immunosorbent assays for measuring anticardiolipin antibodies over previous methods available in Belfast particularly those employing the VDRL cardiolipin as antigen.

CASE REPORT. A 58 year old Caucasian woman presented to the Rheumatology Unit with a 3 day history of progressive weakness and numbness in her legs, vague lower back pain and urinary incontinence. A diagnosis of systemic lupus erythematosus (SLE) had been made twelve years previously on the basis of arthritis, pleurisy, a "butterfly" facial rash and a positive antinuclear antibody. She described three similar episodes requiring hospital admission during the previous three years. On each occasion she had received oral corticosteroids, with gradual, albeit incomplete, improvement in her clinical condition. Examination showed severe weakness of the left lower limb and moderate weakness on the right in a pyramidal pattern. There was a sensory level to pinprick sensation below T8 on the right side and impaired posterior column sensation on the left. Deep tendon reflexes were increased in the lower limbs with bilateral extensor plantar responses. The cranial nerves and upper limbs were normal. These signs suggested an incomplete spinal cord lesion in the region of T8.

Initial investigations were as follows:

ESR 45mm/hr (Westergren); Full blood picture normal; C-reactive protein (CRP) 6mg/1 (normal range < 1 Omg/l); Renal function normal; Antinuclear antibody IgG 160, IgM 80; antinucleolar antibody IgG 320, IgM negative; antibody to double stranded DNA 6.6 (normal range 0-Smg/l); antibodies to Ro, La and Sm were all positive; pANCA 80, anti-myeloperoxidase antibodies negative; immunoglobulins, C3, C4 and CH50 were all within the normal range with no circulating immune complexes detected. Antibody to anticardiolipin (VDRL Antigen) was negative on repeated testing. The ELISA test for anticardiolipin (aCL) was, retrospectively performed on 7 serum samples stored during the previous 2 years, with aCL IgG elevated on 2 of these occasions at levels of 24.2 and 32.7 GPL units/mL (normal range < 23) and aCL IgM elevated on one occasion at a level of 13.5 MPL units/mL (normal range <11). Visual and sensory

Department of Rheumatology, Musgrave Park Hospital, Belfast BT9 7JB and Department of Immunology, Belfast City Hospital*.

Anita Smyth, MB, MRCP, Rheumatology Research Fellow.

I N Bruce, MD, MRCP, Registrar in Rheumatology.

A L Bell, MD, FRCP, Senior Lecturer and Consultant in Rheumatology.

Department of Immunology, Belfast City Hospital.

S A McMillan, BSc, PhD, Clinical Scientist.

Correspondence to Dr Smyth

evoked responses were all normal. Magnetic resonance imaging (MRI) of the dorsal spine and brain showedno spinal abnormalitybutmultifocal cerebral infarctions were reported as being suggestive of vasculitis. Cerebrospinal fluid examination revealed only amoderately increased protein level (0.64mg/1) with remaining parameters being normal. CT myelogram performed during a previous hospital admission was normal. Echocardiogram showed no evidence of endocarditis. A diagnosis of recurrent transverse myelitis complicating SLE was made and treatment was commenced with pulsed intravenous cyclophosphamide (350mg) and methylprednisolone (SOOmg) on every sixth day. Her subsequent inpatient course was complicated by recurrent urinary tract infections, necessitating a change in her immunosuppressive regime from cyclophosphamide to methotrexate. There was little improvement in her condition on either drug and a course of intravenous immunoglobulin was therefore introduced with some benefit. Prior to discharge she was commenced on maintenance oral therapy with cyclophosphamide lOOmg/day and prednisolone 15mg/day.

Nine weeks from her initial presentation she developed a deep venous thrombosis in her left leg despite routine heparin prophylaxis of 12,500 IU given daily by subcutaneous injection, following which she was commenced on long term warfarin therapy maintaining the international normalised ratio (INR) at a level greater than 3.0. Eleven months after initial presentation to our unit she had grade 3/5 power of the right hip flexors and grade 4/5 power on the left. She continued to have regular outpatient physiotherapy.

DISCUSSION

Neuropsychiatric manifestations of SLE occur in up to 50% of patients, ranking only second to renal complications as the leading cause of death in SLE.[1] Transverse myelitis is uncommon, occurring in less than 1% of patients and is generally associated with a poor prognosis.[2] The myelopathy usually presents acutely with paraethesia in the legs, ascending to the thorax within 24-48 hours. Other consistent features include paraplegia, back pain and loss of sphincter control.[3] In SLE the occurrence of transverse myelitis is strongly associated with the presence of elevated levels of antiphospholipid antibody (APA). In one large study 12 patients with SLE found to have transverse myelitis were all positive for anticardiolipin antibody.[4] It is of note that patients with the clinically similar Jamaican myelopathy frequently have chronic false positive tests for syphilis.[5] The diagnosis of transverse myelitis was initially made on clinical grounds aided by serological tests and imaging modalities primarily aimed at excluding other pathology. The value of CSF examination is controversial but abnormalities reported include elevated protein, pleocytosis, low C4, low glucose, altered immunoglobulin concentration and immune complexes.[6] MRI is the procedure of choice for detecting lesions of the spinal cord and several case reports have shown abnormal signals at the level of the patients' tranverse myelitis. This suggests it may have an additional role in the diagnosis of transverse myelitis and in monitoring the response to treatment.[2,7]

The antiphospholipid syndrome (APS) was initially described in SLE patients as a triad of venous or arterial thrombosis, recurrent foetal loss and thrombocytopenia associated with the presence of an antiphospholipid antibody[8] (Table 1). Since the original description further clinical manifestations have been found to correlate with elevated antiphospholipid antibody levels in SLE [9] (Table 2). It has also become clear that 'primary' antiphospholipid syndrome can also occur in the absence of clinical or serological evidence of SLE.[10]

There are three main ways of detecting APA in serum or plasma.[11] The first consists of serological tests used in the diagnosis of syphilis, as the antigenic material used in the VDRL test contains the anionic phospholipid cardiolipin. This performs poorly in screening for APS and was negative on several occasions in our patient. The second is the lupus anticoagulant test (LA) which is detected as a paradoxical prolongation of the partial thromboplastin time that cannot be corrected by the addition of normal human plasma in vitro. It has been shown to be mediated by antibodies which bind to anionic phospholipids.

The LA test was not determined in our patient as prophylactic heparin had been commenced from the time of admission and the test would therefore have been invalid. Finally, an enzyme linked immunosorbent assay (ELISA) has been developed to measure anticardiolipin antibody levels (aCL) directed against the cardiolipin diphosphatidyl glycerol from calf heart. This has

TABLE 1

Original Diagnostic Criteria For The Antiphospholipid Syndrome (after GRV Hughes et al Reference 8)

Clinical Features	*Laboratory*
Venous thrombosis	1gG aCL (elevated levels)
Arterial thrombosis	1gM aCL (elevated levels)
Recurrent foetal loss	Positive LA test
Thrombocytopenia	

Patients with the syndrome required at least one clinical plus one laboratory finding during their disease. The laboratory test must be positive on at least two occasions.

several benefits in that it can be used on banked frozen sera, anticoagulants do not affect results and identification and quantification of different aCL isotypes is possible. The ELISA is more sensitive at detecting aCL, thus manyregard it as the most clinically useful screening test. However, the LA test appears to be more specific for predicting clinical features other than transverse myelitis which has not been formally tested. Unfortunately, the ELISA test was not available in Belfast during this patient' s initial presentation and the elevated aCL was detected on banked frozen sera 2 years later. Sera from 94 healthy blood donors have been tested by the Sigma immunoassay currently used in Belfast; the mean + 2 SD (standard deviation) values obtained were 12 + 10.6 GPL units/mL for IgG and 5 + 5.6 MPL units/mL for IgM. The frequency of aCL positivity in SLE patients ranges from 17-61%.[11] In a series of 95 Irish patients it was found to be 44%.[12]

The pathogenic mechanisms underlying transverse myelitis are unknown, although vasculitis and ischaemia have been described at postmortemexamination.[6,13] The almost universal finding of antiphospholipid antibodies in such patients can be interpreted in different ways; for instance APA might simply result from inflammatory vascular damage. There is, however, good evidence that they contribute directly to a procoagulant state[5] so that vascular occlusive myelitis secondary to thrombosis must be considered. Finally direct interaction between APA and spinal cord phospholipids in the presence of a co-factor, a B-2 glycoprotein I has been postulated.[5, 14] In our patient, vasculitis should not be assumed on the basis of the cerebral MRI findings, since similar appearances have been reported in primary APA syndrome[9] and in addition she had no clinical features to suggest widespread lupus vasculitis.

The treatment regimes available include high dose steroids and immunosuppressive agents, which suppress the autoimmune response and inflammation involved in the vasculitic process. The value of isolated cases reported as showing improvement with plasma exchange and hydroxychloroquine have yet to be validated. In summary, this case emphasises the need to test for antiphospholipid antibodies, ideally by all three methods, in all patients presenting with transverse myelitis whether known to have SLE or not. As antibody levels vary with time and disease activity repeated measurements are advised.[9] While consensus has yet to be reached on some aspects of treatment in the APS it is accepted that those individuals with elevated APA and a history of previous thrombosis require long term anticoagulation with warfarin.[14, 15] Recent evidence suggests that maintenance of the INR at greater than 3.0 is required for secondary prevention of thrombosis in this condition.[16]

While continuation of traditional treatment regimes for transverse myelitis are appropriate the presence of an elevated APA should alert the clinician to the possible thrombotic mechanism, and the need for the prompt initiation of adequate anticoagulation.

The authors wish to acknowledge the help of Dr B B Sawhney, Consultant Neurophysiologist and Dr K E Bell, Consultant Neuroradiologist in the investigation of this case.

TABLE II

Clinical Manifestations in SLE and Anticardiolipin Status. (after Alarcon-Segovia et al Reference 9)

Clinical manifestation	*Number of patients with*	*% with positive aCL*
Liovedo reticularis	162	62
Thrombocytopenia	88	66
Recurrent foetal loss	43	60
Venous thrombosis	36	83
Haemolytic anaemia	25	72
Arterial occlusion	16	62
Leg ulcer	15	87
Pulmonary hypertension	5	80
Transverse myelitis	4	100

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Case Report

Synovial Chondromatosis of the Cubometatarsal Joint

P T Kennedy, G F McCoy

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Synovial chondromatosis is a benign metaplastic condition, and results in either an intraarticular or extraarticular mass lesion. The most common presentation is with a long history of localised pain. It is characterised by large numbers of cartilaginous or ossified rice-like loose bodies, and plain radiographs may reveal these as multiple small heterogeneous opacities.

We present a case of cubometatarsal joint synovial chondromatosis, which is an unusual site for this rare disease.

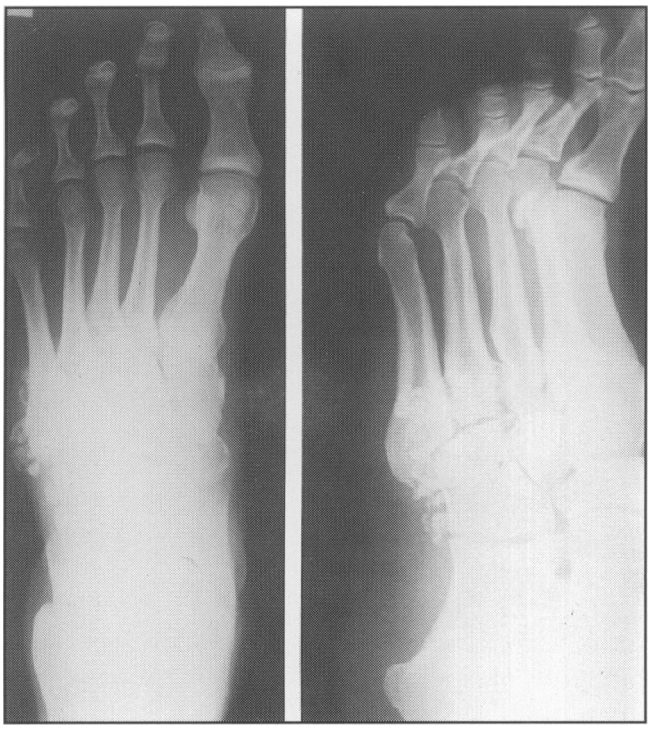

Fig. 1 PA and oblique views of the foot.

CASE REPORT. A 31 year old man presented complaining of a swelling on the sole of his foot and numbness along its lateral border. Examination revealed a tender fullness on the sole of his foot, but no sensory loss.

A plain radiograph showed discrete areas of calcification around the cuboid and bases of his 4th and 5th metatarsals, with scalloping of the cuboid in keeping with a long standing pressure effect (fig. 1); these features were reported as being consistent with synovial chondromatosis. Magnetic resonance imaging (MRI) confirmed the diagnosis by revealing multiple foci of low signal intensity surrounded by fluid (fig. 2). The cubometatarsal joint was later explored, a myriad of loose bodies of approximately 5 mm in size were removed, and an open synovectomy done. Histopathology confirmed synovial chondromatosis. When reviewed after four weeks he was pain free with a full range of movement.

DISCUSSION

Synovial chondromatosis is a metaplastic condition affecting the synovium and similar linings. The stimulus which causes the metaplasia is unknown. There is a slight preponderance of females[1] and it affects a wide age range, although most commonly those in their 3rd and 4th decades.[2] Large variations in reported incidence stem from a difficulty in definition. Milgram has classified the disease into three stages:[3] an early stage where metaplastic cells are seen *within* the synovium, but there are no loose bodies, a transitional stage where the same active process is seen, and loose bodies have been secreted into the joint cavity or bursa, and lastly a quiescent stage in which the epithelial changes are no longer seen, but there are loose bodies within the cavity. It is the last stage which gives rise to the difficulty as some degenerative processes result in loose bodies forming within the joint cavity, without epithelial changes and are therefore difficult to distinguish from quiescent synovial chondromatosis

Department of Orthopaedic Surgery, Musgrave Park Hospital, Stockman's Lane, Belfast BT9 7JB.

P T Kennedy, FRCSI, Registrar.

G F McCoy, MD, FRCS, Consultant Orthopaedic Surgeon.

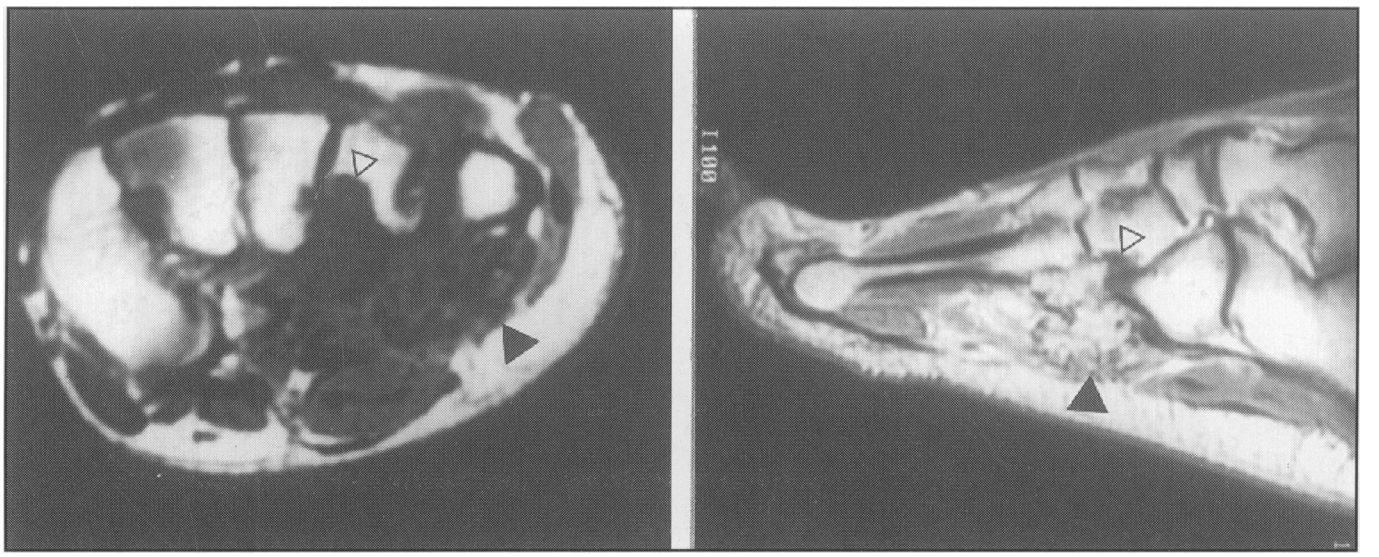

Fig 2(a). Coronal view Tl weighted MRI Low signal tissue is seen adjacent to the base of the 4th and 5th metatarsals (closed arrow head); it has the same signal strength as the surrounding muscle. Within this region there are multiple foci with very low signal in keeping with calcification. The low signal soft tissue is seen eroding into the plantar aspect of the 4th metatarsal (open arrow head).

Fig 2(b). Sagital T2 weighted MRI The soft tissue mass shows higher signal than the surrounding muscle indicating increased fluid within the tissue, in this case synovial fluid (closed arrow head). Again discrete areas of low signal are seen, representing the rice-like loose bodies. Erosion into the lateral cuneiform bone is indicated by the open arrow head.

The most commonly affected joint is the knee: one of the larger studies showed only two cases out of 53 in which ajoint of the foot was involved,[1] extrasynovial involvement of the synovium in tendon sheaths is not uncommon,[4] but more bizarre situations have included the bursa overlying an osteochondroma,[5] or within the iliopectineal bursa. Macroscopically there are multiple, smooth, well circumscribed loose bodies in a clear viscous synovial fluid. The loose bodies are usually less than 10 mm in size, but have been reported up to 50 mm. They may be purely cartilaginous, or heterogeneous in their degree of calcification. The presenting symptoms vary depending on how the mass effect is exerted: the most common symptom is intermittent long-standing pain focused at a joint, sometimes associated with a palpable mass. Other manifestations include joint locking, decreased range of movement and a limp.

The initial investigation is plain film radiography: the only changes visible may be those of non specific degenerative disease or of a soft tissue mass, but up to 88% of plain films may show discrete radio opacities within the affected joint.[1] Pressure erosion of bone is seen in approximately 11% of cases, particularly of the anterior aspect of the distal femur in knee involvement, and is caused by the pressure effect of a bulky synovium.

The malignant potential of synovial chondromatosis is uncertain: there are several well documented case reports showing histologically proven progression into extraskeletal myxoid chondrosarcoma with metastatic spread.[6] However without metastatic spread the histopathology alone is not conclusive: synovial chondromatosis which follows a benign course may on histology display several features normally associated with malignancy, for example a variation in nuclear size and staining characteristics, an increase in nuclear cytoplasmic ratio, two or more nuclei per lacunar space and a pleomorphic growth pattern.[7] Furthermore it may also become locally invasive, for example breaching the joint capsule and spreading throughout neighbouring soft tissues. Conversely extraskeletal myxoid chondrosarcoma tends to follow a benign course when compared with chondrosarcoma arising from bone – there are several reports of patients living for may years following positive identification of metastases.[8] Thus it has long been accepted that the clinician must be cautious when diagnosing malignancy on the basis of some cellular atypia, but it also

raises the possibility that so called synovial chondromatosis which was thought to have progressed to malignancy, may in fact always have been a low grade extraskeletal myxoid chondrosarcoma.

The standard treatment for intraarticular synovial chondromatosis is arthrotomy, removal of loose bodies and synovectomy; it has been argued that if the synovium looks macroscopically normal it may be assumed that the active disease is burnt out (Milgram stage 3) and therefore the synovium may be left intact.[9]

ACKNOWLEDGMENT

We would like to thank Dr M Crone for his help with interpretation of the MRI.

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Book Reviews

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It is a series of chapters by appropriate experts ranging in subject from molecular genetics, through clinical presentation, investigations to the various forms of management. It is up-to-date. The book's editors are well known and credible - a neurosurgeon and a neuropathologist.

There are two good statements in the preface that "there is some optimism that matters albeit slowly will change for the better" and "perhaps as never before, it is appreciated that a multidisciplinary approach to these difficult tumours is required".

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D P BYRNES

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A J WILKINSON

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In some places it is rather simplistic particularly when it deals with the biology of the immune response while in others, such as the chapter relating to catalytic antibodies, the complexity is such that individuals not working in the field of organic chemistry would find it rather difficult to follow.

There are a number of areas such as the use of antibodies within previously immunised hens' eggs for the treatment of gastro-intestinal diseases which I found novel and interesting. Although the chapter relating to the therapeutic use of antibodies to snake venom is perhaps a little irrelevant to clinicians working in this country.

Overall, however, I found it a very enjoyable book to read. It was quite thought provoking and the underlying message appears to be that although much interest has centred on the development and use of monoclonal antibodies, there is still

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As a result of dealing with the two problems separately there is, undoubtedly repetition but it allows the reader easy access to information on specific questions. Overall however this book, whilst being a useful review, does not contain anything new and its main interest lies in the distillate of a lifetime's experience in the field of Crohn's disease from Alexander-Williams. It will prove to be a useful reference work.

A J WILKINSON

"Therapeutic Antibodies". Editors: J Landon and T Chard. Publisher: Springer-Verlag. ISBN 3-40-19722-2. ISBN 0387-19722-2. No of pages-231.

This book gives a very comprehensive account of the uses of monoclonal and polyclonal antibodies both for the diagnosis and treatment of a variety of disorders. Seventeen individual authors contribute chapters in this book and like many books with multiple authors, the style, complexity and degree of enthusiasm varies from chapter to chapter.

In some places it is rather simplistic particularly when it deals with the biology of the immune response while in others, such as the chapter relating to catalytic antibodies, the complexity is such that individuals not working in the field of organic chemistry would find it rather difficult to follow.

There are a number of areas such as the use of antibodies within previously immunised hens' eggs for the treatment of gastro-intestinal diseases which I found novel and interesting. Although the chapter relating to the therapeutic use of antibodies to snake venom is perhaps a little irrelevant to clinicians working in this country.

Overall, however, I found it a very enjoyable book to read. It was quite thought provoking and the underlying message appears to be that although much interest has centred on the development and use of monoclonal antibodies, there is still

tremendous potential for using polyclonal antibodies, raised in animals, both for the diagnosis and treatment of common diseases.

I would not recommend this book for undergraduate students but it would be an excellent book for those involved in clinical research as it clearly outlines the function and uses of these antibodies both in the laboratory and in the clinical setting.

D R McCLUSKEY

Tumours in urology. D E Neal. pp 298. No price stated. London: Springer-Verlag 1994.

Urological oncology is arguably one of the most rapidly advancing and diverse growth areas in both the basic research and clinical fields today. By the very nature of this progress, an expanding chasm lies between the basic science and clinical strata. This book aims to bridge this gap, so it will prove both interesting and valuable to urologists of all grades as well as oncologists and scientists. The authors, predominantly urologists, are drawn from mainly European centres, with a few highly relevant contributions from America.

This book is divided into sections on bladder, prostate, renal and testicular tumours. The latter is undoubtedly the book's greatest weakness, being unduly focused on the relatively narrow area of retroperitoneal lymphadenectomy. The renal cancer section, whilst dealing with topics such as immunotherapy in excellent detail, addresses the molecular biological and clinical aspects somewhat superficially.

It is in the bladder and prostate tumour sections that this book excels. The editor's personal interest in bladder cancer is reflected in the comprehensive section devoted to this broad subject. The molecular biology of bladder cancer is explained clearly and the authors have no difficulty in bringing the reader up to date with all current work, including their own. Oncogenesis and growth factors are covered more than adequately, although tumour markers and prognostic parameters are only briefly alluded to throughout the book. All aspects of prostate cancer are discussed well. The current controversies surrounding screening and the role of surgery are dealt with in a balanced manner although the author's views on this matter are unsurprisingly European. This conservative bias is reflected in the substantial text dedicated to biochemistry, endocrinology and their clinical application to prostate cancer. The surgical approach to treatment is additionally covered with a thorough attention to detail from an American perspective.

This relatively short textbook more than adequately addresses the basic science and clinical aspects of urological tumours. However the rapid advances in this exciting field will require an updated version of this attractive book before long.

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How to organise a year abroad *

D C Wilson

Accepted 1 March 1996

Many trainees in hospital medicine will want to organise a year working in another country. This review describes the issues that lead to the choice of a particular centre, the bureaucratic process, funding, and practical issues. Some foreseen and unforeseen obstacles that previous trainees have encountered are discussed.

INTRODUCTION

This article is intended to give advice for trainees in hospital specialties or subspecialties, and will be of very limited use to those wishing to do GP work or else work in the developing world. There is published advice available, but it tends to be country specific and has a tendency to get out of date very quickly.[1,2] Examples in this review are given for various countries and disciplines, but tend to be from my own experience of a paediatric subspecialist fellowship in Canada.

Advice given here is to aid and abet your efforts in going abroad. There are quite a few headaches and usually considerable financial loss, but remember – it is a great opportunity.

PLANNING AHEAD

WHERE? There are many places where fellowships are available. As an example, people who were students during my time at Queen's University Belfast (QUB) have done fellowships in the United States of America (USA), Canada, South Africa, New Zealand, Australia, France, Germany and Hong Kong.

WHY? Many wish to advance their career by gaining new skills, consolidating knowledge and experience in one area or improving their research skills. Others want to gain experience of working in a different culture. Some wish to travel. Most of us want to do all three.

WHAT? The choice is between clinical and research appointments. In North America, it is much easier to get one year in research rather than in a clinical job; few North American trainees wish to move into an academic post, preferring the acquisition of vast wealth. However, if you are going to stay for 2-3 years, a combined fellowship is easier to obtain. Clinical jobs are easier to get in New Zealand, Australia and South Africa.

WHEN? It is essential to apply early. Although jobs can be picked up at short notice, usually due to withdrawal of applicants, it can be difficult to get visas sorted out (see below). Most North American centres finalise trainee lists in June for the next July. This leaves a time period of about 15 months minimum from first contact to commencing a job. Note that Australian and New Zealand job years begin in December.

HOW? If you are unsure, write to the Dean of the Medical Faculty or the Chief of the Specialty at the hospital, although it is best to contact the designated Director of Training at the institution and in the discipline in which you wish to work. Personal contacts are very useful, especially a senior registrar or consultant who has previously trained at the institution concerned. Specialist literature is useful – for example, a full list of available North American programmes with contact addresses and closing dates is published each January in the Journal of Paediatrics.

I and others have been surprised to learn that the protracted training period that we undergo in Northern Ireland makes us attractive to programme directors in even the most prestigious of institutions. In North America, fellowship applicants are midway through their four year

Department of Child Health, The Queen's University of Belfast, Northern Ireland.

D C Wilson, MD, MRCP, Fellow in Gastroenterology and Nutrition. (Hospital for Sick Children Toronto, Canada.)

* Based on a talk given to the Northern Irish Paediatricians in Training, NIPIT Summer Meeting, June 1995.

residency, entered direct from medical school, and may have even less publications than you. Good referees are vital, and again personal contacts will be of great assistance.

ORGANISATION: BUREAUCRACY STRIKES BACK

Getting the job that you want is not the end. It is the beginning of a long and frequently trying relationship with bureaucrats. This is where that seemingly huge gap before starting gets whittled away by delays, contradictory demands and impossible requests.

THE JOB APPOINTMENT – The amount of paperwork needed will vary. In all cases, multiple copies of your curriculum vitae will eventually be needed. Remember to internationalise it (not every one knows our local geography or understands our Health Service structure) and expand descriptions of experience and skills obtained during every job. If you have to fill in an application form, this will be structured for graduates of the relevant country, so alternatives may be needed for some answers (see below). Once appointed, contact the administrator designated to deal with foreign medical graduates. Note their name, direct telephone number and fax number and be prepared to use the latter two. If in North America, you may discover the electronic wasteland of voice mail, but keep persevering.

VISA – Basically, you need a job to get one. The time lag involved will vary, but is usually at least 3 months. In most cases, the relevant office is in London, such as the New Zealand High Commission and the Canadian Consulate, but occasionally is in Belfast, as for the US Consulate General. The name of the document varies – J-1 exchange visitor visa for USA, employment authorization for Canada – but the first step will be the prospective employing institution sending a validated job offer to the relevant immigration office. Supporting documents needed will include British or Irish passport, passport size photographs, birth certificate, money draft and possibly the results of a medical examination. The involvement of the supporting institution will vary, so don't leave it up to others to sort this out, and also allow enough time.

If a partner is accompanying you, their visa (eg J-2 dependent's visa in USA) will often preclude working in the host country, unless a job appointment and separate visa is organised in advance.

REGISTRATION – It is usual to need to register with a medical authority, such as a State Licensing Body in USA, College of Physicians and Surgeons in Canada, or the New Zealand Medical Council. This can often be one of the most time consuming and frustrating tasks, as they usually require multiple documents plus a large amount of cash (as an international money order). Some of the documents that I and others have needed, with translations to our version of the English language, are listed below:

(i) Original medical degree.

(ii) Certificate of Medical School Graduation – This is different from (i), but will be supplied by the Medical Faculty Office at QUB.

(iii) Original postgraduate examination diplomas.

(iv) Curriculum vitae (multiple copies).

(v) Medical School Transcript – This is needed for North American programmes, where all student attachments are marked and recorded, not just formal examinations. Again, the Medical Faculty Office at QUB will supply a rather bland version of this, which is begrudgingly accepted by North American institutions.

(vi) Specialty Certification – This has a separate meaning in the North American version of English, but a copy of your current Annual Registration Certificate from the General Medical Council is accepted.

(vii) Evidence of standing – North American institutions will provide forms to be filled in from "medical licensing authorities in every jurisdiction where you have practised medicine", with a Consent of Release of Information form. There is no British equivalent, so a certificate of Good Standing can be purchased from the General Medical Council (for about £50) and used instead. The GMC will refuse to fill in any of the forms mentioned above.

UNIVERSITY AFFILIATION – It is often necessary to register with a postgraduate training programme in the local university. This will require more form filling, many of the documents listed above, and a generous supply of money (as

an international money order). One benefit is that you may, at an advanced age, regain a student card and re-enter the world of cheaper travel and entrance tickets.

MEDICAL DEFENCE/INDEMNITY – This will need to be obtained in the country where you are going to work. In some places, the host institution will pay or else reimburse you, in others it will be yet another expense to bear. In some countries, like the USA, it is impossible to do clinical work without it, whereas in others, like Canada, it is not compulsory. However, it is advisable in any litigious country – for example, my host institution successfully prosecuted two residents who had been found liable in a court ruling, and the hospital wanted to get some of their lost money back.

EXAMINATIONS

It is necessary to do yet more exams to work in some countries. For the USA, the United States Medical Licensing Examination (USMLE) has now replaced previous examinations. It is a 3 part exam with the final part being done in USA. It is hard to escape doing this exam if you are doing any clinical work in USA. Most people combine the 3rd part exam with a visit to the prospective destination in the USA. Canadian institutions require the Medical Council of Canada Evaluating Examination, but it is possible to avoid this by claiming that you are an "advanced trainee". There are no other countries where an entrance exam is required.

FUNDING

Funding by the institution is not always available, so again it is important to find out early. Even if it is, it is important to know that, in North America, basic pay is less than here and there is no pay for on-call commitment. Other sources include (i) Northern Ireland Council for Postgraduate Medical Education – who are very helpful indeed but need to know by the October prior to the academic year in which you wish to leave. Contact their office for details. (ii) QUB – A letter stating your aims for the year, with a photo and copy of your curriculum vitae should be sent to the Scholarships Committee of the Faculty of medicine. There may be specialist funding available also – contact the Postgraduate Adviser in your department. (iii) Travel Bursaries are available from Royal Colleges and various professional bodies – a bit of detective work is needed, so again early application is recommended. (iv) Pharmaceutical companies can rarely be of direct help, unless they have an established fellowship or travel grant. (v) MRC and Wellcome Trust have research fellowships available. Again, it is recommended to contact these bodies well in advance, as closing dates are in autumn for the next academic year.

GETTING THERE: THE LONG AND WINDING ROAD

TRAVEL

The cost of travel is one of the many delights in store. Apex return fares are not available for more than 6 months, nor are many charters. Single fares are expensive. Open return tickets can be hard to obtain. If you are fortunate enough to have small children, consider sedation. For you, not the children.

Some centres, for example New Zealand, will reimburse some of the travel costs, but these are a definite minority. It is important to remember that Immigration and Customs affairs need to be settled at port of entry, regardless of onward travel, lost baggage, marital discord or childhood rebellion.

FREIGHT

If household and personal possessions are being brought, there are several routes. One way is to bring them on the plane as excess baggage, and pay the resulting charges. Air freight is in two price bands, for delivery within days or within weeks. Sea freight is cheapest, but trunks may need to be sent 3 months in advance. Freight companies are listed in the telephone book yellow pages.

ACCOMMODATION

The choice of accommodation may be decided in advance or once arrived in the country. Often, hospitals may be in less than salubrious inner city areas, with accommodation at close hand. It is usually easy to obtain a flat in such a residence. Furnished apartments may be available from the institution for short term use, which is of benefit while arranging accommodation in a suitable residential area. Most apartments are unfurnished, except for cooker and fridge. Furniture can be rented, but it is easy to furnish via garage sales and discount warehouses. If an institution has a high volume of overseas fellows, it may be possible to take over a predecessor's furnishings.

DRIVING

In a few cities, there is such good public transport that there is no need to own a car, with the use of hire cars or taxis when needed. However, in most a car is needed. A second-hand car can often be bought from previous fellows. If buying second-hand cars from a dealer, choose one where there is an AA or equivalent person to give independent advice. Bring your own driving licence; an international driving licence is rarely needed. Local driving tests may be required from as early as within 3 months, or not until 12 months.

CONTACTS

Always make contact in advance with the person you are replacing, if applicable, or another foreigner in the work site. They will not only tell you the real story, but can be a source of mutually beneficial trading. Friends and relatives in the country are also invaluable.

LOCAL BUREAUCRACY

Large hospitals will often have induction days for new residents and fellows, with representatives from banks, social insurance, medical and dental insurance. If not, these need to be arranged individually.

Banking – This is easy in most countries, with a bank draft or travelling cheques being enough to secure a bank account and credit card. In North America, being a newcomer means having no credit rating. Again, a bank draft or traveller cheques will allow the opening of an account, but a credit card may be more difficult to obtain. Some options are to storm off to a different bank, to use a credit card from home and arrange payment from your home bank account, or to lay down a money collateral (usually 125% of the monthly credit limit). North American credit cards have annual charges: It is worth trying to get a gold card which comes with perks such as automatic coverage on rental car insurance.

Social Insurance Numbers (SIN) – In the relevant countries, this may be arranged by the host institution, or a visit to the nearest federal office or employment centre is necessary.

Health Coverage – In many countries, there is a reciprocal arrangement with the United Kingdom. In Canada, each province provides basic health coverage after a gap of time to temporary workers, but not to their families. Families in Canada and everyone in USA needs to purchase health insurance for the full visit; workers in Canada for a few months until the province takes over. It is never an economy to scrimp on health insurance. Everyone in North America needs to purchase dental insurance.

Taxes – This will be arranged by your employer. It is important to fill in a tax return if the tax year is different from home – an unexpected cash bonus will usually result.

Work for your Partner – Professional work is easy to arrange in Australia, New Zealand and South Africa. It is exceptionally hard in North America, unless a visa has been issued for work prior to arrival.

Electricity – Remember that the UK has a unique electrical arrangement. If bringing electrical goods, purchase an international adaptor prior to leaving. Precious goods, such as lap top computers, will need transformers to guard against power surges. Most small appliances can be purchased second-hand at reasonable cost, and then resold on leaving.

HOME FINANCIAL MATTERS

Banking – Discuss your plans in advance with your bank, and consider arrangements for automatic payment of credit card bills, insurance policies, mortgage etc. Money can be transferred from a savings account to a current account on a regular basis.

Power of Attorney – consider appointing a relative or reliable friend to this position in case of emergencies. Also consider making a will prior to departure.

Superannuation – It is wise to arrange to continue to pay your contributions by standing order while away. Contact your current employer prior to departure, who will continue to pay their contribution. This arrangement only lasts for 12 months.

Taxes – Contact the local tax office in writing when your plans are formalised. If absent for a complete tax year (April to April) and still paid from home, you will not be liable for tax on these earnings. There is also a 365-day tax relief, claimed if paid from home, but are out of the country for 365 days. There are also taxing arrangements with some countries, particularly the USA, whereby taxes will be reduced. The Inland Revenue leaflet "Going to Work Abroad" is of value.

Medical Idemnity – Medical Defence Organisations will not provide coverage if working abroad; notify the organisation in advance and membership will be suspended.

Property – Letting property should allow mortgage repayments to be paid while away. It can be complicated, so it is essential to consult a solicitor. Most people employ an agent, despite the fee involved, because of the potential problems.

The building society or bank should be informed; they will wish to see a legal contract for letting.

You are usually responsible for taxes, but not television, telephone or electricity bills. Again, arrange for a friend to handle routine correspondence on your behalf and to forward relevant letters.

LECTURES

Bring relevant slides from any original work from home, which may save preparing a new talk. Many suggest enhancing these up with geographical and cultural slides but I never had the nerve to do so.

CHILDREN

Inform relevant education authorities of your plans, to ensure a place for your children to return to. The host institution often will provide help in arranging schooling. Immunization schedules for school age children are often different, but this can be arranged when settled in the new country.

Consider the needs of your children, or your partner if you have a baby, when choosing accommodation – many people do not consider the tension that social isolation of a partner will engender.

GETTING HOME AGAIN

Attention to some of the details discussed above should smooth the eventual return home. You may be considerably poorer than before, but at least the bank will still recognise you, the taxman will still be on friendly terms, and your mortgage not have been foreclosed. Furniture and other goods can be recycled to an incoming fellow. Return freight costs are often more expensive. Keep an eye on the local press for possible cheap flights home. It is important to watch your visa deadline, so that a holiday at the end of your fellowship does not convert you into an illegal alien.

PRACTICAL POINTS

1. Enquire early – 18 months is a practical time to allow for deadlines and organisation.
2. Never underestimate the bureaucracy ahead of you.
3. Replace any missing original documents (birth certificates, medical degree, specialty examination certificates) at an early stage.
4. Be prepared for financial loss.
5. Consider what your partner will do.
6. On arrival, play up your Irish identity – a winner every time.
7. Seize the opportunity to travel – during and after the job year.

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