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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 74 No. 1, pp. 1-2, May 2005.

Editorial

Undergraduate medical education – future directions

The responsibility to educate doctors was one of the earliest traditions of medicine. For instance the first section of the Hippocratic oath provides the first written framework for valuing education in medicine and laying upon doctors the duty to pass on their skills and learning.[1] It is only after this section that the oath turns to the more familiar duty of a doctor to patients. It is interesting therefore that in one of the earliest written codes of practice setting clear standards for those engaged in the profession of Medicine the responsibility for teaching was placed in pole position. Education has therefore been at the heart of the ethos of medicine since the earliest days of the Western tradition.

Since the time of the Hippocratic School medical teaching has developed considerably, yet along distinct lines with a changing emphasis on two particular priorities, the need for a firm grounding in the scientific basis of the field and the practical skills necessary for diagnosis and the management of patients. The importance of the patient in education was summed up by William Osier as follows: "He who studies medicine without books sails an uncharted sea, but he who studies medicine without patients does not go to sea at all." For many years, though, there have been additional mounting tensions generated largely because of the increasingly rapid growth of medical knowledge and the need to rationalise how much of this plethora of information is transmitted to students. Even before the exponential increase in medical knowledge of the past forty years there were concerns about information overload, described prosaically as the "overburdening of young minds". The traditional approach to undergraduate medical training characterised by the explicit division of courses into biomedical science and clinical training also came under scrutiny as ideally these should interweave throughout medical training; it was also felt that that formal instruction in those characteristics of a doctor that should provide the basis for ideal patient care, such as skills in communication, should form an early part of the medical curriculum. In the UK this culminated in the publication of a new vision of the aims, objectives and methods of undergraduate training by the General Medical Council (GMC), Tomorrows doctors in 1993 and subsequently modified in 2003.[2] This laid down a clear statement of the expectations of the newly qualified medical graduate with a strong emphasis on patient-centered education and people skills, vertical integration of learning. It also made it a requirement to provide, in up to a third of the course, a selection of relevant modules which would be chosen by the students themselves, now known as the student selected components.

The curriculum at Queens has remained responsive to change and variation. Broadly speaking, while it retains clearly recognisable elements of basic medical sciences such as anatomy and physiology, from the outset students are taught clinical skills that are fundamental to communicating with and caring for patients. In the later years the students learn medicine and surgery along with the specialities. During this period they also receive training in other basic elements of medicine from disease mechanisms to the legal aspects of medicine. This is not a static position and medical curricula continue to grow, adapt and contract to take account of changes in teaching methods and needs. A number of changes have been made in the past few years in the undergraduate medical curriculum in Queens and reflect this responsiveness to re-evaluation of the course; these include the introduction of a module on the mechanisms of disease and a total revision of the final year so that work shadowing, which is intended to hone the skills needed by PRHOs, is timetabled after finals. Anatomy is taught alongside the application of imaging techniques in medicine and in child health there is a special focus on the development of the doctor nurse team. We have recently introduced a new structure, the Institute of Medical Education, to foster teaching and teachers. These are but a few examples of the changes.[3]

The biggest challenge for the next couple of years is the enlargement of the medical course in Queens to accommodate an extra 80 medical students who

will be needed to make good the short fall in the complement of doctors in Northern Ireland.[3] This has resulted in an expansion programme involving a building schedule with the construction of a new medical school on the BCH site and a new clinical skills centre, the revision of the curriculum and a recruitment drive to bring in an additional 28 clinical academic staff over the next few years. There is much to be done before the new intake starts in September. While the challenges of medical education and the prospect of enlarging the School and its staff provide us all with a stimulus it would be wrong to ignore clouds on the horizon. Many are problems that beset all educational initiatives in the UK. Foremost amongst these are the pressures on time resulting from the introduction of the new consultant contract and the European working hours directive both of which attempt to confine activity within a defined weekly schedule. The pressures on consultant and general practitioner time have been underestimated in most health service planning and even before the arrival of the new consultant contract time available to carry out audit, governance tasks, keeping abreast of medical advances or even to talk with one colleagues was at a premium.[4] There is a risk to the training of all health care professionals if the time needed to provide education at all levels within the health service is regarded as a optional call on a busy schedule. In addition Universities, continually subject to research assessment, have inevitably placed a premium on high quality research. Delivering a complex educational agenda while maintaining both clinical and research excellence is a daunting task and arguably only achievable in a much extended, but hopefully fulfilling, working week. Curricular change has reduced some of the fundaments of basic training in order to provide more flexible opportunities for student learning and a wider spectrum of teaching opportunities for doctors. Yet staffing these student selected components with teachers will pose a severe challenge in the next few years. These factors, amongst others, continue to exert pressure on doctors.

Will these changes produce a better doctor? The quality of young doctors graduating from our system remains high and apparently little affected by this change. However there are some signs that there are benefits from the focus on communication skills early in the medical educational pathway. For instance the fourth year students working outside the main campuses have been complemented on their heightened confidence and abilities in dealing with and relating to patients. It remains important though in something as important as medical education that the changes we introduce follow the principles of good practice and are not driven by fashion or whim. The course will continue to change but this should be by rational and assessable evolution which is easier to achieve where many of the practising doctors trained locally. It is also important that this is not driven by something that we now teach our students to regard with extreme suspicion - practice based on inadequate evidence.[5] In Northern Ireland we have the opportunity to do something that would be difficult elsewhere in the UK – to assess the effect of changes of medical training on our graduates and to base alterations on solid evidence.

RJ Hay, DM, FRCP, FRCPath and Head, School of Medicine, Queen's University Belfast.

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"To see ourselves as others see us"

Presidential Address to the Ulster Medical Society

14 October 2004

Domhnall MacAuley, MD, FRCGP, FFPHNI, FFSEM

Oh wad some power the giftie gie us
To see ourselves as others see us!
It wad frae monie a blunder free us,
An' foolish notion.

To a Louse. Robert Burns 1759-1796

DREAMS

We all had dreams, ideals, and aspirations: Caring for the sick, heroic surgery, becoming, perhaps, a world famous medical researcher. Most of us do not achieve the dizzy height of our ambitions, but it is useful to measure ourselves against our hopes and expectations. Margaret Cook[1] put it eloquently "I had a romantic notion of myself in medical research, complete with daydreams of Nobel prizes, reincarnating Marie Curie, winning an immortal reputation." Similarly we have an image of the traditional family doctor that has changed little over the years. Life published a photo essay on Dr Ernest Ceriani, that set America thinking. In June 1990 they returned to Belfast (pop 6500) Maine, to revisit that story and photographed Dr David Loxtercamp at work.[2] "He cares about all the right things-about love and honour and ethics and community. He has faith in himself, in his profession and in those he serves" These are familiar sentiments. But, in the modern world, we must ask ourselves if they are still relevant. Time and medicine have moved on.

Contemporary literature can give us some idea of the changing role of the doctor in society. Nick Hornby shows us a different world in his novel "How to be good".[3] The central figure is a woman, a general practitioner: "Listen: I'm not a bad person. One of the reasons I wanted to become a doctor was because I thought it would be good-as in Good, rather than exciting or well-paid or glamorous thing to do. "I'm a GP in a small North London practice". I thought it made me seem just right-professional, kind of brainy, not too flashy, respectable, mature, caring."

The reality is not, however, a glamorous, prestigious and honoured role in society. Nick Hornby portrayed it eloquently through his narrator: "And I'll tell you something for nothing. All my life I've wanted to help people. That's why I wanted to be a doctor. And because of that I work ten hour days and I get threatened by junkies, and I constantly let people down because I promise them hospital appointments that never come and I give them drugs that never work. And having failed at that, I come home and fail at being a wife and mother".

John Diamond, another contemporary commentator, who has since died of cancer of the throat, did not shy away from telling us: "We used to like doctors, of course, or have some respect for them at least, but that was in the days when there was some communal respect for people who knew things that we didn't. . . . We like nurses, because they don't get paid much, tend to use the same pubs that we do and we know that if we were willing to spend a couple of weeks . . . we could do the job just as well. But doctors. No".[4]

What is a good doctor? A recent edition of the BMJ,[5] tried to help us decide what we valued in the medical profession, and the cover featured some well known faces in medicine ranging from criminal to celebrity. But it is difficult to identify what factors determine the standing of the profession. Recent surveys may give us some insight into public opinion. Trust is important in any professional relationship and, in a recent survey [6] 92% of the public trust their doctors. This is reassuring and, indeed, doctors polled highest of any profession. But, in another part of this study, the public were more satisfied with nurses than with doctors. In a similar poll, commissioned by the Irish College of General

Professor Domhnall MacAuley, Hillhead Family Practice, 33 Stewartstown Road, Belfast BT11 9FZ.

Practitioners, the public were asked who they held in high esteem. Of the professions, 72% held nurses in very high esteem in contrast to 60% who held general practitioners in very high esteem. Perhaps we should ask ourselves why there is such a difference in the public perception of two professions working in a similar caring medical context. Why does the public hold our nursing colleagues in higher esteem? Exploring further we find that the public consider doctors to be helpful, hardworking, committed and patient-focused, but a significant proportion considered doctors to be aloof [16%] inefficient [13%] overpaid [16%] and financially-driven [19%]. Figures worth reflection.

In the national survey of patients,[7] the public perception of general practitioners was generally very favourable. The vast majority of respondents (around 90%) had positive views of GPs' skills, knowledge, attitude and ability to communicate but their views on nurses were even more positive. Those with less favourable views of doctors were younger people, those living in London and those from minority ethnic groups. The authors warned, however, that to keep that status, doctors will need to measure up to patient's higher expectations of care.

"MEDICINE WILL HAVE TO SAY SORRY FOR ITS PAST MISTAKES AND MEAN IT"

Any smug self satisfaction evaporates after reading a few lines of "Rebuilding Trust in Health Care.[8] Reviewing a catalogue of medical mistakes, hospital mismanagement, misinformation, subterfuge, and murder, the authors show how the medical profession deserves the loss of esteem. Doctors can no longer take respect for granted. If it wasn't all entirely true, we could hide behind excuses. While events surrounding such dramatic medical scandals as Bristol, Shipman, and Alder Hey are familiar, the raw facts make horrific reading. Presenting the case that we have failed our patients, the blunt message that "medicine will have to say it is sorry for past mistakes and mean it" resonates. In Alder Hey, one pathologist erred but many others in the university and health service were complicit by their silence. If ever we doubt the impact of these events we should remind ourselves that the families felt so strongly, they asked doctors and hospital administrators not to attend the church memorial service.

Major scandals like those above make headlines, but there are many smaller issues that should make us think. We speak of the importance of medical confidentiality. Our behaviour may contradict. A small study buried in the BMJ[9] should jar complacency: Medical students listened to casual conversation in the hospital elevators and found that caregivers made 18 comments deemed to compromise a patient's confidentiality on 13 of 113 lift journeys with multiple comments on some journeys. Doctors made the most comments, then allied health professionals, and then a nurse. On two occasions medical students asked that the conversation be continued in another location. Patient confidentiality was compromised on more than one in ten lift journeys. Similarly, we might ask how often medical confidentiality is compromised by lecturers showing illustrations or presenting medical histories without written informed consent, or in hospital canteens or social meetings away from the hospital.

A good doctor or a nice doctor? Harold Shipman was clearly a nice doctor, well liked by his patients and this may be one reason why he remained undetected for so long. But we must ask how we would have reacted if he had been neighbouring colleague.[10] Professor Richard Baker suggested that we each look inwards ". . . calling for GPs to take responsibility for the killer's legacy and question their trust in each other." We can no longer shirk our responsibility to our patients, just by turning a blind eye to a colleague's errant behaviour, but we must take some collegiate responsibility. In response,[11] Prof Sir Graeme Catto, President of the General Medical Council, reflecting on our individual responsibility suggested that "The doctor-patient relationship must become more open and straightforward and be made less prone to the manipulation and paternalism which featured so strongly in Shipman's practice." And perhaps we are each a little guilty, seduced by the often praised doctor-patient relationship. Liam Farrell, whose satire[12] often finds the profession's weaknesses, wrote about the change in out of hours commitment ". . . my patients are getting along very well without me, thanks very much: any competent doctor is quite acceptable. . . I guess most of all I miss being needed."

At the Bristol Royal Infirmary, three doctors were found guilty of serious professional misconduct by doctors' regulatory body, the General Medical Council, for failing to stop heart operations on babies, despite the fact that their death rate was much higher than the national average. Twenty-nine babies died following heart operations at the hospital. The fate of the three doctors has been well documented. But what happened to the whistleblower? The NHS has a long history of treating whistleblwers badly. Many

whistle blowers find their career, physical health and mental health all suffer and Stephen Bolsin, of the Bristol Royal Infirmary, claimed that victimisation arising from his actions cost him his career. Surely it is time to put into place a system of honesty, transparency and truth, where the whistle blower is not a victim but respected for his integrity. We know why doctors keep so quiet about incompetent colleagues. They pay a huge price. Is this right?

OPENNESS AND TRANSPARENCY

Which are the best hospitals or practices? In choosing almost every other service from schools to supermarkets, there is some transparent measure of quality. But, when we try to look at options in measuring the quality of hospital or medical care, there is little available. In contrast, most doctors know to whom they would refer themselves or their family if they were ill. But, it seems, they are reluctant to let it be known to patients. Patients would value such a resource. Claire Rayner, President of the Patients' Association, commenting on publications from the Dr Foster organisation[13] which publishes a number of consumer oriented titles, said "This is a truly remarkable resource. For the first time, I can find out what I want to know about local health services. It's the most authoritative measure of healthcare standards available anywhere in the world".

Who are the best doctors? For a start, we are unsure who the good ones are. Appraisal is the proposed quality mark of professional competence and already some branches of the profession are well advanced. The quality of training and appraisal of doctors is sometimes compared to airline pilots although some mischievously suggest that doctors only use this when it suits them. A letter to the BMJ[14] puts this comparison into perspective: Imagine two airlines: In the first, Airline A, 'pilots undergo regular flight simulator skills tests, including rarely met but crucial challenges and a thorough medical examination. Airline B, in contrast, has informal personal development plans agreed privately with a colleague, maybe of their choice, supported by cabin crew and passenger surveys of the gentleness of their landings and the clarity of their communications together with a self declaration of sobriety, health, and honesty. With whom would you fly?

The relationship between doctors and the drug industry is complex and difficult. No one would argue that we need a vibrant drug research programme to maintain progress in therapeutics. But we must question the close, and sometimes too close, relationship between the drug industry and the profession. It is difficult to defend a wealthy profession that seems unwilling to fund its own medical education without considerable financial support from the pharmaceutical industry, where influential consultants are funded to attend medical meetings in exotic foreign locations, and that doctors are wined and dined by representatives almost every night of the week. This complex relationship was the subject of an entire issue of the British Medical Journal. As Ray Moynihan,[15] one of the key authors, observed "Food flattery and friendship are all powerful tools of persuasion".

"No free lunch" is an organisation that campaigns against this cosy relationship.[16] A presentation accessible on their website points out that gifts from the pharmaceutical industry are not without strings, carry entitlement, and are demeaning to the profession. They include examples of this pervasive persuasion. In contention, the drug industry will argue that they invest heavily in research, and they do, with 22% of their workforce employed in research. But 39% are employed in marketing. Marcia Angell, former editor of the New England Journal of Medicine addresses the topic in her book: "The truth about drug companies. How they deceive us and what to do about it.[17] Next time you are invited to a drug sponsored event in a luxury location and offered good food and wine, imagine what the restaurant staff might think of you. They are your patients.

CARING FOR EACH OTHER

In this caring profession, do we care for each other? The British Medical Association, in their report "Racism in the medical profession. The experience UK graduates"[18] tells it as it is: Racism is manifest in access to training and careers, and in norms of acceptable behaviour. The system is sustained by the reluctance of trainees to complain and the widely held view within the profession that problems encountered by trainees from an ethnic minority are due to valid reasons such as 'not understanding English culture'. But, surely, the medical profession is not deliberately racist. The report[19] of the Department of Health [2003] Medical and dental workforce census England illustrates the pattern of employment. White doctors are over represented in the consultant grades and non white doctors are over represented in the staff grades and associate specialists. Esmail[20] points out, in a BMJ editorial, that he has rarely met doctors who are obviously bigoted, but many who deny the problem of racism but act in ways that result in

certain groups of people being disadvantaged. His quotation from "A suitable boy" by Vikram Seth [21] is apt: "If it is only bad people who are prejudiced, that would not have such a strong effect. . . . It is the prejudices of good people that are so dangerous." "What people think is not what matters – what they do is what matters and in that respect the medical profession in the United Kingdom has a long way to go." In Northern Ireland, we have had relatively fewer doctors from ethnic minorities than in other areas in the UK but we should still ask ourselves if there has ever been discrimination on race or, indeed, on grounds of religion.

We aim to give the best medical care to all patients. But it seems we have different standards in dealing with our colleagues. A qualitative study of general practitioners[22] in Northern Ireland, highlighted the problem. The authors described a perceived need to portray a healthy image to both patients and colleagues, that there was embarrassment in adopting the role of a patient, and that this attitude impeded access to healthcare for ourselves, families and our colleagues. There was an expectation that we would work through illness and that we would expect our colleagues to do likewise. The strength of the message was in the quotations: "unless you're unable to get out of bed you'll crawl in and work" and "a terrible sense of duty of letting your partners down if you don't go in" and that "doctors feel they shouldn't be sick . . . you don't want to go and see your local psychiatrist in case one of your patients is sitting beside you".

Doctors with disabilities describe a similar experience. A piece in the jobs supplement of the BMJ[23] describing career barriers in medicine highlighted how doctors with disabilities felt that "It is difficult to talk about your weaknesses . . . We are expected to conform to a certain standard and I think if you have a weakness you keep it hidden, you don't want to talk about it.' More alarming: '[You] would expect tolerance from doctors, but this is the worst group when dealing with their own ... most people don't want to know . . . medicine has a "survival of the fittest" style.'

Not all doctors remain in the profession. In their study of doctors leaving the profession, Mike Goldacre and colleagues[24] found that 15% of graduates were not working in the NHS two years after graduation, 18% after 5 years, 19% after 15 years and 23% after 20 years. And their feelings: "Those who left felt dispensible and that no one cared what happened to them. Their treatment in the NHS contrasted starkly with their experience of working as doctors in other countries and in the private sector". This year we see the introduction of the European Working Time Directive which has greatly changed medical training. Some senior consultants feel that 58 hours each week is too little for adequate training and hospital administrators worry about staffing the hospital. Few seem to consider that 58 hours of work each week is so much more than we would expect of any other profession. And, on top of this we expect junior doctors to undertake additional study and prepare for postgraduate examinations. "What is the role of doctors in the future? A lot of people who are burning out are some of the most sensitive, thoughtful and caring people, We want a sensitive, caring, thoughtful organisation, yet we are driving people like that out".[25]

CHANGING FACE OF MEDICINE

General practice is undergoing some major changes with a new contract in 2004 and a recruitment crisis. Many general practitioners have their own stories to tell, but recent quotations from the BMA Junior members forum[26] might make us think: "one hospital consultant said to me that the MRCGP was given away with cheese and crackers", "this attitude that GPs are second-rate doctors is dissuading people from entering general practice", "why do you want to be a GP? That will be the end of your life". Similarly, medical students from Dundee and Leicester universities at a BMA conference on recruitment:[27] "lecturers often gave the impression that GPs spent their whole day referring patients to secondary care . . . medical students do generally listen to their exciting cardiology lecturer". If we wish to see a monetary reflection of the importance attached to general practice research within the wider medical research community, we need only look at the tiny funding allocation to general practice research in Northern Ireland compared to overall medical funding.

"My son the doctor" are famously the four favourite words of Jewish immigrants to America. This headlined an article in The Times[28] discussing the findings of a study by Goldacre showing that of UK-domiciled, UK trained graduates, the percentage of non-whites increased from 1.6% of graduates in 1974 to 21.5% in 2000 and will approach 30% by 2005. White men comprise little more than a quarter of all UK medical students. It seems that the male white doctor is endangered, soon to be extinct. Carol Black President of the Royal College of Physicians courted controversy in stating:[29] "Women did

better than men at medical school but there was no female dean of a medical school, no female head of a department of surgery, and no female head of a department of medicine in the UK." "Family commitments made it more difficult for them to rise to the top of the profession".

PUBLIC PROFILE

The medical community has another skeleton lurking: Research misconduct. Various shades of research misdemeanor include duplicate publication, salami publication, authorship (order, gift, and ghost), plagiarism, fraud, conflict of interest. Some cases have made national and international news. The case of Malcolm Pearce is probably the best known. But Peter Wilmshurst, an indefatigable detective of medial research has described what he considered to be institutional corruption in medicine.[30]

Doctors may claim that the media is responsible for the bad press.[31] One study of the national press found that numbers of negative, positive and neutral articles has increased significantly. The ratio of negative to positive was 2.33 with no change over the period of the study. The number of lines in each article and the median ratio of the number of lines portraying negative to positive was 2.98 with no significant change over time. Data suggest that newspapers respond to incidents rather than deliberately hounding doctors. There were not unexpected peaks in negative reports in 1986-7 and in 96-2000.

CONCLUSION

Medicine is not all that we might hope. There are problems, and problem doctors, that we cannot ignore. Richard Smith, editor of the BMJ for 13 years was never afraid to address the controversial issues and pointed out: "Medical systems and doctors are measured not by how they manage the grateful patient brings whisky but by how they care for terrorists, monsters and the marginal".[32] In a world that neglects the poor, where the greatest epidemiological risk factor is social inequality and where we read of doctors' complicity in torture, we do need to ask some serious questions.

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Total ankle replacement.

Early experiences with STAR prosthesis

JM Murnaghan, DS Warnock, SA Henderson

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SUMMARY

Early designs of Total Ankle Replacement (TAR) had a high failure rate. More recent experience with the 3-piece, meniscal bearing, total ankle replacement has been more promising. We report a review of the early results of our first 22 prostheses in 20 patients undergoing Scandinavian Total Ankle Replacement (STAR) in Northern Ireland. There was a mean follow-up time of 26 months. Seventeen patients are pain-free at the ankle joint during normal daily activities. Two of the early cases have required revision surgery due to technical errors. Other complications have included malleolar fractures, poor wound healing and postoperative stiffness.

These early results show high levels of patient satisfaction, and we are encouraged to continue with total ankle arthroplasty. There is a steep initial learning curve and use of TAR should be restricted to foot and ankle surgeons.

INTRODUCTION

End-stage degenerative disease of the ankle is uncommon when compared with the hip and knee. Common causes include trauma, primary osteoarthritis, rheumatoid arthritis and other inflammatory arthritides. However, unlike degenerative disease in the larger joints such as the hip and knee which is frequently due to primary osteoarthritis or inflammatory disease, the ankle is most frequently affected by post-traumatic arthritis (up to 80% of cases). This tends to occur in the younger patient, and is commonly associated with trauma to the soft tissue envelope. In the ankle this is thin, and often becomes scarred and inelastic.[1,2] This in itself can lead to a decreased range of motion of the joint and can also be a predisposing factor to wound healing difficulties during subsequent surgery.

Many patients obtain good symptom relief from non-surgical care including orthotics, shoe modifications, splints, physiotherapy and judicious use of intra-articular steroid injections. Ankle arthrodesis remains the gold standard for treatment of intractable pain unresponsive to non-surgical care, and has been reported as producing a painless stable foot in 59-95% [3,4,5,6] of patients. Unfortunately ankle arthrodesis has a significant complication rate with problems in both the short and long term. Specifically it has been reported to be associated with a non-union rate of 0-20%.[7,8] There is a requirement for prolonged immobilisation, and loss of ankle motion results in difficulties on inclined surfaces and loss of proprioception that can contribute to a sense of imbalance and loss of stability. Fusion of the ankle leads to greater force transmission through adjacent joints with Bauer reporting up to 80% of patients developing radiological evidence of arthritis at these joints 12 years following ankle arthrodesis.[9] While arthrodesis may provide good early pain relief, it is associated with premature

Department of Trauma and Orthopaedics, Queen's University Belfast, Musculoskeletal Research and Education Unit, Musgrave Park Hospital, Belfast BT9 7JB.

JM Murnaghan, MB, BCh, MRCS(Ed), SpR, Trauma and Orthopaedics.

DS Warnock, MB, BCh, FRCS(Tr&Orth), Consultant Orthopaedic Surgeon.

SA Henderson, BSc, MD, FRCS(Ed), Consultant Orthopaedic Surgeon.

Correspondence to Dr Murnaghan

E-mail: m.murnaghan@gub.ac.uk

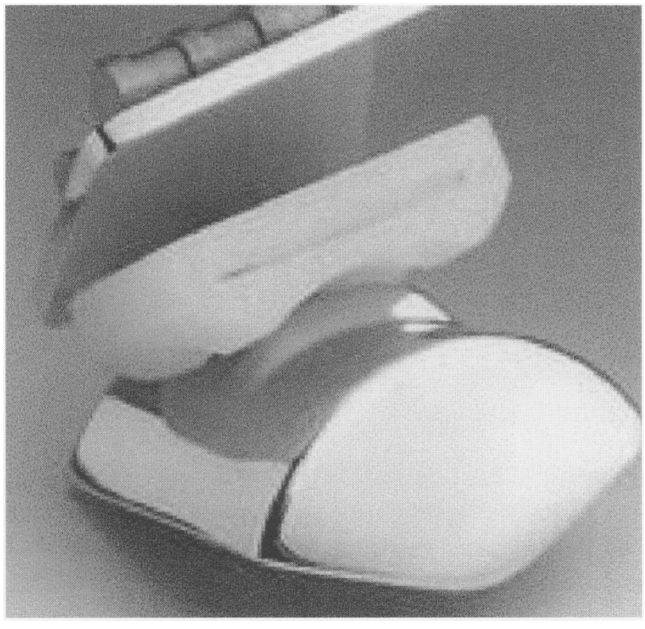


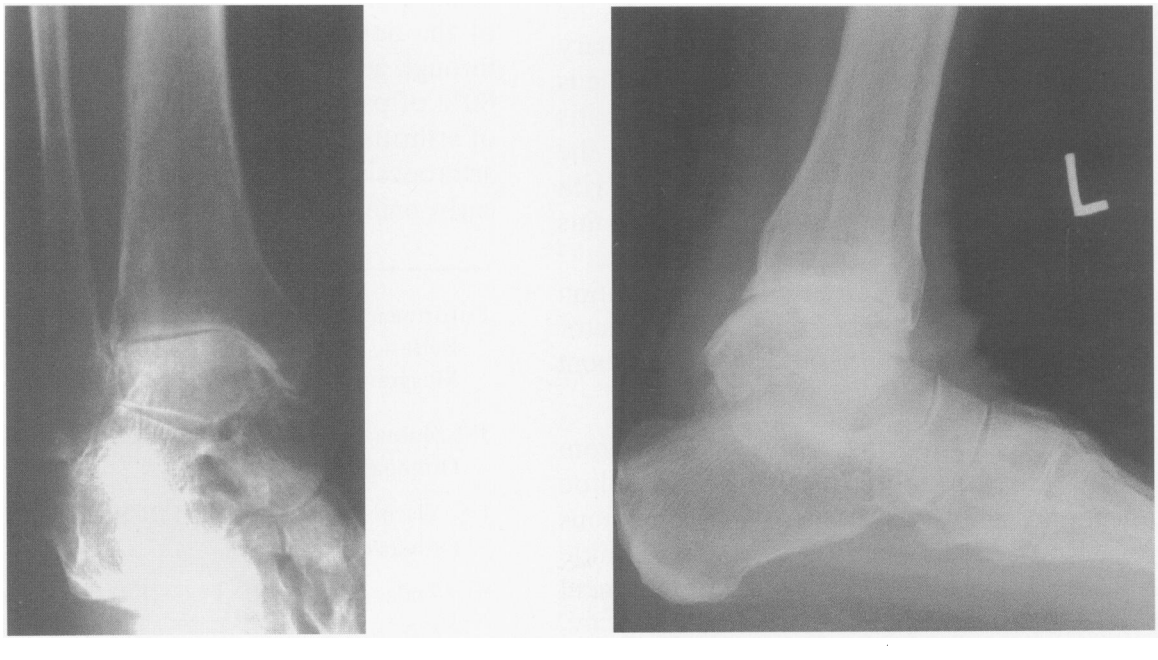
Fig 1. Scandinavian Total Ankle Replacement (STAR) components.

deterioration of other joints of the foot and eventual arthritis, pain and dysfunction. There is frequently a decreased functional ability with a greater need for ambulatory aids and permanent shoe modifications.[10] The concept of Total Ankle Replacement (TAR) to overcome these problems is therefore attractive.

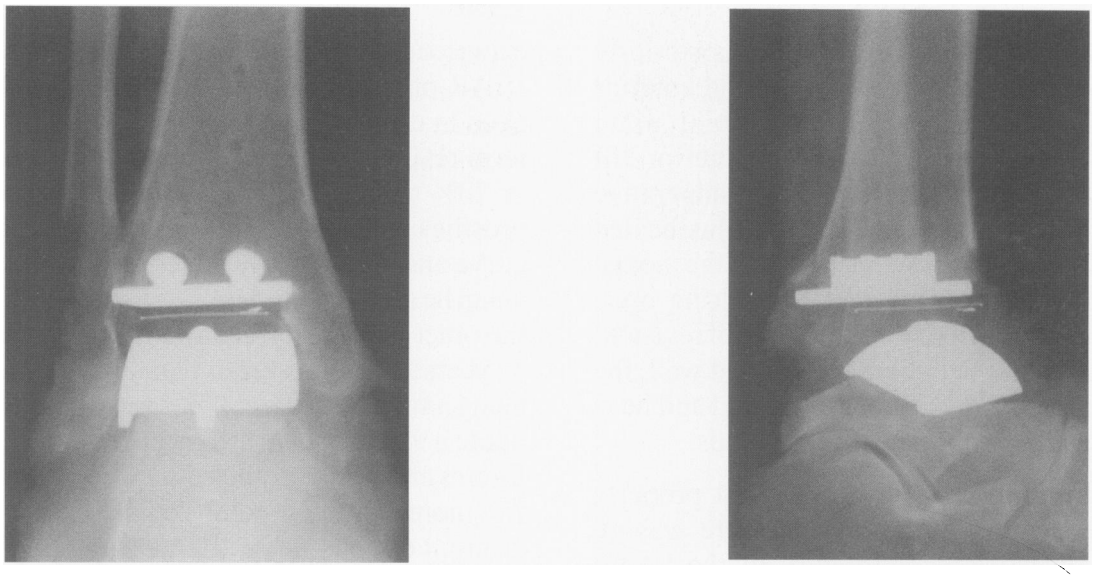
Following on from the successes of total hip and knee arthroplasty, TAR was first performed in the early 1970's. Initial results were however associated with high rates of loosening, due to a failure fully to appreciate normal ankle biomechanics. In the 1980's second generation ankle prostheses were developed. These devices allow both flexion-extension and also a degree of rotation (via a polyethylene meniscus) and attempt to replicate the complex multi-axial motion that occurs at the ankle. Prostheses were implanted without the aid of cement which is believed to be partly responsible for a decrease in loosening rates. It is one such three-component, uncemented prosthesis that is implanted in our institution (see Figure 1). We report our early experiences of the first 20 patients in Northern Ireland undergoing Scandinavian Total Ankle Replacement (STAR).

MATERIALS AND METHODS

The ankle joint is approached under spinal anaesthesia via an anterior mid-line incision, between the anterior tibial and extensor hallucis longus tendons.[11] Following appropriate preparation of the bony surfaces the metal tibial and talar prostheses are inserted. The polyethylene bearing is then introduced between the components by forceful distraction of the ankle joint. Postoperatively the ankle is immobilised in short-leg plaster of paris for up to 6 weeks, allowing increasing weight bearing as tolerated. Review with clinical assessment and screening x-rays is arranged postoperatively at 6 weeks, 3 months, 6 months and yearly thereafter (Figures 2a-d).



Figs 2a and b. Preoperative AP and lateral x-rays showing tibio-talar degeneration with relative preservation of the talo-calcaneal and talo-navicular joints.



Figs 2 c and d. Post-operative x-rays with S.T.A.R. prosthesus in situ.

We present the results of the first 22 Scandinavian Total Ankle Replacements (STAR) in our institution (two patients required revision surgery), looking at outcome as assessed by patient satisfaction, mobility and complications. This has been performed by retrospective chart review and clinical assessment at a follow-up clinic.

All patients had an assessment of their ankle function using the Kofoed scoring system.[12] This scoring system has been widely published in reviews of ankle replacement and therefore allows for comparison of our results to that of the world literature. Review of x-rays was performed to assess any complications at the time of surgery and subsequent subsidence or loosening.

RESULTS

Of the 20 patients, 12 were male and 8 female. Osteoarthritis was the diagnosis in 14, while six had rheumatoid disease. Patient's age at surgery ranged from 31 to 77 years with a mean of 60 years. Eight of the cases had previously undergone other joint surgery. All patients had undergone preoperative treatment including joint injections and ankle-foot orthosis with limited effect. All patients had complained preoperatively of decreased and painful mobility with 12 of the cases complaining of night pain.

Follow-up ranged from eight to 46 months with a mean of 26 months. 75% of patients expressed complete pain relief at the operative site during normal activities of daily living (*Table I*), and only 10% require walking aids during their ADL's due to difficulties in the ankle joint (Table II). The patient's postoperative range of flexion-extension was from 10° to 51° with a mean of 28° resulting in a mean postoperative Kofoed score of 75 (range 19-96).

TABLE I

Pain levels Patient	*Number*
Painfree during ADLs	15
Anterior impingement	1
Loading/start-up pain	2
Lateral discomfort	2

TABLE II

Mobility	*Patient Number*
Full ADLs without aids	15
Crutches (due to discomfort/instability of ankle joint)	2
Crutches (due to co-existing arthritis in other joints)	1
Wheelchair (due to co-existing arthritis in other joints)	2

COMPLICATIONS

Revisions subsequent surgery

Three patients required secondary surgery with two of these requiring revision of the prosthesis.

Case 1. The tibial plate inserted too posteriorly such that the anterior lip was behind the anterior tibial cortex and as a result the tibial plate developed marked and progressive anterior tilt and loosening. He also sustained an intraoperative bimalleolar fracture. The lateral malleolus healed with conservative management; however the medial malleolus developed a non-union requiring open reduction and internal fixation at the time of revision. Following revision the patient progressed well, the lucency has regressed, the fracture healed and he is now painfree, and mobilising without aids.

Case 2. The tibial plate failed to seat properly on the cut surface posteriorly, and there was an undisplaced intraoperative fracture of the lateral malleolus. The fracture healed with conservative managemen; however the tibial tray was revised. The patient is now mobilising without any aids and has minimal start-up pain only.

Case 3. The patient complained of significant lateral discomfort while mobilising X-rays suggested a fibular impingement, and this along with some dense scar tissue was excised via a lateral approach. He now has no rest or nocturnal pain though does complain of pain while walking on uneven ground.

Fractures

Five patients suffered intraoperative fractures of the malleoli. (The two referred to above and 3 others). All, aside from the patient in case one, healed satisfactorily following treatment in POP.

Lucency

Six patients were noted to have lucent areas around the tibial plates on postoperative films; however in all but one of these this lucency resolved, and there was no clinical suggestion of infection or loosening. In one case (referred to above) this lucency did progress; however it resolved following revision.

Wound healing

There were two cases of delayed wound healing, one patient developed a small anterior ulcer, which resolved within four weeks and the other patient developed a superficial wound infection in the early postoperative period that resolved with oral antibiotics.

CONCLUSIONS

Early models of Total Ankle Replacements had a high failure rate, with early loosening and failure. They also had difficulties in wound healing. More recent experience using a 3 component design such as the STAR prosthesis has been more successful. It has been in use for 17 years and has good intermediate term results. Anderson *et al* quote a mean survival of 70% at five years using the uncemented STAR prosthesis, though did note a very steep learning curve and significantly better results were obtained when he analysed his last 31/51 cases.[13] Kofoed[14] on the other hand describes a 95% survivorship rate at 12 years using the same implant, while Knecht *et al*,[15] using a slightly different prosthesis (Agility Ankle), quote a 92% survival at a mean of nine years. These figures are not greatly dissimilar from those reported for more common joint replacements. Total hip arthroplasty has survival figures ranging from 96% at 10 years[16] to 90% at 20 years,[17] while long term results for total knee replacement are in the range of 95 to 88% at 10 and 15 years respectively.[18,19]

The indications for ankle arthroplasty are expanding and it has now been shown to be equally effective in patients both under and over 50.[20] The ideal patient is an elderly person who has low physical demands, good bone stock, normal vascular status, no immuno-suppression and excellent hindfoot-ankle alignment. The patient who has bilateral ankle arthritis or ipsilateral hindfoot arthritis requiring fusion is particularly likely to benefit, as the results of bilateral fusion or pan-talar fusion are often poor.[21] Contraindications to surgery include talar avascular necrosis, neuropathic degenerative disease (Charcot joint), sensory or motor dysfunction of the lower leg, severe tibio-talar malposition, and acute or chronic infection.

Ankle arthroplasty has now been performed in our institution for four years, with 28 cases being completed. In this early review of the first 20 patients with an average of follow-up of 26 months, 15 of the patients are now entirely pain free during normal activities of daily living while only two of the patients require use of walking aids due to difficulties at the operative joint. These results, although still only short-term, are comparable to those in the world literature. On the basis of these early results ankle arthroplasty will continue to be offered as an alternative to ankle arthrodesis in our institution. It is clear however that TAR is technically demanding and has a steep learning curve. It is also clear that TAR should be limited to centres where surgeons with an interest in foot and ankle disease have the caseload to master this steep curve.

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Review

Hereditary Non-Polyposis colon cancer

LA Devlin, JH Price, PJ Morrison

INTRODUCTION

Colorectal cancer is the second most common cause of cancer related death and the third most common cancer in the United Kingdom.[1, 2] Around 80% of cases present with spread to the bowel wall. Early diagnosis and recognition of symptoms can now be achieved by screening asymptomatic persons.[3]

We now know that between 5-15% of colorectal cancer is hereditary in nature. Various genetic disorders exist that predispose individuals to colorectal cancer (CRC), including Familial Adenomatous Polyposis (Gardner's syndrome,/ Turcot's syndrome), Peutz-Jeghers syndrome, Juvenile Polyposis syndrome and Hereditary Non Polyposis Colorectal Cancer (HNPCC).

This is an autosomal dominant highly penetrant cancer-susceptibility syndrome caused by germline mutations in one of the DNA mismatch repair genes, MLH1, MSH2, MSH6, PMS2 and PMS1. Affected individuals have a predisposition to developing early onset colorectal cancer and endometrial cancer, and less commonly ovarian, small intestine, stomach, biliary tract, pancreatic, brain and uroepithelial tract cancer.

In contrast to Familial adenomatous polyposis and other colorectal cancer syndromes, HNPCC lacks distinctive clinical features. Traditionally associated with an increased susceptibility to CRC, the extending clinical phenotype with a susceptibility to other cancers makes diagnosis increasingly difficult. Under-diagnosis leaves families susceptible to cancer, whereas over diagnosis commits families to a prolonged screening program that is not without its complications.

Various criteria have been developed to aid in the diagnosis of HNPCC and select families for molecular testing of mismatch repair genes, the Amsterdam and Bethesda criteria being the most widely used (Boxes 1-3). Difficulties arise in families who do not meet these criteria, but have a significant history of HNPCC related cancers.

HISTORICAL BACKGROUND

One of the first HNPCC families described was "Family G", by Warthin in 1913.[4] Warthin's interest in the hereditary nature of certain cancers was stimulated by the depressed thoughts from his seamstress who had told him that she would die at an early age from cancer of the colon, or cancer of the female organs, as had many of her relatives. He analysed 3600 cases of neoplasm at the pathological laboratory of the University of Michigan between the years of 1895 to 1913. From looking at family histories he identified those with multiple occurrence of carcinoma. The incidence of cancer in these families was so striking that he interpreted them as showing an inherited susceptibility to cancer.

His seamstress later died of endometrial carcinoma, but her family, "Family G" showed a predominance of uterine, gastric and colon cancer. Warthin's study looked at three successive generations; forty-eight descendants of a grandfather with cancer of the stomach/intestine. Ten cases of carcinoma of the uterus and seven of the stomach were described.

He noted that uterus, breast, gastrointestinal tract and mouth are the parts of the body most frequently involved in the case of these family cancers. Cancer

Belfast City Hospital, Lisburn Road, Belfast BT9 7AB.

Department of Medical Genetics:

LA Devlin, MB, BCh, MRCPCH, Research Fellow.

PJ Morrison, MD, FRCPCH, FFPHMI, Professor of Human Genetics.

Department of Gynaecological Surgery:

JH Price, MD, FRCOG, Consultant Gynaecologist.

Correspondence to Professor Morrison.

of the lip and rodent ulcer of the face also show a tendency to familial occurrence.

Lynch revisited the family in the 1960's,[5] with more than 650 descendants. He noted the increased incidences of adenocarcinoma, predominantely of the colon and endometrium. One particular branch of the family (from a sibship of ten, from the original progenitor) initially showed a paucity of cancer until further generations developed chronic lymphocytic leukaemia and lymphosarcoma (3 out of seven members of a sibship).

Several members of the other branches of the family also developed chronic lymphocytic leukaemia, sarcomas and brain tumours.

Lynch concluded that the cancer family syndrome was characterised by: (1) increased occurrences of adenocarcinoma, primarily of the colon and endometrium; (2) increased incidence of multiple primary malignant neoplasms; (3) autosomal dominant inheritance; and (4) early age of onset of cancer. "Family G" differed from other families with the cancer family syndrome in the development of sarcomas and leukaemias in some family members.

He named the purely colon type 'Lynch type 1' and families with extra colonic cancers including ovarian and endometrial, 'Lynch type 2'. We now know that several genes cause the different phenotypes and the term HNPCC is generally used.

MOLECULAR GENETICS

HNPCC is caused by mutations in mismatch repair genes, MLH1, MSH2, MSH6, PMS2 and PMS1. MLH1 and MSH2 account for the majority of families with HNPCC. The prevalence of mutations in these two genes in HNPCC families depends on the chosen population and inclusion criteria used for molecular screening, but can be as high as 86%.[6] Founder effects in this Finnish population may account for the relatively high mutation detection rate and the prevalence of MLH1 and MSH2 mutations in other HNPCC kindreds meeting the Amsterdam criteria have been 39-49%.[7,8] The same studies found the prevalence of MLH1 and MSH2 mutations in kindreds who are "Amsterdam Like", showing familial clustering of colorectal and other related cancers, to be between 8 and 16.7%, depending on the specific subgroup tested. The population carrier frequencies of MLH1 and MSH2 have been estimated at 1:3139 in the Scottish population.[9]

Recently, it has been noted that large genomic rearrangements, that traditionally would not be picked up on genomic sequencing, account for more than 50% of pathogenic mutations in MLH1/MSH2 in families meeting the Amsterdam criteria.[10]

MSH6 mutations are less common; 3.8% of total families, and 14.7% of all families with DNA mismatch repair gene mutations in a German HNPCC cohort,[11] had MSH6 gene mutations. They had a later age of disease onset and a lower incidence of CRC, hence almost two-thirds of families carrying MSH6 mutations would have been missed if the Amsterdam criteria were applied as a 'checklist' to be met prior to molecular testing.

A deletion in PMS2 and one nonsense mutation in PMS1 have been described in HNPCC families,[12] however a more recent study by Liu *et al*[13] failed to identify any clear cut pathogenic mutations in 84 HNPCC and HNPCC like kindreds without known mutations in the other three known DNA mismatch repair genes.

At present, testing in the NHS is offered on a diagnostic basis for germline mutations in MLH1 and MSH2 to families fulfilling the modified Amsterdam criteria in most regions.

Molecular analysis of these mismatch repair genes is expensive and very labour intense; therefore selection of families for molecular analysis of MLH1 and MSH2 must be aimed at those likely to have a mutation in either of the two genes.

No definite criteria exist for the diagnosis of HNPCC and there are various factors that will influence the likelihood of a mutation in one of the mismatch repair genes known to be involved.

DIAGNOSTIC CRITERIA

The Amsterdam criteria were developed in 1991 by the International Collaborative Group on Hereditary Non-polyposis Colorectal Cancer (ICG-HNPCC),[14] in an attempt to standardise diagnostic criteria in recruitment of HNPCC patients for comparative multicentre studies. These were modified in 1999 to include other HNPCC related cancers.[15]

Since then, the Amsterdam criteria have been commonly used to diagnose HNPCC and to select families for molecular analysis of mismatch repair genes.

Application of the Amsterdam criteria to molecular testing will increase the chance of a germline mutation in MSH2 and MLH1, but may indeed

miss a significant number of families carrying an MSH6 mutation.

Box 1:

Amsterdam criteria I

There should be at least three relatives with histologically verified CRC; all of the following criteria should be present:

One should be a first degree relative of the other two:

At least two successive generations should be affected:

At least one CRC should be diagnosed before age 50:

FAP should be excluded in the CRC case:

Tumours should be verified by pathological examination.

Box 2:

Modified Amsterdam criteria (Amsterdam II)

There are at least three relatives with an HNPCC associated cancer (large bowel, endometrium, small bowel, ureter, or renal pelvis, though not including stomach ovary, brain, bladder or skin):

One affected person is a first degree relative of the other two:

At least two successive generations are affected:

At least one person was diagnosed before the age of 50 years:

Familial adenomatous polyposis has been excluded:

Tumours have been verified by pathological examination.

MICROSATELLITE INSTABILITY (MSI) AND IMMUNOHISTOCHEMISTRY (IHC)

Microsatellite instability is characteristic of tumours from individuals with a mutation in one of the mismatch repair genes. These are length variations of short repetitive DNA sequences in the tumour, and occur in more than 80% of HNPCC tumours. As many as 15% of sporadic colorectal cancer also display MSI.[16]

MSI can therefore be used as a screening tool to try and identify patients who are likely to have a mutation in one of these genes. The Bethesda guidelines were introduced in 1997[17] to indicate which families should proceed to MSI testing prior to molecular analysis (Box 3).

These Bethesda Guidelines were revised in relation to their performance, sensitivity and specificity in 2002, following a HNPCC workshop at the National Cancer Institute, Bethesda, MD,[18] (Box 4).

Box 3:

The Bethesda criteria for MSI testing of tumours: tumours from any of the following should be tested for MSI (or by immunohistochemistry) and then positive patients should continue for MMR testing.

Individuals with cancer in families that meet the Amsterdam Criteria:

Individuals with two HNPCC-associated cancers, including synchronous and metachronous CRC or associated extracolonic cancers:

Individuals with CRC and a first-degree relative with CRC and/or HNPCC-related extracolonic cancer and/or a colorectal adenoma diagnosed at age < 40 years:

Individuals with CRC or endometrial cancer diagnosed at age < 45 years:

Individuals with right sided CRC with an undifferentiated pattern (solid or cribiform) on histopathology diagnosed at age < 45 years:

Individuals with signet-ring-cell-type CRC diagnosed at age < 45 years:

Individuals with adenomas diagnosed at age < 40 years.

Immunohistochemical loss of expression of the affected MMR protein is another characteristic feature of HNPCC tumours. This too can be used as a screening, in combination with MSI, prior to molecular testing.

MSI and IHC have both been shown to be highly sensitive and specific in predicting a germline mutation (97 and 83% respectively for MSI, 79 and 89% respectively for IHC),19 and are reliable to be used to identify patients suitable for molecular analysis, in patients suspected of HNPCC.[20] Tumours resulting from a germline mutation in MSH6 may exhibit a lower degree of MSI,[21] and therefore an MSI-low phenotype cannot be considered an exclusion criterion for mutation testing of MSH6.

Box 4:

Revised Bethesda Guidelines for testing colorectal tumours for microsatelllite instability (MSI).

Tumours from individuals should be tested for MSI in the following situations:

1) Colorectal cancer diagnosed in a patient who is less than 50 years of age.
2) Presence of synchronous, metachronous colorectal, or other HNPCC associated tumours*, regardless of age.
3) Colorectal cancer with the MSI-H† histology‡ diagnosed in a patient who is less than 60 years of age_.
4) Colorectal cancer diagnosed in one or more first degree relatives with an HNPCC-related tumour, with one of the cancers being diagnosed less than 50 years.
5) Colorectal cancer diagnosed in two or more first- or second-degree relatives with HNPCC-related tumours, regardless of age.

*HNPCC related tumours include colorectal, endometrial, stomach, ovarian, pancreas, ureter and renal pelvis, biliary tract, and brain (usually glioblastoma as seen in Turcot syndrome) tumours, sebaceous gland adenomas and keratoacanthomas in Muir-Torre syndrome, and carcinoma of the small bowel.

†MSI-H = microsatellite instability-high in tumours refers to changes in two or more of the five National Cancer Institute-recommended panels of microsatellite markers.

‡Presence of tumour infiltrating lymphocytes, Crohn's-like lymphocytic reactions, mucinous/signet-ring differentiation, or medullary growth pattern.

_There was no consensus among the Workshop participants on whether to include the age criteria in guideline 3 above; participants voted to keep less than 60 years of age in the guidelines.

A review carried out by Grady calculated the likelihood of mutation detection in MLH1/MSH2 in HNPCC families depending on the clinical criteria used; The Amsterdam I criteria have the highest predictive value for the identification of a mutation in MLH1 and MSH2 genes (40-60% likelihood of mutation detection), but this is met only in larger families.[22] The likelihood of finding a mutation fell to 18% for the Amsterdam II criteria, and to 20-30% for the original Bethesda guidelines. Interestingly there was a 28% chance of identifying a germline mutation in MLH1/MSH2 in an individual who developed CRC less than 30 years.

Syngal *et al* calculated similar sensitivity of the Amsterdam criteria for detecting a germline mutation in MLH1/MSH2; 61% with a specificity of 67%. Higher sensitivities are however reported for Amsterdam II and the Bethesda criteria; 78% and 94% respectively.[23]

No perfect criteria exist for the diagnosis of HNPCC or indeed for predicting the likelihood of a MMR gene mutation, and difficulty arises in trying to obtain an adequate balance between sensitivity and specificity.

CANCER RISK ASSOCIATED WITH HNPCC

The lifetime risk of any cancer to mutation carriers in HNPCC is 91% for males, and 69% for females, with a 74% and 30% risk by age 70 for colorectal cancer respectively in each sex. The risk of ovarian cancer in females (*figure 1*) is around 10% by age 70 years,[24] and endometrial cancer around 40% by age 70 years (*figure 2*). MSH6 is associated with a slightly different tumour phenotype (later age of disease onset and lower incidence of CRC),[11] and an estimated lifetime cancer risk of 60%.[25] Presentation may be with only endometrial cancer in families and we have ascertained some cases through gynaecology clinics.

Fig 1. Ovarian cancer.

GENETIC COUNSELLING

Guidelines exist for segregating colon cancer risk into high (greater than 1 in 10), medium (less than 1 in 10 to 1 in 20), and low risk (less than 1 in 20 – ~1 in 50 (the population level) – *see table 1*). Most cancer genetic screening programs offer a "triage" system of referrals where patients fill in a detailed questionnaire to allow accurate confirmation of cancers in the family and the drawing of an accurate family tree. This enables the genetic team of clinical

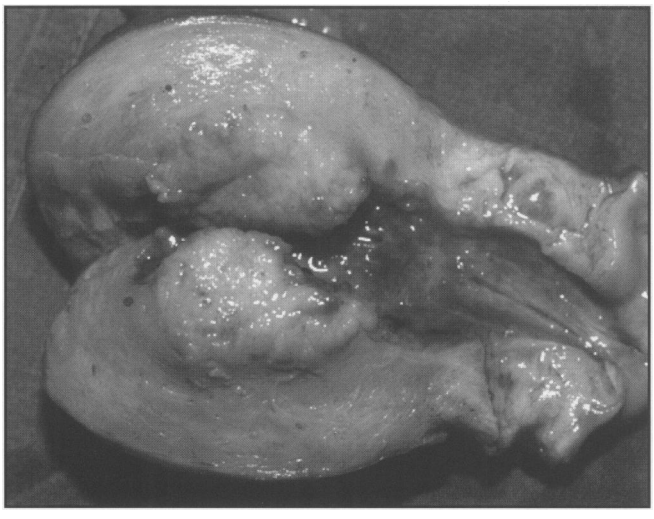

Fig 2. Endometrial cancer.

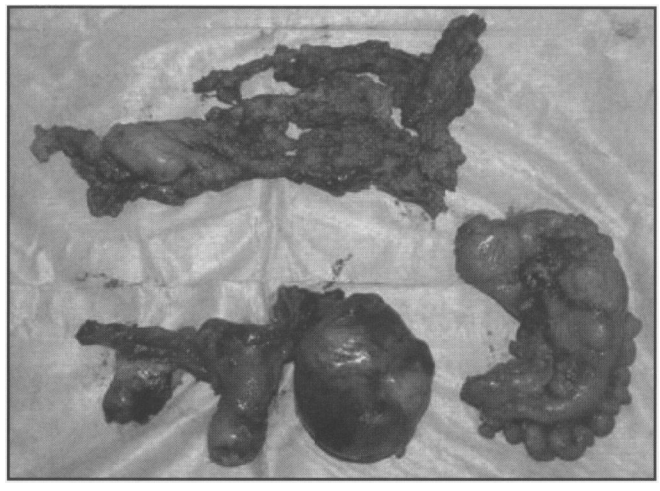

Fig 3. Ovarian cancer with resection of colorectal tumour.

geneticist and genetic counsellors or genetic associates to work out an accurate individual risk for the proband.

Confirmation of cancers is important for two reasons. Firstly some patients may not know the exact cancers their relatives suffered from, or whether the cancer from which they died was primary or secondary. This is particularly important in patients with ovarian and colon cancers when it is important to distinguish which is the primary and which is the secondary cancer or if there are indeed two separate primaries (*figure 3*), as the risk to relatives will vary depending on the number of cancers in the family as to and whether the family fits medium or high risk screening criteria. Secondly some suspected cancers may actually be benign (e.g. ovarian cysts or endometrial fibroids), and the risk to the family may be very low.

Rarely, some patients may fabricate a family history, as they may be suffering from other problems of a nonphysical nature, or to seek attention, and these patients require special help in dealing with their problems. We have had some cases in our own practice, and GP's and surgeons should be aware of the possibility that this may occur, even if it is uncommon.

If patients are in the low risk category after preliminary risk estimation, management is usually by telephone and written contact to the patient with copies to the general practitioner, detailing that the patient is at low risk and giving reassurance and an offer of further risk evaluation if the family history changes (e.g. another relative becomes affected). Patients often find this very helpful, especially as they do not need to attend a hospital clinic. Medium risk patients are offered screening at an appropriate secondary level clinic with colonoscopy at defined intervals. Often this will be an 'entry' and 'exit' regime with initial colonoscopy at ~35 years and later colonoscopy at 50-55 years. This covers the main time that polyps will grow in the colon and allows prevention. High-risk patients are offered a consultation with a geneticist for consideration of genetic testing and a range of screening and preventative measures including colonoscopy at 2 yearly intervals from 25, or 5 years younger than the earliest affected case in the family (whichever comes first), up to age 75 years.

Surveillance programmes in the UK are based upon a study carried out by a group at Leiden University, Netherlands, who looked at 114 families with an identified mismatch repair gene defect and/or met the clinical criteria for HNPCC, and looked at the interval between surveillance and colorectal cancer.[26] They recommend colonoscopy with an interval of not more than two years for HNPCC families.

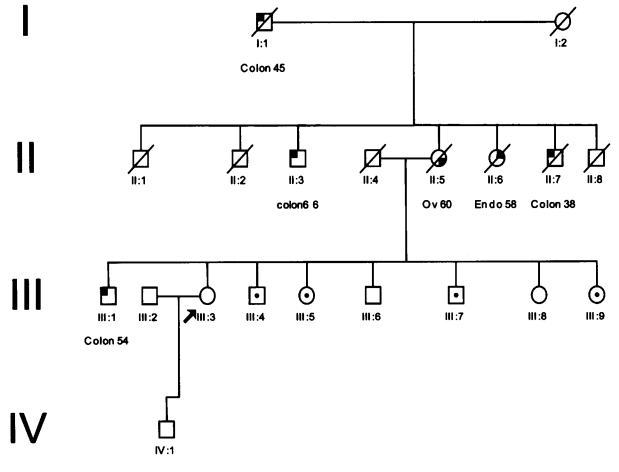

Fig 4. Pedigree showing typical referral for HNPCC.

TABLE I

Colorectal Cancer risks (population risk = 1 in 50)

Family History of Colorectal Cancer	*Lifetime Risks*	*Low Risk –*	*Medium Risk*	*High Risk*
1 RELATIVE				
>45 yrs	1 in 17	Yes		
<45 yrs	1 in 10		Yes	
2 RELATIVES				
one 1st degree and one 2nd degree	1 in 12	Yes		
two 1st degree relatives ave <60	1 in 6		Yes	
two 1st degree relatives ave >70	1 in 10	Yes		
3 OR MORE RELATIVES dominant pedigree or Amsterdam criteria HNPCC family	1 in 2 - 1 in 3			Yes

Discussion of the ovarian cancer risk (population risk 1 in 70 increasing to around 10-15% in cases of HNPCC) and endometrial cancer risk (population risk 1 in 75 increasing to around 30-40% in cases of HNPCC, and may be higher in MSH6 genetic mutations) is important in females with a history of HNPCC. Ovarian and uterine ultrasound with pipelle biopsy and CA125 tumour markers provide some reassurance although clinical trials are underway to determine the efficacy of this screening. Preventative oophorectomy/hysterectomy, and other surgical options are also discussed. Upper GI endoscopy needs to be considered if there is a history of stomach cancer in the family.

The family tree (*figure 4*) is a typical referral with the index case, III.3 (arrowed), being referred because of her family history which includes brother, III.1, with colon cancer at age 54, mother with ovarian cancer age 60, two maternal uncles with colon cancer (II.3 age 66 and II.7 age 38) and a maternal aunt with endometrial cancer aged 58. The family fit the Amsterdam criteria with 3 affected cases of HNPCC related cancer (CRC, endometrial cancer etc.), at least one (here 2 cases) with colon cancer under 50 and 2 generations being affected. Genetic testing of the index case's, brother III.1, confirmed a mutation in the MSH2 gene consistent with HNPCC. Carrier testing was then offered to all family members and the index patient was shown not to carry the mutation although four of her siblings (dot indicates carrier) were found to be carriers of the mutation. This is powerful genetic information as the risk to the index case is reduced to the population risk of 1 in 50 (for CRC), and no additional screening is necessary for either her or her children (she cannot pass on a gene mutation she does not have). Her siblings, who are carriers, should have 2 yearly colonoscopies from 25 years and her two carrier sisters should also have endometrial and ovarian screening starting in their mid thirties.

Following genetic testing, if a mutation is found in a HNPCC family, other at risk family members should be offered testing as in the example above. If they prove to be negative for the family mutation, then further surveillance is not necessary, but it is important that they should be reminded that a background population risk for colorectal cancer still exists and lifestyle measures including a diet including fruit and vegetables and exercise may be helpful. Other issues including insurance risks can

be covered although this is less of a problem in the United Kingdom as there is a moratorium on the use of genetic tests,[27] which was extended in March 2005 from 5 to 10 years in a concordat between the insurance industry and the government and will be reviewed in 2008 before the 10 year moratorium ends in November 2011.[28]

Families in which a mutation is not identified need to continue with ongoing surveillance until future genetic testing eventually allows clarification of the risks in the family with new genes being tested for as they are found.

CONCLUSIONS

The diagnosis of HNPCC allows early detection and prevention of HNPCC related cancers. Criteria exist to aid diagnosis for HNPCC and also to aid in selection of patients for molecular analysis of mismatch repair genes, although such testing is expensive and labour intense. Other candidate genes may be involved and may account for families with a phenotype not consistent with the Amsterdam criteria, and the current criteria may fail to diagnose families with MSH6 or other rare mutations.

HNPCC is an important condition relevant to the practice of medical practitioners from various specialties, particularly those who see and treat cancer patients. The condition is complex and all potential patients should be referred to a regional clinical genetics department where full assessment and counselling of the proband (and later the entire family) can be carried out, and screening programmes instigated through onward referral to colonoscopy services, or reassurance can be given in low risk cases.

ACKNOWLEDGEMENTS

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Social deprivation and childhood injuries in North and West Belfast

JA Silversides,[1] A Gibson,[1] JFT Glasgow,[1,2*] R Mercer,[4] GW Cran[3]

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SUMMARY

Injuries in childhood represent a major public health concern. North and West Belfast is an area in which a high rate of emergency department attendance due to injury has been observed, and in which social deprivation is widespread. We carried out a cross sectional survey of 479 injuries in children aged 0-12 years presenting to four emergency departments serving North and West Belfast. Injury rates were compared between the most deprived and least deprived areas, selected on the basis of Noble Economic Deprivation scores. A significant correlation between economic deprivation and injury rate was demonstrated (r =2.14, p≤ 0.001). Children living within the most deprived areas were particularly likely to be involved in road traffic accidents (relative risk RR=3.25, p=0.002). We conclude that children living within the most deprived areas of North and West Belfast are at greater risk of injury than those in less deprived areas. Specific causes of injury, for example burns and scalds, high falls, and motor vehicle accidents are particularly associated with deprivation. Targeting should be taken into account when injury prevention strategies are being developed.

INTRODUCTION

Epidemiology of Injuries to Children

Injuries represent a major cause of morbidity and mortality in the paediatric and young adult population of the developed world. In Northern Ireland, with an under-16 population of 398,000, 100,000 injured children seek medical attention each year, of whom over 5,000 are admitted to hospital, and 50 succumb.[1-2] Epidemiological studies have tended to use injury-related mortality as a surrogate for injury rate, and have shown that over the past two decades there has been a significant decline in deaths.[3] It seems, however, that this is due at least in part to improved hospital care of seriously injured patients (i.e. tertiary prevention) rather than a true decline in incidence of injuries.[4]

Relationship between Socio-Economic Status and Injuries

Understanding the socio-economic patterns of injury is important for provision of services and the targeting of resources toward accident/injury prevention. In addition, the magnitude of any injury risk gradient between affluent and deprived groups gives an indication of the potential for improvement if inequalities are addressed. Furthermore, an understanding of the mechanisms by which socio-economic status influences the risk of injury may allow for better understanding of the causation of injuries.[5]

Higher rates of injury have been found in the lower socio-economic groups in several studies worldwide.[6-9] In the United Kingdom, mortality rates

1. Royal Belfast Hospital for Sick Children.
2. Departments of Child Health & of
3. Epidemiology & Public Health.
4. Queen's University of Belfast and Child Accident Prevention Trust, Northern Ireland.

* Correspondence to JFTG, 12 Old Coach Road, Belfast BT9 5PR, Northern Ireland.

due to injury show a steeper social class gradient than any other cause of death.[10] In the Trent region, Hippisley-Cox *et al*[11] studied a total of 56,629 hospital admissions in the age range 0-14 years, and found higher injury rates and greater severity of injuries in electoral wards with greater deprivation; and identified specific causes of injury most closely associated with deprivation.

It has been suggested not only that a socio-economic gradient in injury rate exists, but that this is widening, as accident prevention initiatives meet with more success among more affluent segments of society.[12, 3] Greater understanding of causative factors in childhood injury is therefore required if injury prevention initiatives are to be successful across the socio-economic gradient.

North and West Belfast

North and West Belfast (NWB) is an area with a high rate of emergency department attendance due to injury, and is also an area where social deprivation is widespread.[13] We therefore designed a study to examine the relationship between social deprivation and childhood injury in NWB.

METHODS

We utilised information captured from emergency department attendances after childhood injury to compare calculated injury rates between the most and least deprived districts, and to compare causes, location, and severity of injuries in the two groups. This was part of a broader prospective study of the injury profile in NWB for which AG was immediately responsible.

Patient Sampling

The four study centres involved were the paediatric emergency department at the Royal Belfast Hospital for Sick Children (RBHSC) and three general emergency departments at Belfast City Hospital, Lagan Valley Hospital and Mater Infirmorum Hospital, none of which provides secondary care paediatrics.

Children aged 0-12 years who attended any of these departments following injury and whose home address was within the postal districts BT 11-15 and BT17 were eligible for inclusion in this study. The sample was collected every fourth day over the 12-month period from 2nd January to 31st December 2001.

Data Recording

A dedicated Injury Surveillance Module (ISM) computer package was used to record injury data in the RBHSC. Clerical staff and triage nurses were asked to input data on a number of variables relating to the injury, including location (eq home, school etc.) and cause, of which there are 31 in all, based on the Victorian Emergency Minimum Dataset.[14] For ease of analysis these were condensed into 13 categories; eg bicycle, vehicle etc. Anatomical diagnosis was also recorded. All staff using the ISM underwent training in its use. In the absence of the ISM in the other three centres, data was obtained at regular intervals by AG visiting the departments in person and scrutinising the clinical records, to add to the dataset. A patient was included in the study only if there was a one-to-one match between the BT address code and an enumeration district (defined below).

Patient "disposal" was used as a simple indicator of seventy. Injuries treated solely in the emergency department were classified as minor; those for which outpatient follow-up was thought necessary, as moderate; and those requiring hospital admission as severe.

Noble Index

The Noble Index ,[13] a measure of social deprivation specifically designed to provide detailed information for Northern Ireland, is based on a total of 45 indicators. Examples of indicators used to calculate the Noble Index include uptake of state benefits, crime rates and unemployment rates. A Noble Index Multiple Deprivation Score is available for each electoral ward in the Province. A number of subdivisions of the overall Noble Index are also available, including economic, social environment, and education-related indices, some of which are available at enumeration district (ED) level. Enumeration districts are small units comprised of around 200 households, into which electoral wards are divided. We used economic deprivation scores as a measure of socio-economic status; a high Noble deprivation score implies greater deprivation, and vice versa.

Demographic Information

Northern Ireland mid-census estimates of population were obtained (NISRA, personal communication).

TABLE

Comparison of Injury Rates by Cause of Injury

Cause of Injury	EDs Under Study (n=20)	Mean Injury Rate by Cause (per 1000 Children)	Std. Deviation	Relative Risk	p
Vehicle	Least Deprived	0.94	2.99		
	Most Deprived	2.70	5.75	2.88	0.23
Bicycle	Least Deprived	0.95	2.33		
	Most Deprived	2.30	4.25	2.43	0.22
Pedestrian	Least Deprived	0.74	2.30		
	Most Deprived	0.97	2.49	1.32	0.76
Other Transport	Least Deprived	1.34	3.38		
	Most Deprived	1.60	3.32	1.19	0.80
Animal-related	Least Deprived	0.00	0.00		
	Most Deprived	1.08	3.06	NIA	0.13
Burns and Scalds	Least Deprived	0.46	2.06		
	Most Deprived	1.66	2.74	3.65	0.13
Collision with Object	Least Deprived	5.19	6.83		
	Most Deprived	11.36	10.86	2.19	0.04
Collision with Person	Least Deprived	0.80	2.49		
	Most Deprived	2.26	4.27	2.83	0.20
Foreign Body	Least Deprived	0.89	2.74		
	Most Deprived	2.56	4.05	2.89	0.14
High Fall (>1 metre)	Least Deprived	0.80	2.50		
	Most Deprived	2.82	4.52	3.52	0.09
Low Fall (<1 metre)	Least Deprived	12.31	9.16		
	Most Deprived	23.34	18.35	1.90	0.02
Ingestion	Least Deprived	0.00	0.00		
	Most Deprived	2.08	5.92	N/A	0.13
Miscellaneous	Most Affluent	0.92	2.89		
	Most Deprived	0.91	2.36	10.99	0.99

Year-specific age data are not available in the public domain; the availbale 0-15 years population data multiplied by 0.81 were usd to estimate the 0-12 years population data within each ED. The latter are appropriate denominators for calculating injury rates for the majority of the causes of injury in the Table. One cause of injury for which the use of such denominators is inappropriate is bicycle – the correct denominator would depend on rates of bicycle ownership and helmet wearing, and perhaps traffic densities.

Data Compilation and Statistical Analysis

Microsoft Excel was used to compile a dataset for each ED in the study containing information on economic deprivation level, the estimated number of children under 12, the number of injuries, cause, location, and clinical diagnosis. From these data were derived both overall injury rates and injury rates categorised according to cause, location, severity, and anatomical diagnosis. Statistical analysis was carried out using SPSS v 11. Student's t-test was used to compare rates between the most deprived and least deprived areas. The significance level for all calculations was 5%.

RESULTS

The sample consisted of 479 injuries from 91 Enumeration Districts. A description of the injury profile will be given in another paper.

Economic Deprivation and Injury Rates

Noble economic deprivation scores and injury rates were plotted for each of the 91 EDs in question (*Figure 1*). Correlation analysis showed a significant positive correlation between economic deprivation and rates of injury for the EDs studied ($r = 0.25$, $p = 0.001$).

We selected the twenty EDs with the highest Noble Economic Deprivation scores (range 50.11 to 85.14, mean = 59.42), and the twenty with the lowest (range 0.47 to 16.49, mean = 7.71) – i.e. the most deprived and the least deprived – for further analysis. A highly significant difference in rates of injury was present between the most and least deprived EDs (mean injury rate/1,000 children 60.3 vs 28.2, $p < 0.001$, RR=2.14).

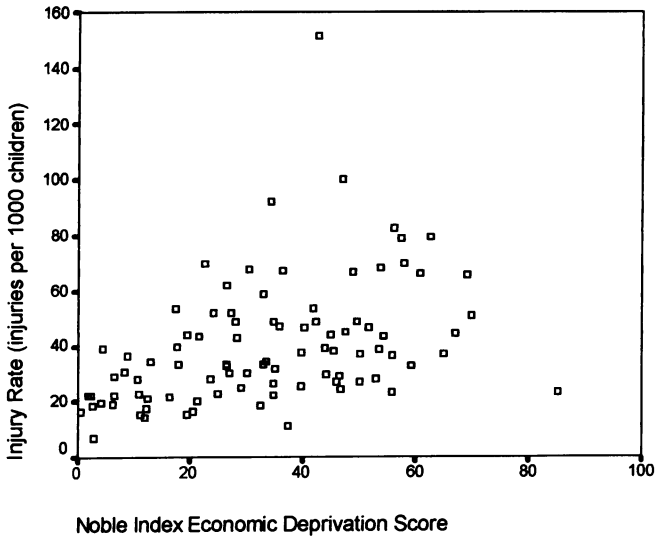

Fig 1. Scatter Diagram of Injury Rate against Economic Deprivation. Each point on the graph represents an ED.

Economic Deprivation and Causes of Injury

Thirteen coding options were available to record cause of injury. For each of these, we compared the rate of injury between the most deprived and least deprived groups (Table). In all but one, the rate of injury was greater in the most deprived districts compared with the relatively less deprived districts. However, this reached statistical significance in only two of the 13 causes of injury – namely, low falls and collisions with an object.

Economic Deprivation and Location of Injury

Significant differences were present between the most and least deprived areas in rates of injury both within the home (mean injury rate 24.5 vs 13.3 /1000 children, $p = 0.01$, RR = 1.84) and outside the home (including schools, roads, etc) (mean injury rate 24.6 vs 10.7/1000 children, $p = 0.001$, RR = 2.29). However, the difference was greater for injuries outwith the home than for home injuries (RR=2.29 vs 1.84).

Within the group of injuries occurring outwith the home, a highly significant difference was evident in injuries due to accidents on the road (mean injury rate 16.8 vs 5.1 / 1000 children, $p = 0.002$, RR=3.25). When road accidents were excluded, however, this difference was no longer present.

Severity of Injuries

Likewise we compared severity of injuries between the most deprived and least deprived areas (*Figure 2*).

The rates for mild injuries (38.0 vs 17.0/1000 children, p ≤(0.001, RR = 2.24) and moderate injuries (18.5 vs 8.7/1000 children, p = 0.001, RR = 2.12) were significantly higher among children in the more deprived EDs. This was not true, however, for injuries classed as severe (3.84 vs 2.51/1000 children, p = 0.38, RR = 1.53).

Since the rate of severe injury was low, we selected fractures as an objective marker of relatively severe injury - i.e. some requiring admission, but all in need of some follow up. The rate of fractures differed significantly between the two groups (8.0 vs 3.6/1000 children, p = 0.04, RR = 2.24). There was no relationship between the presence of a fracture and the cause of injury – likely due to small numbers.

DISCUSSION

Economic Deprivation and Injury Rates

We found a statistically significant correlation between economic deprivation and rate of injury. For further work, we compared directly the most deprived areas with the least deprived. By comparing an average injury rate for the 20 most deprived EDs with that in the 20 least deprived, we confirmed the previously noted correlation between economic deprivation and injury rate, with a relative risk of injury of 2.14 ≤(P0.001) for the most deprived over the least deprived districts.

The most recent population figures available were mid-census estimates dating from 1996, and were thus 5 years older than the actual injury data. This anomaly might be sufficient to explain our findings only if the number of under-12 year olds had dramatically increased in the most deprived areas between 1996 and 2001. This would lead to an underestimate of the number of children in these more deprived areas and a falsely high estimate of injury rates. Conversely, if the number of children in the less deprived areas had declined significantly, this could result in a similar bias. Within the context of the area under study, we are unaware of evidence to support either of these putative demographic trends.

Our findings accord with other literature on this topic. They were, for example, comparable to those of Hippisley-Cox et al,11 who found the difference in injury-related paediatric hospital admissions between the 20% most deprived electoral wards compared to the least deprived to be highly significant (RR=1.96).

Causes of Injury

We compared rates of injury due to each cause or mechanism of injury between the most and least deprived EDs *(Table)*. For all causes of injury except the miscellaneous category, the rate was higher in the more deprived areas. For several categories,

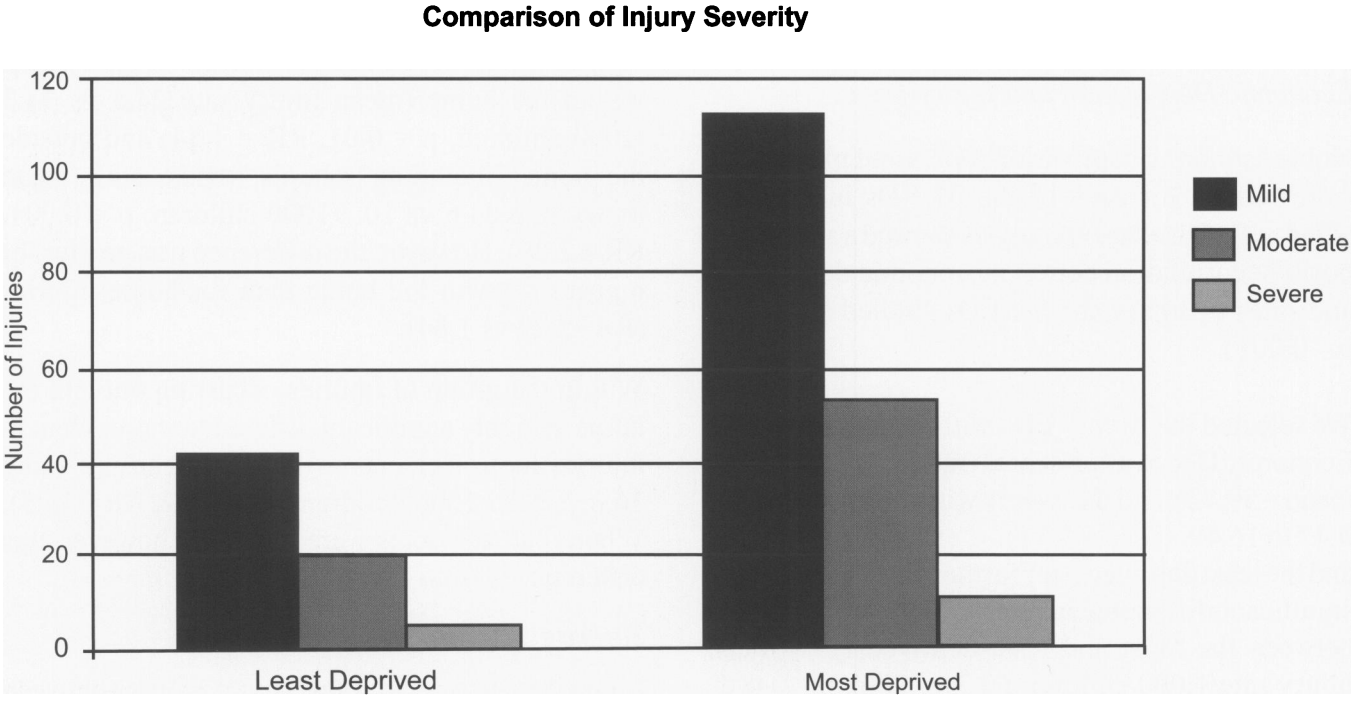

Fig 2. Injury Severity compared between Most and Least Deprived Areas.

the relative risk of injury due to the specific cause exceeded 2.0. Although statistical significance was not reached for the majority of causes, this probably reflects the small numbers involved.

In the study by Hippisley-Cox *et al*,[11] six causes of injury were shown to be significantly associated with deprivation: pedestrian injuries (RR = 3.65), burns and scalds (RR = 3.49), ingestion of toxic substances (RR = 2.98), bicycle-related injuries (RR = 1.61) falls (RR = 1.53), and other transport injuries (RR = 1.25). Our findings were consistent with this much larger study.

Location of Injury

Injuries outwith the home were more strongly associated with economic deprivation than injuries within the home, a finding that is accounted for almost entirely by injuries on roads. This finding is noteworthy since it identifies a specific location where inequalities are important in determining risk. There are many potential factors which may form the basis for this finding: differential impact of road safety initiatives across the socioeconomic gradient, access to safe play areas, and differences in driver behaviour or alternatively, risk-taking behaviour by children. This is a challenge for various groups and professions as diverse as the Department of Environment and Belfast City Council, the police, as well as health professionals – not to mention parents themselves. Moreover, our findings suggest that greater effort should be focused upon more deprived areas rather than more generally as might be the case at present.

Seventy of Injury

We found a strong association with economic deprivation for minor and moderate injuries. Statistical significance was, however, not reached for severe injuries. Although this would suggest attendance bias as an explanation for our positive findings, there is little evidence in the literature to suggest that attendance rates are directly related to socioeconomic status. Distance from an accident and emergency department has, however, been shown to correlate inversely with attendance.[15-16] Since accident and emergency departments tend to be located closer to inner city areas than more affluent suburbs, this is a potential confounding variable. However, in our study, the most and least deprived areas were in close proximity (although the entire area under study could be described as deprived), and the most likely explanation for the failure to detect a difference in rates of severe injuries is therefore the relatively small numbers of injuries in this category.

On the basis of earlier work in NWB carried out by one of us (JFTG), it is known that 77% of injured children are brought directly to an emergency department; few of those seen at general practice required onward referral (4%).[17] However, any attendance bias is likely to apply equally to the most and the least deprived EDs. In addition, the severity scale used was somewhat crude. For these reasons we selected fractures as an example of more severe injury that because of the degree and uniformity of symptoms we would expect virtually 100% attendance at casualty, thus further eliminating possible bias; and in the work just cited, seven of the eight who sustained bony injury did not go to a GP but attended emergency directly.[17] A significantly higher rate of fractures in more deprived areas therefore gives further credence to the overall finding of higher injury rates in this socio-economic group.

CONCLUSIONS

This small prospective study based on data collection every fourth day throughout 2001 demonstrated an association between socioeconomic deprivation (as measured using a locally specific index) and childhood injuries within North and West Belfast. It identifies a number of causes of injury which show a particularly strong association with economic deprivation, particularly those outside the home (i.e. motor vehicle accidents). These findings suggest pointers for future research, and further, that injury prevention initiatives be focused particularly in the most deprived districts of Northern Ireland.

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Magnetic Resonance (MR) imaging of lumbar spine:

Use of a shortened protocol for initial investigation of degenerative disease

CP Mullan, BE Kelly

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SUMMARY

Purpose: **To assess the potential use of shortened protocol MRI of lumbar spine in the investigation of degenerative disc disease in Northern Ireland.**

Materials & Methods: **Prospective study of 35 patients having MR imaging of lumbar spine performed during a 12-month period by one consultant radiologist. T1-weighted and T2-weighted sagittal images of lumbar spine were obtained in all cases, as well as T2-weighted axial images. The detection of degenerative disc disease by sagittal T2-weighted imaging alone was compared with the diagnostic information obtained by combined use of axial T2 and sagittal T1 and T2 images.**

Results: **In comparison with the full protocol, the shortened protocol had 100% sensitivity and 100% specificity in detecting loss of disc hydration and loss of disc height. In the detection of disc prolapse, the sensitivity was 87% and the specificity was 91% using the shortened protocol. The sensitivity was 35% for detection of thecal sac indentation, and 33% for nerve root encroachment. Therefore, the shortened protocol had high sensitivity and specificity in the detection of disc degeneration and prolapse, but was less sensitive in the detection of nerve root or thecal sac encroachment.**

INTRODUCTION

Degenerative disease of the lumbar spine is a common cause of low back and lower extremity pain. Patients presenting with these symptoms often have imaging studies performed to determine if there is a significant structural abnormality in the lumbar spine. Plain film examination of the lumbar spine is the usual initial imaging technique but provides only limited diagnostic information.[1] Myelography-based examinations have largely been replaced by magnetic resonance imaging (MRI) and computed tomography (CT). MR imaging has a high degree of accuracy in delineating disc abnormalities and demonstrating whether neural tissue is compressed. Figure shows a selected image from a sagittal T2-weighted MR sequence, demonstrating loss of hydration of the L415 disc due to degenerative disease.

Magnetic resonance scans of lumbar spine form a substantial proportion of MR examinations performed in many centres.[2] Despite advances in scanning techniques, MR imaging requires relatively long scan times, limiting the number of examinations which can be performed. A study performed by Robertson *et al* indicated that a rapid MR protocol was an accurate screening investigation

Royal Victoria Hospital, Grosvenor Road, Belfast BT12 6BA

Department of Radiology:

CP Mullan, MRCP, Specialist Registrar in Radiology

BE Kelly, MD, FRCS, FRCR, FFRRCSI, Consultant Radiologist

Correspondence to Dr Kelly

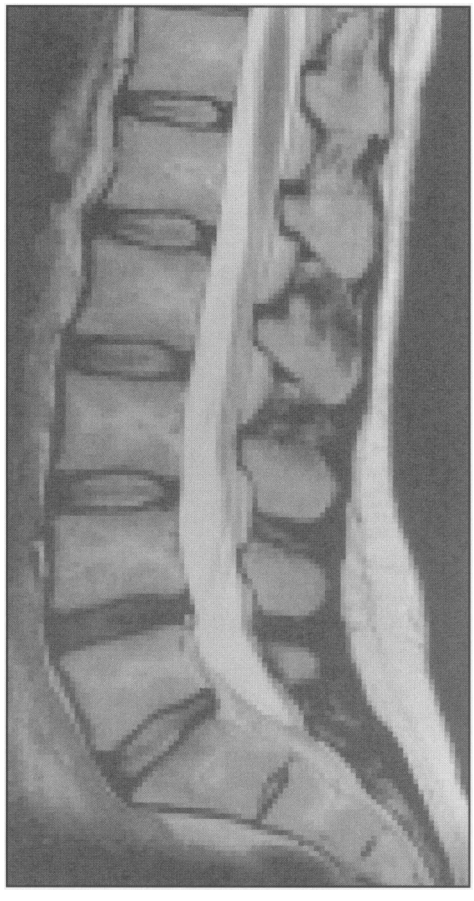

Figure Selected image from sagittal T2-weighted MR sequence of lumbar spine.

for lumbar spondylosis.[1] The aim of our study was to determine the potential application of shortened protocol MR in local clinical practice, in light of the recent expansion of MR facilities in Northern Ireland. If sufficient diagnostic information can be obtained with a shorter acquisition time, it would be possible to image a larger number of patients and reduce waiting times.

METHOD

This was a prospective study of 35 sequential patients having MR examination performed for suspected lumbar spine degenerative disease over a 12-month period. Sagittal T1-weighted, sagittal T2-weighted, and axial T2-weighted sequences were obtained by standard technique in all cases. The diagnostic information obtained from the sagittal T2-weighted sequence was first recorded. The final report was subsequently compiled by interpretation of all 3 sequences. Comparison was therefore made between the diagnostic information obtained by the full protocol and the proposed shortened protocol of sagittal T2-weighted images only. All scans were interpreted by one consultant radiologist. The presence of disc prolapse was assessed at each of 5 intervertebral levels, ie L1/2, L2/3, L3/4, L4/5, L5/S1. In addition, the following items were assessed as present or absent – loss of disc height, loss of disc hydration, annular disc tears, nerve root encroachment, and thecal sac indentation.

Patients were imaged using a 1.5 tesla Philips Intera system. The sagittal T1-weighted sequence was performed using TR 400 ms, TE 11 ms, matrix 512 x 384, slice thickness 4.4 mm, interslice gap 0.4 mm, field of view 325 mm, acquisition time 4 min 24 sec. The sagittal T2-weighted sequence was performed using TR 3500 ms, TE 120 ms, matrix 512 x 384, slice thickness 4.4 mm, interslice gap 0.4 mm, field of view 325 mm, acquisition time 3min 54 sec. The axial T2-weighted sequence was performed using TR 2500 ms, TE 120 ms, matrix 512 x 384, slice thickness 4.0 mm, interslice gap 0.4 mm, field of view 225 mm, acquisition time 4 min 52 sec.

RESULTS

The mean age of the patients studied was 54.5 years (standard deviation 18.1 years), with male: female ratio 0.84. Five disc levels were assessed for each of the 35 patients, yielding 175 disc evaluations in all. The sensitivity and specificity of the shortened protocol was calculated using the detailed protocol as the reference standard. In comparison to the

TABLE I

Sensitivity and specificity of shortened protocol for various parameters.

	Sensitivity %	Specificity %
Loss disc height	100	100
Loss disc hydration	100	100
Annular disc tears	73.7	100
All disc prolapses	86.7	90.8
Central prolapse	87.5	90.4
Lateral prolapse	40.0	100
Thecal indentation	35.3	100
Nerve root encroach	25.0	100

TABLE II

Detection of all types of disc prolapse

	Positive on full protocol	*Negative on full protocol*
Positive on shortened protocol	39	12
Negative on shortened protocol	6	118

TABLE IV

Detection of lateral disc prolapse

	Positive on full protocol	*Negative on full protocol*
Positive on shortened protocol	4	0
Negative on shortened protocol	6	165

full protocol, the shortened protocol had 100% sensitivity and 100% specificity in detecting loss of disc hydration and loss of disc height (*Table I*). For annular disc tears, the sensitivity was 73.7% and the specificity was 100% (*Table I*).

Table II shows the detection of all types of disc prolapse by the full and shortened imaging protocols. The detailed protocol demonstrated a total of 45 disc prolapses in the group of 175 discs evaluated. 39 of the 45 prolapses were detected on the shortened protocol, while 12 discs declared prolapsed on the shortened protocol were found to be normal on the full protocol. This resulted in sensitivity of 86.7% and specificity of 90.8% for the shortened protocol in the detection of all types of disc prolapse.

Of the 40 central disc prolapses found on the full protocol, 35 were detected on the shortened protocol (*Table III*). The calculated sensitivity was 87.5% and the specificity was 90.4% in the detection of central disc prolapses. Table IV shows the detection of lateral prolapse of intervertebral discs. A total of 10 lateral disc prolapses were detected using the full protocol,

TABLE III

Detection of central disc prolapse

	Positive on full protocol	*Negative on full protocol*
Positive on shortened protocol	35	13
Negative on shortened protocol	5	122

four of which were seen on the shortened protocol. The sensitivity was 40.0% and the specificity was 100% for the shortened protocol in the detection of lateral disc prolapse.

CONCLUSIONS

The shortened protocol would be a suitable initial investigation for suspected degenerative disc disease, in view of the short acquisition time required. More detailed imaging would be indicated for patients with significant abnormality on the shortened MR examination. Initial investigation by MR would reduce radiation exposure incurred in lumbar spine radiographs and provide greater diagnostic information.

The detailed protocol detected 17 prolapsed discs which were causing thecal sac indentation, with only six of these discs detected by the shortened protocol. The shortened protocol therefore had sensitivity of 35.3% and specificity of 100% in the detection of thecal sac indentation. Of the four discs causing nerve root encroachment on the detailed protocol, one was detected on the shortened protocol. The sensitivity was 25.0% and the specificity 100% for nerve root encroachment by prolapsed discs.

DISCUSSION

The shortened protocol was reliable in the detection of disc degeneration, with high sensitivity and specificity for loss of disc height and loss of disc hydration. The shortened MR imaging protocol was mostly reliable in visualising annular disc tears, with sensitivity of 73.7% and specificity of 100%. In the detection of all types of disc prolapse, the shortened protocol was relatively accurate with sensitivity of 86.7% and specificity of 90.8%. In

particular, the shorter examination was reliable in visualising central prolapse, the most common type of intervertebral disc prolapse in the study. However, the shortened protocol was less satisfactory in detecting lateral disc prolapses, with sensitivity of 40%. The sensitivity of the shorter MR examination in the detection of thecal sac indentation (35.3%) and nerve root encroachment (25%) was also relatively low, although specificity was 100%.

Overall, the shortened protocol for MR imaging of the lumbar spine was satisfactory in assessing disc degeneration, disc tears, and most types of disc prolapse. The shorter examination was limited in the ability to detect lateral disc prolapse, thecal sac indentation and nerve root encroachment. However, all of the patients with lateral disc prolapses which were not detected on the shortened protocol had other evidence of degenerative disease that was found on this protocol. This demonstrates that MR imaging with the shortened protocol would be a suitable initial investigation for patients with low back pain due to suspected degenerative disc disease. Detailed MR examination would be indicated for those patients with significant anomalies detected on the shortened protocol, such as large disc protrusions, abnormal bone marrow or spinal cord lesions.

MR facilities are becoming more widely available in hospitals throughout Northern Ireland. As access to MRI increases, a shortened protocol such as that used in this study could replace plain films as the initial imaging investigation for low back pain. The yield of plain films in the work-up of patients with low back pain is low.[1] The Royal College of Radiologists recommends MRI as the first-choice investigation for patients with persistent or severe back pain.[4]

TABLE V

NRPB reference does for lumbar spine radiographs

View	*Dose Area Product*
Lumbar spine AP	1600 mGy cm2
Lumbar spine lateral	3000 mGy cm2
Lumbar spine LSJ	3000 mGy cm2
Total for 3 views	7600 nGy cm2

MRI of lumbar spine enables visualisation of disc hydration changes, end plate changes, and the nature of disc prolapse. This approach would also reduce medical radiation exposure as MRI does not involve the use of ionising radiation. As shown in Table V the national reference radiation dose for plain film lumbar spine examination with three views is dose area product (DAP) of 7600 mGy cm2.[3] Accordingly, the calculated risk of inducing a fatal cancer due to a plain film examination of lumbar spine is 1 in 15,400. The calculated risk of inducing non-fatal cancer is 1 in 2,080. Approximately 21,000 plain film lumbar spine examinations are performed each year in Northern Ireland, therefore inducing 1.36 fatal cancers and 10.10 non-fatal cancers.

In summary, this study shows that a shortened MR examination of lumbar spine using a sagittal T2-weighted sequence is effective in detecting degenerative disc changes and most types of disc prolapse. The vast majority of treatable lesions will therefore be detected by use of the shortened protocol. The shorter acquisition time and the increasing availability of MRI facilities mean that this examination is becoming more suitable than plain film radiography in the initial assessment of patients with low back pain. This approach would improve diagnostic yield and reduce the risk of radiation-induced malignancy due to medical exposure in the Northern Ireland population. Widespread implementation of the shortened protocol examination would require sufficient resources to maximise the use of MRI facilities.

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If I can see so far

Annual Oration: Royal Victoria Hospital Belfast, October 2004

JM Hood

The title of this oration is based upon a quotation from a letter which Sir Isaac Newton wrote to Robert Hooke, the well known 17th century scientist; and among other things, the inventor of the compound microscope. The letter was written in February 1675. "If I have seen further it is because I stand on the shoulders of those giants that have gone before".

I must thank the Medical Staff of the Royal Victoria Hospital for the great honour that they have bestowed upon me today in asking me to deliver the 2004 Oration. It is interesting to note that in 1852, when Dr Andrew George Malcolm was giving this oration he stated that the oration was "an old established custom". From the first Oration in 1827 until 1883 the opening address probably took the form of the 1st clinical lecture of the teaching year. In 1883 it is recorded in the Medical Staff Minutes of the Belfast Royal Hospital that there should be "an introductory address" given annually, and so the tradition continues to this day.

"The Science of Medicine has for its object the emancipation from disease of those who are afflicted by it, and the preservation of the health of those who possess it".

This is not a definition of medical practice obtained from a recent textbook but rather that of the ancient Indian physician Sush Mita, writing sometime around 500-600AD. I think that the second part of the definition is the most remarkable, as it clearly alludes to the role of medicine in preventing disease as well as its role in treatment.

Over the years many have argued as to whether surgery is an art or a science. I think that the answer cannot be better stated than in the words of St Francis of Assisi (1181-1226), who wrote many years ago:

> "He who works with his hands is a labourer.
> He who works with his hands and his head is a craftsman.
> He who works with his hands, his head and his heart is an artist".

I suggest to you today that the last line denotes the essential requirements for a surgeon. All three components are necessary attributes for a successful surgeon ie manual dexterity, intellectual ability and compassion for ones fellow man. Students present who wish to pursue a surgical career would do well to remember this, and to work towards achieving expertise in all three areas. Manual dexterity comes with practice, knowledge from learning, but compassion comes from within.

One other wise piece of advice for us all, and for the students in particular, comes from a famous medical author. One not best known for his textbooks, but rather his novels none other than Sir Arthur Conan Doyle. In one of his Sherlock Holmes novels, "A Study in Scarlet" he writes:

> "You see. I consider that a man's brain originally is like a little empty attic and you have to stock it with furniture as you choose. A fool takes in all lumber of every sort that he comes across, so that the knowledge which might be useful to him gets crowded out, or at best is jumbled up with a lot of other things so that he has difficulty in laying his hands upon it. Now the skilful workman is very careful indeed as to what he takes into his brain attic."

This morning I want to reflect upon some of our predecessors who have made significant contributions to our current knowledge in the medical field. I would liken this knowledge to an as yet incomplete jigsaw to which many have contributed pieces both large and small but all fit together – eventually – to give us a more complete picture.

As yet, many parts are missing, and it is for you, the students and young doctors in the audience, to contribute further pieces to our puzzle.

JM Hood, Mphil, FRCS, Consultant Vascular Surgeon, Royal Victoria Hospital, Grosvenor Road, Belfast BT12 6BA.

Clearly it is impossible to mention all who have made contributions to our jigsaw, so I claim the orator's privilege to single out a number of people who in my opinion have made significant advances. Some of these are well known and some not so. Many are international figures and some have associations with our Medical School and in particular the Royal Victoria Hospital. In making my selections I have been interested not only in the contribution that these individuals have made to medical progress, but also in looking at what personal attributes they had, apart of course, from the ability to have original ideas, or in modern parlance "to think outside the box".

I would like to focus on the branches of surgery with which my professional career has been most closely associated, namely vascular and transplantation surgery.

The transformation of a part of one individual into another has been a recurring theme throughout lore and literature since the earliest time and an abundance of examples exist. To name but a few, snakes coiled from Medusas' scalp: those who caught her glance turned to stone. Homer sang of the Sailors of Ulysses transmogrified into swine by the enchantress Circe. Indeed, his chimera, part goat, part lion, and part dragon, has become a modern symbol of clinical transplantation.

In the Bible Christ restored the ear of a servant of the High Priest following its amputation by an angry Simon Peter. St Peter having witnessed this accomplishment, was later able to replace the breasts of St Agatha which had been pulled off with tongs during torture.

Probably the best known early record of transplantation is that attributed to the third century twin brothers Cosmas and Damien. They were born in Cilicia in Asia Minor. They were Christians who performed great deeds of charity never accepting a fee for their services. An elderly servant of the church who was to become St Justinian, developed a gangrenous leg. Following a long prayer to one of his patrons, Justinian fell asleep, and Cosmas and Damien appeared before him. The brothers amputated his diseased leg and thereupon remarked that a Moorish slave had been buried on the same day at St Peters cemetery. Cosmas and Damien went to the slave's grave, exhumed the body, and amputated the dead man's leg. They then reattached it to their patient's stump. When Justinian awoke he had one black and one white leg. Unsure of whether or not he had been dreaming, Justinian went to the cemetery and there next to the slave lay his diseased white leg. There are many paintings of this feat. This particular one hangs in the Prado Museum in Madrid. Cosmas and Damien died martyrs, and are widely regarded today as patron saints of transplantation. (Illustration 1).

Figure 1

Vascular Surgery now has an increasingly wide remit, but a very important area concerns the repair of aneurysms. Antyllus was a pioneering Greek surgeon living in the late 3rd and early 4th century. He wrote extensively on the pathology and surgical treatment of aneurysms. The following is a quotation from his writings sorted by Oribasus –

> "There are two kinds of aneurysms. In the first the artery has undergone a local dilatation; in the second the artery has been ruptured. The aneurysms that are due to dilatation are longer than the others. The aneurysms caused by rupture are more rounded. To refuse to treat any aneurysm, as the ancient surgeons advised, is unwise; but it is also dangerous to operate upon all of them. We should refuse, therefore, to treat aneurysms which are situated in the axilla, in the groin, and in the neck, by reason of the volume of the vessels and the impossibility and danger of isolating and tying them. We should not touch an aneurysm of large volume even when it is situated in some other part of the body."

Antyllus went on to describe ligation of the artery both proximal and distal to the aneurysm, followed by opening the sac and evacuating the contents. This method of treating aneurysms was forgotten for centuries until, as you will hear later in this oration, it was "rediscovered" by Rudolph Matas in 1888.

For many centuries vascular surgery made little or no progress until another of the early surgical "Giants" appeared on the scene. I allude to Ambrose Paré (1510-90). In 1536 he joined the French Infantry and his first campaign was in the same year in Northern Italy against Charles V. The Battle of Chateau de Villane was especially fierce, and there were so many casualties that Paré ran out of supplies of oil which, at that time was boiled and applied to wounds, especially amputation stumps. He therefore had to develop an alternative. He described the circumstance of his discovery thus. "I was at that time a fresh-water surgeon, since I had not yet seen treated, wounds made by firearms. It is true I had read Chapter 8 of Jean de Vigo's book. *Wounds in General,* in which it is stated that wounds made by firearms are poisoned by the gun powder. For their cure he advised cauterization with oil of elders mixed with a little theriac. To not fail, this oil must be applied boiling, even though this would cause the wounded extreme pain. I wished to know how the other Surgeons did their first dressings, which was to apply the oil as hot as possible. So I took heart to do as they did. Finally my oil was exhausted and I was forced to apply instead a digestive made of egg yolk, rose oil and turpentine. That night 1 could not sleep easily, thinking that by failure of cauterizing, I would find the wounded in whom I had failed to put the oil, dead of poisoning. This made me get up early in the morning to visit them. Then, beyond my hope, I found those on whom I had used the digestive medication, feeling little pain in their wounds, without inflammation and swelling, having rested well through the night. The others on whom I had used the oil, I found feverish, with great pain, swelling and inflammation around their wounds. Then I resolved never again to so cruelly burn the poor wounded by gunshot".

His important book Dix Livres de Cherugu was published in 1564, making three very important points. Firstly the abandonment of hot cautery, secondly the role of ligation of bleeding vessels in deep wounds and thirdly the benefit of ligating vessels during the course of an amputation, as opposed to the old practice of applying a red hot cautery iron to an amputation stump.

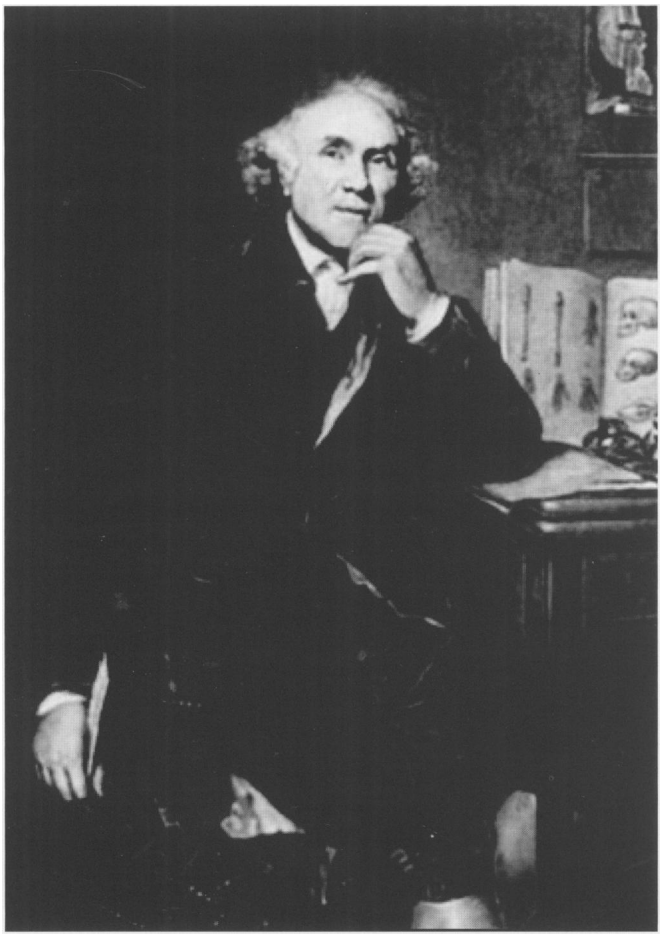
Paré was a good anatomist and by far the greatest surgeon of his time. He was the friend of four successive kings of France, Henry II, Francis II, Charles IX and Henry III, and he was said to be the only Protestant in Paris to survive the St Bartholomew's Day Massacre on August 24th 1572. This was attributed to the direct actions of the king.

Any consideration of the history of Vascular Surgery would be very incomplete without a mention of the two famous Hunter brothers. Their father was a Scottish farmer who farmed at Long Calderwood near East Kilbride. The elder brother William was born in 1718. He received a good classical education and went to study medicine at Edinburgh University.

William Hunter taught anatomy at various locations, culminating in the establishment of the famous Great Windmill Street School of Anatomy (near Covent Garden). He was a passionate and gifted teacher believing that a man could do far more for the public by teaching his art than by practicing it. He pointed out that only the few individuals for whom he could care benefited from his practice, but "the influence of a teacher extends itself to the whole nation and descends to posterity".

As well as teaching, William Hunter had a particular interest in aneurysms, publishing two major works on the subject, the first in 1757 and the second in 1761. In the latter publication he was critical of the attempts at treatment of aneurysms at this time and wrote "Ignorance is rash and fearless: knowledge is always cautious and circumspect. The first, amidst much mischief, boasts now and then a random cure: the other, though active when there is a prospect of success, is frequently restrained by the fear of doing harm". This, I would suggest, is another piece of excellent advice far ahead of its time, and still very apposite to the practicing surgeon today.

John Hunter was born 10 years after his brother William and had a very different childhood. He demonstrated no interest in learning and by all accounts his childhood was rather wild. In 1748 at age 20, he went to join his brother in London working in his anatomy school. Here he soon found his vocation showing exceptional ability. Whilst William was mainly an anatomist and teacher, John became a surgeon, and he is known today for putting surgery on a scientific basis as he carried out much research. He is best known for his contribution to the surgical treatment of aneurysms and in particular



John Hunter (1728 - 1793)

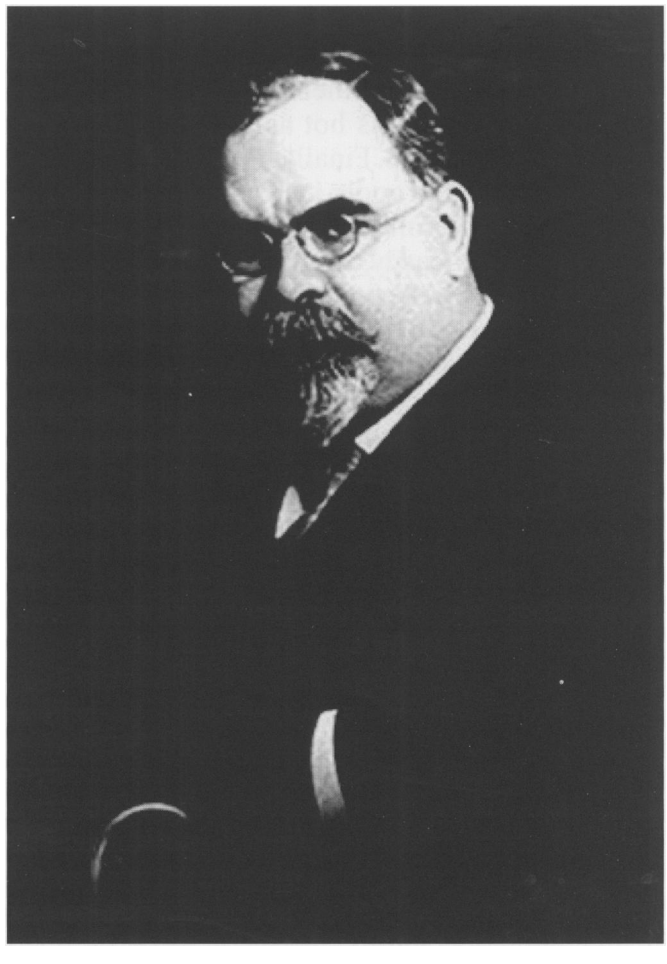
popliteal aneurysms. His most famous patient "A.B." was a 45 year old London coachman who begged John Hunter not to amputate his leg and to do anything he could to save it so that he could continue to earn his living. Over the previous 3 years AB had developed an enlarging pulsatile swelling in his left popliteal fossa. In December 1785, having sedated AB with laudanum, he operated, placing no less than 4 ligatures on the artery well proximal to the aneurysm itself. This proved effective. AB recovered only to die of pneumonia about 1 year later. The operation was recorded for posterity by Hunter's brother-inlaw Everard Home, who was himself a surgeon.

Hunter later modified the operation using only 1 proximal ligature. Over the next couple of years he went on to perform 4 further operations for popliteal aneurysm of which the first died, but the other 3 survived without limb loss. After this he handed his aneurysm patients over to his brother-in-law Everard Home, who performed many successful operations on popliteal and brachial aneurysms, using what became known as the Hunterian method.

Up until the latter half of the 19th Century all of the major advances in vascular surgery came from Europe, but on the 11th September 1860 a child was born on a remote Louisiana cotton plantation called Bonnet Carre. This child was named Rudolph Matas and he was destined to make a major contribution to vascular surgery. His parents had emigrated from Europe four years earlier, his father, Narciso, obtained a degree in pharmacy from New Orleans College of Medicine in 1858, and in the following year a medical degree. His first post was as a doctor to the cotton plantation on which Rudolph was born

Rudolph's early education was in many locations including Paris, Barcelona, New Orleans and Brownsville Texas. He entered the University of Louisiana (Illustration 3), later Tulane University, and graduated in medicine in 1880. Following this he worked in Charity Hospital New Orleans.

In January of 1888 a young 26 year old plantation worker, Manuel Harris was out shooting rabbits with some friends. He sustained an accidental shotgun wound to his left upper arm. Little could he have known that the treatment of this injury would lead



Rudolph Matas (1860 - 1957)

to surgical advances which would change the field of vascular surgery for ever. Two weeks after the injury Manuel noticed a pulsatile swelling on the medial aspect of his left upper arm. He attended Charity Hosptial where he came under the care of Rudolph Matas. In a situation very reminiscent of John Hunter's patient, the coachman, with a popliteal aneurysm almost 100 years earlier, Manuel impressed upon Matas how important his arm was to him otherwise he would not be able to earn a living. Matas therefore tried to thrombose the aneurysm with both digital compression and compression by means of an Esmarch tourniquet. All failed, and so he operated on Manuel on 23rd April 1888 and performed the standard Hunterian operation of proximal ligation. Initially this seemed successful but within 48 hours the pulsation in the aneurysm returned. Matas re-operated on 2nd May when he performed both proximal and distal ligation, plus opening of the aneurysmal sac to occlude any branches which were back bleeding into it.

Thus the operation, now known as endoaneurysmorraphy, was rediscovered some 15 centuries after Antyllus's original description.
In 1895 Matas was appointed Chief of the Department of Surgery at Tulane University, a post which he held until his retirement in 1927.
In 1923 Matas was the first to successfully ligate an abdominal aortic aneurysm.
In 1949 at the age of 80 years, he reported his personal experience of treating various types of aneurysm to the American Surgical Society. He had performed 620 operations of which 101 were by the technique of endoaneurysmorraphy. The most remarkable aspect of his experience was that these operations were performed with a mortality rate of less than 5%. He also claimed that none of the procedures resulted in gangrene. Vascular surgeons of today would be proud of these results.
Matas was a man of great intellect and sensitivity and in one of his more famous lectures delivered in 1915 entitled "The Soul of the Surgeon", he warned of those who would disgrace their profession for money and fame, and of others who would allow their vanity to eclipse reason and morality. I'm sure you will agree that these are thoughts entirely appropriate to the 21st century.
Matas died at the grand old age of 97 years on 23rd September 1957.

Meanwhile during the late 18th and 19th century the City of Belfast was growing rapidly driven by the industrial revolution, and in particular the role the city played in the production of linen. With the increasing population, so the need for a hospital grew, hence in 1797 in Factory Row "The Belfast Dispensary and Fever Hospital" opened. This was the precursor of the Royal Victoria Hospital of today. In 1815 the need for expansion of the hospital was accepted, and so the foundation stone for a new hospital was laid in Frederick Street. Two years later on 1st August. 1817 the Belfast General Hospital opened. In 1875 the Royal Charter was granted, and the hospital became the Royal Belfast Hospital, only to change its name again in 1899 to the Royal Victoria Hospital Belfast. On 27th July 1903 the new hospital on the Grosvenor Road site was opened by King Edward VII and Queen Alexandra. Most recently, the first phase of the major redevelopment of the hospital was opened by HRH Prince Charles on 2nd September 2003.

The 19th century saw some of the greatest advances in surgery of any century either before or since. Among these advances was the introduction of anaesthesia. The first use of the word anaesthesia is attributed to Oliver Wendell Holmes of Boston (1809-1894). In a letter to William Morton dated 21st November 1845 he used it to describe the state induced by ether. The introduction of anaesthesia resulted in effective pain relief for surgical procedures for the first time.

Chloroform was first used as an anaesthetic in the United Kingdom by John Snow (1813-58), in St Georges Hospital London in 1846. It is interesting to note that the medical staff of the Belfast General Hospital were quick to embrace the new advance. The first mention of the use of chloroform in the Belfast General Hospital was in the Surgical report for the years 1848-49 which was given by Doctor Stewart. It is recorded "42 surgical operations have been performed, several of them under the influence of chloroform. The facts in relation to this agent are not yet sufficiently numerous to enable us to recommend or condone its general use. It is perhaps, however, only right that we take this opportunity of stating that it requires great caution and considerable experience to render its administration safe".

Three years later when the report for the years 1851-52 was being delivered by Dr James Moore, he said that chloroform was being used "in about every case of surgical operation".

Not long after this in 1866, ether came into use but it was not until 1900 that the Royal Victoria Hospital appointed its first two anaesthetists, Victor GL Fielden and RJ Johnstone.

As well as the advent of anaesthesia the 19th century saw another important advance, namely the use of antiseptics as introduced by Joseph Lister in Glasgow.

From 1861-65 between 45-50% of Lister's amputations for trauma died from sepsis. In 1865 Louis Pasteur suggested that sepsis was due to living organisms in the air which entered wounds and caused infection. Lister was quick to recognise the importance of this and he began to use carbolic acid to clean and dress wounds. The first use of carbolic acid in the Belfast General Hospital was also in 1865. Two years later at the annual BMA meeting, Lister was able to make the remarkable statement that no wound infections had occurred in his wards for 9 months, since he had started to use carbolic acid. Later as the nature of bacteria and infection became more fully understood, antiseptic surgery evolved into aseptic surgery.

Returning to developments in Belfast, shortly after the opening of the new hospital in Frederick Street in 1817, the staff proposed that medical teaching should commence and in 1820 the management committee of the hospital accepted this proposal. The following year formal teaching commenced, the first registered pupil being a Mr W Bingham, who after qualifying, practiced in Downpatrick until his death in 1848. Although teaching began in 1820, it wasn't until 1830 that the Royal College of Surgeons of Edinburgh and the University of Glasgow recognised teaching in the hospital as equivalent of any other hospital in the UK.

During those early years of the hospital the students had to obtain their degrees in medicine in some of the universities with medical faculties, eg Edinburgh, Dublin. It was therefore a logical step to set up a Medical School in Belfast and this was eventually established at Inst in 1835, before moving in 1849 to the newly established Queens College, Belfast.

There were a number of important figures involved in the setting up of our medical school, but I want to single out a father and son whose lives spanned the whole of the 19th century. They are Henry MacCormac born in 1800 and his son William who died in 1901, the former a physician, the latter a surgeon. I am indebted to the late Sir Ian Fraser for much of the material on these two interesting men. Sir Ian gave his Presidential address to the Ulster Medical Society in October 1967 on the MacCormacs. Later in October 1982 he delivered the Thomas Vicary Lecture at the College of Surgeons of England on William. I feel that it is time to look at the lives of these two Ulstermen, and to acknowledge their roles in the development of medicine in Ulster, and the United Kingdom as a whole.

Henry was born in Carnan, Co Armagh. His father was a linen merchant who died when Henry was very young leaving his mother with 6 boys and two girls to bring up on a very small income. After an education at the Royal School Armagh he embarked upon medical study in Dublin, Paris and Edinburgh. He obtained his MD from the University of Edinburgh in 1824. He was appointed physician to the General Hospital at age 28 , in 1828. On the establishment of the Medical School in 1835 he became the first Professor of the Theory and Practice of Medicine, a position he held until the establishment of Queen's College, Belfast.

On 17th January 1836 Henry's wife Mary gave birth to her first son (Illustration 4) William in their then residence at 17 Wellington Place. It is probable that he went to school at the nearby "Inst", although there are no records of this. He did attend Queens College

William MacCormac (1836 - 1901)

Belfast, graduating BA in 1855, and MD two years later. He then travelled on the Continent, establishing important and lifelong friendships with surgeons such as Bilroth, Von Esmarch and Lagenbeck. In 1859 he was appointed resident Medical Officer to the Belfast General Hospital at a salary of £100 per annum. In 1864 he obtained the Fellowship of the RCS Ireland, and in the same year was appointed attending surgeon to the Belfast General Hospital.

He was a tall handsome man and not surprisingly was a very eligible bachelor. He eloped with Katherine the daughter of one of the major linen merchants, John Charters. The marriage was a very happy one even though, initially, both families disapproved. The Charters thought their daughter was marrying a penniless surgeon and the McCormacs that their son was marrying into "trade", and not a profession. These views were soon put aside as Williams father in law made a major bequest to the hospital – enabling the Charters Wing to be added to the hospital.

In 1870 William took the very unusual step of resigning from his post in Belfast and going to Paris with Katherine, his aim being to partake in the Franco-Prussian War on the French side.

His first major exposure to war surgery came at Sedan where 12,000 casualties had to be treated. William kept meticulous diaries and among his many observations is one which is of current interest. "Surgeons if constantly overworked, fail to give of their best. It is sound judgement and clear intelligence that begins to fail before actual physical fatigue!"

MacCormac's diary recalled that almost all operations were performed under chloroform anaesthesia, and the wounds were dressed with carbolic acid. This was the first extensive use of these dressings in a war situation.

On many occasions MacCormac repeated what could be a motto for vascular surgeons even today. "A living man with three limbs is better than a dead man with four".

The Franco-Prussian war ended with the siege of Paris, the city capitulating on 28th January 1871.

Just prior to this William MacCormac returned to London. Early in 1871 a vacancy occurred at St Thomas' Hospital, and MacCormac was appointed an Honorary Assistant Surgeon to the hospital at the age of 35 years. Two years later he was appointed to the full surgical staff.

Over the succeeding 20 years MacCormac became a popular figure known to the students as Billy Mac or "The Irish Giant". He frequently attended the wards with his large Newfoundlander dog Baron Bruno, to whom he was devoted. The dog otherwise stayed in his consulting rooms in Harley Street, and was said to be able to tell the difference between old and new patients. When MacCormac went off to his third war, the Boer War, the Turko-Serbian war of 1876 being his second, the dog moped. Although it continued to go for the paper daily, he did so with his tail down. He was delighted to get into the carriage to collect his master on his return. The dog died on 22nd September 1901 at the fair old age of 14 years and it is nice to see that his collar takes pride of place among the large collection of medals and decorations that Sir William accrued during his life time.

Among the many honours bestowed on him was an honorary MCh in 1879 and three years later in 1882 an honorary DSc both bestowed by Queen's University Belfast. In 1881 he was knighted by Queen Victoria. In 1883 he was elected to the council of the RCS England, becoming president in 1896. He had his period of office extended from the then normal 3 years to 4 years, so that he could oversee the centenary celebrations of the college. As far as I am aware he is the only Belfast surgeon to have been president of the English College of Surgeons. In 1897 Queen Victoria made him a Baronet to mark her Golden Jubilee.

After a full and active life he died following a short illness on 4th December 1901 only a few months after his much loved dog Baron Bruno. At the time of his death he was described as the most important Ulsterman since Hans Sloane.

It is impossible to mention all of our predecessors who have made important contributions to the advancement of vascular surgery, but one person deserves a special mention not just for his contributions to vascular surgery, but also his pioneering work in transplantation. That man is Alexis Carrel who was born in the village of Sainte-Foy-des-Lyon a suburb of Lyon on the 28th June 1873. He was baptised Marie Joseph Auguste Balliard but after his father died from pneumonia when Alexis was 4 years old he became known as Alexis Carrel.

Carrel was small in stature, short sighted, with one blue and one brown eye. He commenced his medical education in 1890, and while still a student in 1894 was profoundly affected by an incident when the

then French president, who was visiting Lyon, was stabbed in the abdomen and subsequently died. The cause of death was a laceration of the portal vein which the surgeons were unable to repair. Carrel felt that there was no reason why blood vessels couldn't be sewn, and he decided that he wanted to be able to do this.

At the turn of the century he started experimental work on joining blood vessels, and published his successful early results of anastomosing a dogs femoral artery and vein in 1902.

Because of various disagreements with the medical establishment and his failure to obtain a permanent post in Lyon he left France on 6th May 1904 initially travelling to Montreal. After a short stay he went on to Chicago and obtained a position in the Hull Laboratory of Physiology. Here he encountered Charles Guthrie with whom he would do much experimental surgery.

The techniques which they developed in this period are too many to mention but they included arterial to venous anastomosis, vein interposition grafts, patch grafts on to vessels (still known today as the Carrel patch), and perfection of transplantation anastomotic techniques. If I could single just one important piece of work out, it was the fact that Carrel predicted that the way to repair popliteal aneurysms would not be either that of Hunter or Matas, but would involve the insertion of a vein bypass. This, like much of Carrel's other work, wasn't introduced into clinical practice until after the Second World War.

Guthrie and Carrel carried out work on amputation and re-implantation of dogs legs. It wasn't until 1962 that a successful limb re-implantation was carried out at the Mass General on a 12 year old boy whose arm had been traumatically amputated by a train.

Work on kidney removal followed by re-implantation was performed also in dogs. The first successful kidney transplant in humans was to wait until 1954 when Merril and Murray in Boston, carried out a transplant between identical twins.

In 1906 Carrel moved to the recently established Rockerfeller Institute for medical research where his early work was on the preservation of vein and arterial grafts. In 1909 he began a series of experiments in the field of cardiothoracic surgery: this became possible with the use of endotracheal intubation taught to him by Meltzer. Much work was done on resection and repair of the descending thoracic aorta, and he was the first person to note the occurrence of paraplegia as a consequence of thoracic aortic occlusion. He developed shunts to avoid this complication, several decades before the same techniques were introduced to clinical practice.

In 1912 he received the Nobel Prize for Physiology and Medicine and was the youngest recipient of the prize at 39 years of age.

As well as writing extensively on experimental surgery and physiology, Carrel shared his thoughts about man in the wider scheme of things, and I feel that one quotation is still apposite today. "A great artist, a great scientist, a great philosopher is rarely a great man. He is generally a man of common type, with one side overdeveloped.

Genius can be compared to a tumour growing upon a normal organism. These ill balanced beings are often unhappy, but they give the entire community the benefit of their mighty impulses. Their disharmony results in the progress of civilisation. Humanity has never gained anything from the efforts of the crowd. It is driven onwards by the passion of a few individuals, by the flame of their intelligence, by their ideal of science, of charity and of beauty".

Carrel died in Paris a year before the end of the Second World War, on the 5th November 1944.

One of those individuals whose passion and intelligence has driven forward the development of solid organ transplantation with whom I have had the privilege of working for two very formative years in my career, is Thomas Starzl.

He was born in the small town of Le Mars, Iowa on 11th March 1926. His father owned the local newspaper. Starzl attended Northwestern Medical School in Chicago and went on to Johns Hopkins Hospital Baltimore to do his surgical internship, commencing on July 1st 1952.

The final two years of his residency were completed in Jackson Memorial Hospital Florida.

He then returned to Northwestern to complete a fellowship in thoracic surgery. By then he had decided that he wanted to advance the concept of liver transplantation. Work on dogs started in 1958 and all of the early canine transplants ended in failure with the death of the dog, within, at most, a couple of days. With the support of research grants techniques improved, as did a means of preservation of the donor liver, so that survival for about 1 week became the norm. At this stage rejection occurred.

One of Starzl's major contributions to transplantation was the introduction to clinical practice of the combination of steroids plus azathioprine to control the rejection process. This remained the means of controlling rejection in solid organ transplants until 1979 when Cycloporin A was developed.

In 1962 Starzl moved from Chicago to Denver Colorado, and on 27th March 1962 he carried out the first kidney transplant in Denver – the patient survived for more than 30 years. On 1st March 1963 he performed the first human liver transplant. Unfortunately this proved unsuccessful due to uncontrollable bleeding. The second liver transplant patient survived for 22 days but the following three all died shortly after operation. Therefore in October 1963, having performed 5 transplants, the programme was halted.

In 1967 the scene was set for a further attempt at clinical liver transplantation this time with more, albeit limited, success. Seven children were transplanted, four died after 2, $3^1/_2$, $4^1/_2$ and 6 weeks. Two died with recurrent liver tumours, one aged 19 months at the time of transplant, survived 400 days. The other aged 16 lived for 14 months. The 7th in the series lived for $2^1/_2$ years. In late 1967 a further child had a transplant for biliary atresia, and she was alive, when last heard of, some 23 years post transplant.

I wonder where liver transplantation would be today if Starzl's previous work had been conducted today rather than in the 1960's - 70's. Even for a surgeon with Starzl's amazing determination and drive, I think that it would be difficult to introduce a technique today where all of the first five patients died within a matter of days, what would happen? This was the result of the 1963 initial transplant series. In 1967 when 7 liver transplants were performed 4 died within weeks of operation. I suggest that in the over regulated climate in which we practice today, the PSNI would be asking questions on behalf of HM Coroner. The climate in which we practice today is very different to then. Indeed it is very different to that of only 10 -15 years ago. I do not feel that this altered climate is necessarily in the best interests of the patients.

In my opinion the media must bear a large responsibility for this changed climate. Rather than protecting the public they are more interested in sensationalism. How often do we watch or listen to the news when they report "doctors botch another operation" or some similar headline. Doctor bashing has become more and more commonplace. Having said this, the profession itself is not blameless, and no one would try to justify the appalling exploits of Harold Shipman. This one case has been responsible for major changes as to how the coroner operates, so that now when an unexpected death occurs, the assumption is that a mishap has occurred until proven otherwise. The PSNI now collect statements directly, and even question doctors under caution, whereas formerly a senior medical person would gather such statements before forwarding them to the coroner. The atmosphere is increasingly that of distrust rather than trust which formally existed.

Not all of the blame for these changes can be placed at the door of the media, and the politicians should also accept responsibility. John Major's Patients Charter, whilst having a laudable ethos, gave rise to patients having expectations beyond those which were deliverable with the resources available. The current Labour Government has followed on by setting more and more draconian performance targets in the drive to simply reduce waiting lists, regardless of clinical need. Once more we fail to learn from the past. In 1776 Adam Smith, the Scottish political economist and philosopher published an important book "The Wealth of Nations". In this he wrote "Governments govern best which govern least". I suggest that our government today would do well to relearn this lesson.

Alongside complaints go league tables. Again no reasonable doctor can object to having his/her results monitored and compared to their peers. The problem is that it is very difficult to derive meaningful comparative data, for example, from mortality statistics. Returning to vascular surgery, no two aneurysm patients have the same risk factors and hence comparison of mortality rates at this crude level is of no value. It is only when one develops a complex score for risk factors eg PPOSUM, that a more meaningful comparison can be made.

Despite this, commercial organisations eg CHKS prosper on making crude comparisons between Trusts. On the basis of these errors league tables are complied and published. It is little wonder that many people cast scorn on the results.

Before concluding, no discussion on the history of vascular surgery would be complete without my paying tribute to the role which three of my retired colleagues have played in the establishment and development of the vascular surgical service in this hospital. The unit was initiated through the

vision and foresight of the late Mr JWS Irwin and the late Mr RH Livingston. Throughout the early years of the troubles they dealt with the vascular injuries. Later in 1978 my now retired colleague, Professor AAB Barros D'Sa took up the challenge where Mr Irwin and Mr Livingston left off. I had the privilege of joining him in December 1980 following Mr Livingston's untimely death. In the early 1980s the unit became one of the first pure vascular surgical units in the United Kingdom. 1995 saw the establishment of the third Consultant post with the appointment of Mr PHB Blair. Mr AG McKinley was appointed upon the retirement of Professor AAB Barros D'Sa in the year 2000. Staffing of the unit has been further strengthened this year with the appointment of Mr DW Harkin as Senior Lecturer, and most recently the creation of a joint post with the Belfast City Hospital to which Mr L Lau was appointed last month.

Finally, having metaphorically stood on the shoulders of many giants of the past, I would like to conclude with an extract from the writings of Felix Wurtz of Basle.

> "Skill in surgery is obtained with great painfulness, for it is not gotten with sitting on a cushion at home or by reading and writing. It is not enough to be full of talk and to say such and such and write so and so – a patient is little the better for it if the surgeon hath no skill".

Wurtz was born not in the 20th century but in 1514 and died 60 years later.

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Case Report

Central line-related bacteraemia due to *Tsukamurella tyrosinosolvens* in a haematology patient

S Elshibly, J Doherty, J Xu, RB McClurg, PJ Rooney, BC Millar, H Shah, TCM Morris, HD Alexander, JE Moore

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CASE REPORT A 48-year-old female patient with a six-year history of non-secretory multiple myeloma presented to hospital in September 2001 having felt generally unwell for the preceding two weeks. She lived in an urban area and had limited mobility. She described fevers with rigors on a number of occasions particularly associated with flushing of a Hickman line, which had been *in situ* since July 1999. Her white cell count was 2.7 x 10^9/l and she was mildly pancytopaenic following a course of doxombicin and methylprednisolone, which she had received four weeks previously. Blood culture taken from the central line had grown Gram-positive bacilli and coagulase-negative staphylococci in the first 48 hours from both aerobic and anaerobic bottles drawn from the white and red lumens of the Hickman line. This episode was managed in the community as a central venous catheter infection with oral ciprofloxacin and intravenous teicoplanin as empirical therapy. On review two weeks later, following completion of the 10-day course of antibiotics, the patient continued to be unwell complaining of general malaise and further rigors. At this time, in the absence of any other source of infection, a decision was made to remove the catheter. She dramatically improved thereafter without further antimicrobial therapy.

Phenotypic identification of the Gram-positive organism, (isolate identifier: NIPHL100602/ MK2667), isolated from blood culture was performed employing the API Corynebacterium system (Biomérieux, Las Halles, France) and gave the profile 2150004, which gave an identification of *Rhodococcus* sp. (82.9%), followed by *Corynebacterium* sp. (12.2%). The isolate grew aerobically on blood agar at 37°C forming small, rough, dry yellowish colonies, 2-5 mm in diameter. The isolate was noted to have an unusual colonial morphology, as shown (*Figure*), resembling non-aerial hyphae, similar to fungal growth, which was a useful phenotypic characteristic. The organism was sensitive to erythromycin, clindamycin, fusidic acid, gentamicin, netilmicin, rifampicin, teicoplanin and vancomycin, but was resistant to penicillin, oxacillin, tetracycline, chloramphenicol and trimethoprim, employing a standard *in vitro* antibiotic disk diffusion susceptibility assay. Given the relatively poor phenotypic identification

Belfast City Hospital, Belfast BT9 7AD.

Northern Ireland Public Health Laboratory, Department of Bacteriology:
S Elshibly, MB, Senior House Officer.
J Xu, PhD, Research Fellow.
RB McClurg, Chief Biomedical Scientist.
PJ Rooney, MB, FRCPath, Consultant Microbiologist.
BC Millar, PhD, Senior Clinical Scientist in Molecular Microbiology.
JE Moore, PhD, Principal Clinical Scientist in Medical Microbiology.

Department of Haematology:
J Doherty, MB, SHO.
TCM Morris, MB, MD, FRCPath, Consultant Haematologist.
HD Alexander, PhD, MRCPath, Consultant Clinical Scientist.

Health Protection Agency, 61 Colindale Avenue, London, NW9 5HT.
H Shah, PhD, Head of Identification Services.

School of Biomedical Sciences, University of Ulster, Cromore Road, Coleraine, Co. Londonderry, BT52 1SA.
HD Alexander, PhD, MRCPath, Consultant Clinical Scientist.

Correspondence to Dr Moore.
E-mail: jemoore@niphl.dnet.co.uk

obtained, the isolate was subsequently forwarded for molecular identification through PCR amplification and direct sequencing of a large but partial region of the 16S rRNA gene, corresponding to base position of approximately 811-1374 of *E. coli* ATCC 25922 16S rRNA [GenBank Accession number X80724]. All DNA isolation procedures were carried out in accordance with the DNA contamination management guidelines of Millar *et al.*[1] and in a Class II Biological Safety Cabinet (MicroFlow, England) in a room physically separated from that used to set up nucleic acid amplification reaction mixes and also from the "post-PCR" room in order to minimise contamination and hence the possibility of false positive results. Bacterial DNA was extracted from the isolate employing the Roche High Purity PCR Template Preparation Kit (Roche Ltd., England) in accordance with the manufacturer's instructions. Extracted DNA was transferred to a clean tube and stored at -80°C prior to PCR. For each batch of extractions, a negative extraction control containing all reagents minus isolate, was performed. All reaction mixes were set up in a PCR hood in a room separate from that used to extract DNA and the amplification and post-PCR room in order to minimise contamination. Fifty microlitre reaction mixes were set up as follows:- 10 mM Tris-HC1, pH 8.3, 50 mM KC1, 2.5mM MgCl2 200μM (each) dATP, dCTP, dGTP and dTTP; 1.25U of Taq DNA polymerase (Amplitaq; Perkin Elmer), 0.2μM of the appropriate "broad-range" primers PSL[2] (forward) 5′ -AGG ATT AGA TAC CCT GGT AGT CCA-3′(1) and P13P[3] (reverse.) 5′ - AGG CCC GGG AAC GTA TTC AC -3′[3] and 4μl of DNA template.[2] Prior to PCR cycling, sealed tubes containing DNA template and all PCR reagents were introduced to the thermal cycler at 96°C to avoid non-specific annealing during the initial ramp stage. The reaction mixtures were subjected to the following thermal cycling parameters in a Perkin Elmer Cetus 2400 thermocycler: 96°C for 3 min followed by 40 cycles of 96°C for 1 min, 55°C for 1 min, 72°C for 1 min, followed by a final extension at 72°C for 10 min. During each run molecular grade water was included randomly as several negative controls and DNA templates from *Staphylococcus aureus* was included as a positive control, as appropriate. For each batch of extractions, an extraction control containing all reagents minus bacterial organism, was performed. Following amplification, aliquots (15 μl) were removed from each reaction mixture and examined by electrophoresis (80V, 45 min) in gels composed of 2% (w/v) agarose (Gibco, UK) in TAE buffer (40mM Tris, 20mM acetic acid, 1mM EDTA, pH 8.3), stained with ethidium bromide (5 μg/100 ml). Gels were visualised under UV illumination using a gel image analysis system (UVP Products, England) and all images archived as digital graphic (*.bmp) files. Amplicons chosen for automated sequencing were purified using a QIAquick PCR purification kit (Qiagen Ltd., UK) eluted in Tris-HC1 (10mM, pH 8.5) prior to sequencing, particularly to remove dNTPS, polymerases, salts and primers. The amplicon was sequenced on the ALF II Express® automated sequencer using the primer PSL which was labelled with Cy-5 fluorescent dye (Clarke Stevenson, Oligosynthesis Unit, The Queen's University of Belfast, UK) and used in conjunction with the Thermo Sequenase Fluorescent Labelled Primer Cycle Sequencing Kit (Amersham, UK). The resulting sequence obtained (999 bp) was compared with those stored in the GenBank Data system using FASTA alignment software (http://www.ebi.ac.uk), as well as being deposited in GenBank (Accession number AY259830). On BLAST analysis in combination with previously reported criteria used for interpretation of partial 16S rRNA gene sequences,[4] the sequence gave a 100% identification for *Tsukamurella tyrosinosolvens* (GenBank Accession numbers AY238514, Y12246, Y12245 & Y12247) followed by *T. columbiensis* AF272835 (99% identity), *T. spumae* AY238513

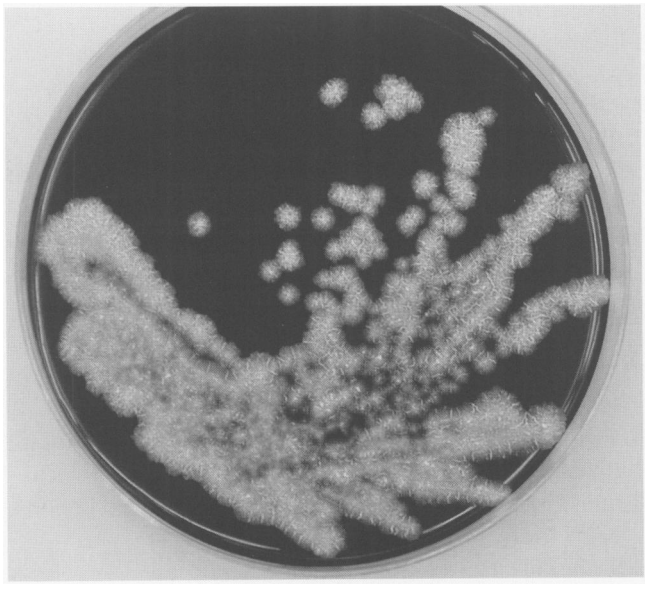

Figure Colonial morphology of *Tsukamurella tyrosinosolvens* NIPHL100602/MK2667 cultured at 37°C Columbia blood agar supplemented with 5% [v/v] defibrinated horse blood. Note the fungal-like hypael appearance of the colonies, which is characteristic of the genus *Tsukamurella*.

(99% identity), *T pulmonis* X92981 (99% identity) and *T. strandjordae* AF283283 (99% identity). The closest *Rhodococcus* neighbour was *Rhodococcus opacus* (AY027586) which was 95% (958/999 bases) similar.

In this case, the patient did not respond to intravenous teicoplanin to which the organism was sensitive for 10 days, thus necessitating the removal of the central line, as this was believed to be the focus of infection. After removal of the line, the patient showed a dramatic response without the use of further antibiotics and continued to remain well (within the limitations of her disease) at 18 months following the *Tsukamurella* infection. We were unable to isolate the coagulase-negative staphylococci or the *Tsukamurella* from the central line tip and this could be explained by the use of teicoplanin therapy, to which the organism was sensitive.

The organism was not identified as *Tsukamurella* until the patient improved. It is therefore important that *Tsukamurella* should be suspected as a possible pathogen in an immunocompromised patient with a foreign implant such as a central line. Previous reports demonstrated that there is a good prognosis by combining the administration of appropriate antibiotic therapy with removal of the catheter, which was the case with our patient.[5]

The genus *Tsukamurella*, was first described by Collins *et al*[6] in 1988 following the reclassification and further molecular and phenotypic charactization of *Gordana aurantiaca, Rhodococcus aurantiaca* and other related organisms, including *Corynebacterium paurometabola* which were distinct from the other mycolic acid-containing actinomycetes. The genus is phylogenetically related to the genera *Nocardia, Gordonia, Streptomyces, Rhodococcus, Corynebacterium* and *Mycobacterium* and taxonomically comprises of at least six described species, including *Tsukamurella inchonensis, T. paurometabola, T. pulmonis, T strandjordii, T. tyrosinosolvens* and *T. wratislaviensis. Tsukamurella* infections have emerged over the last decade as a rare but significant cause of serious infection in immunocompromised individuals. For a comprehensive review of these cases, see Schwartz *et al*.[5] Further to this review, an additional case of line-related sepsis has been shown,[7] as well as a three case of *Tsukamurella* conjunctivitis, which were treated successfully after 10 days with polymyxin B-neomycin or chloramphenicol eyedrops.[8] Consensus opinion from a synthesis of published reports indicates that underlying serious disease, including haematological malignancies, where the patient is immunocompromised combined with indwelling catheters are important risk factors for infection with this genus.[5] Therefore patients with indwelling catheters and haematological malignancies are susceptible populations for *Tsukamurella* infection.

Intravascular catheters have become indispensable in modern medical care. Their use is expected to be increased in the near future with improvement in sophisticated medical care leading to increased numbers of immunocompromised patients, including those with a haematological malignancy, needing indwelling intravascular catheters. The range of catheter-related infection varies from local insertion site infection through to metastatic deepseated infections.

This report highlights the benefits of the integration of a sequence-based typing approach in the identification of difficult-to-identify bacterial isolates employing partial regions of the 16S rRNA gene. Continued routine adoption of such techniques by clinical diagnostic laboratories may prove beneficial for the correct identification of bloodborne infections, as well as for the correct epidemiological characterization of unusual causal agents of bacteraemia in patients with haematological malignancies.

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The authors wish to thank Mr Lester Crothers, Department Bacteriology, Belfast City Hospital, for photographing the isolate (figures).

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Case Report

MR imaging of macrodystrophia lipomatosa

JRA Turkington, AC Grey

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Macrodystrophia lipomatosa is a rare nonhereditary congenital form of localised gigantism usually involving the 2nd or 3rd digit of the hand or foot. Pathologically an increase in adipose tissue involving subcutaneous tissue periosteum and bone marrow is present. Typical clinical and radiological appearances are described in this case report.

Case Report A 36-year-old female presented with enlargement of her right thumb and first metacarpo-phalangeal (MCP) joint since birth. Over the last four years the joints of the thumb had become more painful and had reduced movement. This was impacting on her work as holding a pen and writing was now difficult.

On examination bony enlargement and tenderness were present around the interphalangeal (IP) and MCP joints of the thumb, second MCP joint and the distal radius. Deviation at the IP joint was also present (*Fig 1*).

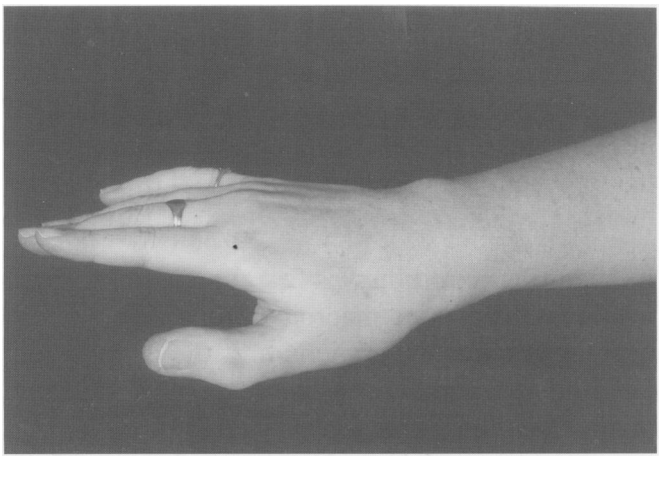

Fig 1. Enlargement of the right thumb and adjacent soft tissues with ulnar deviation of IP joint is demonstrated.

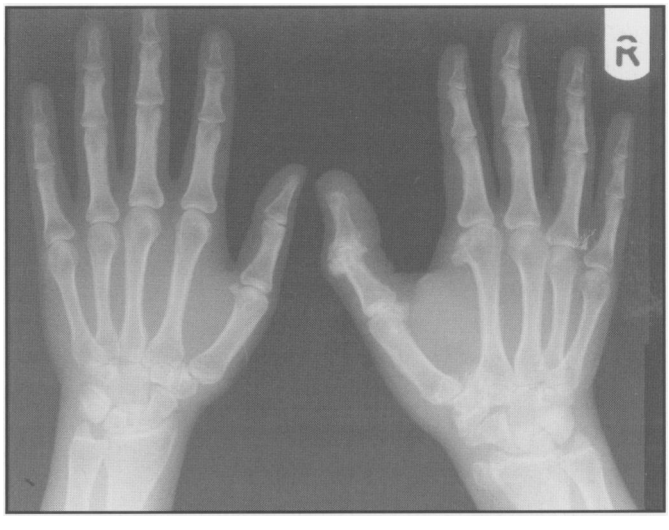

Fig 2. X-ray of both hands showing soft tissue swelling in the thenar eminence of the right thumb, compared to the left. Juxta articular osteopytes and degenerative joint space narrowing of first CMC, MCP and IP joints of the right thumb are demonstrated.

No cutaneous skin lesions, oedema or bruits were present. X-Ray of both hands (*Fig. 2*) and Magnetic Resonance Imaging (MRI) of the right thumb were performed (*Fig 3-5*).

A diagnosis of macrodystrophia lipomatosa was made from the imaging findings.

Musgrave Park Hospital, Stockman's Lane, Belfast BT9 7JB

Department of Radiology:

JRA Turkington, MB, BAO, MRCP(UK), FRCR, Specialist Registrar Radiology

AC Grey, MB, BCH, BAO, FRCR, Consultant Radiologist

Correspondence to Dr Turkington

E-mail: jraturkington@hotmail.com

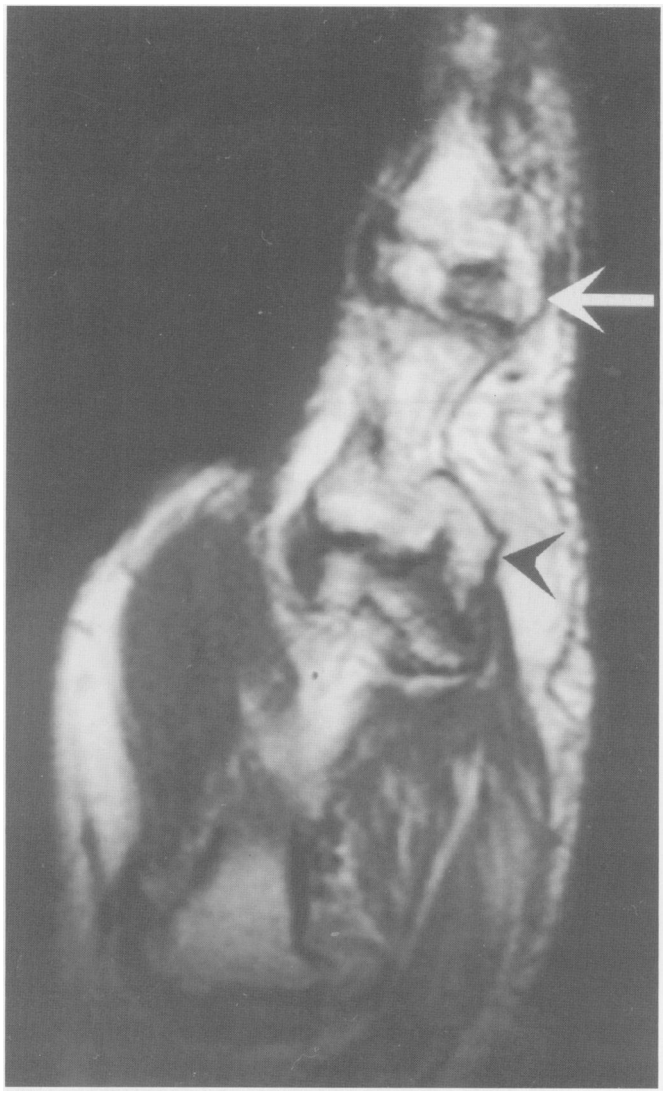

Fig 3. Coronal T1 weighted MRI of right thumb demonstrating the high signal, excess fatty tissue and prominent hook shaped ostephytes at the IP joint (white arrow) and first MCP joint (black arrowhead). Note the low signal fibrous stands within the fatty tissue.

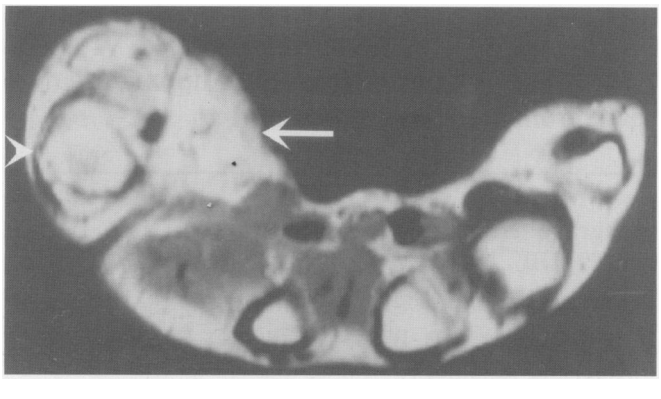

Fig 4. Axial T1 weighted MRI of right thumb again showing the surrounding excess high signal fatty tissue (white arrow). The first metacarpal is labelled (white arrowhead).

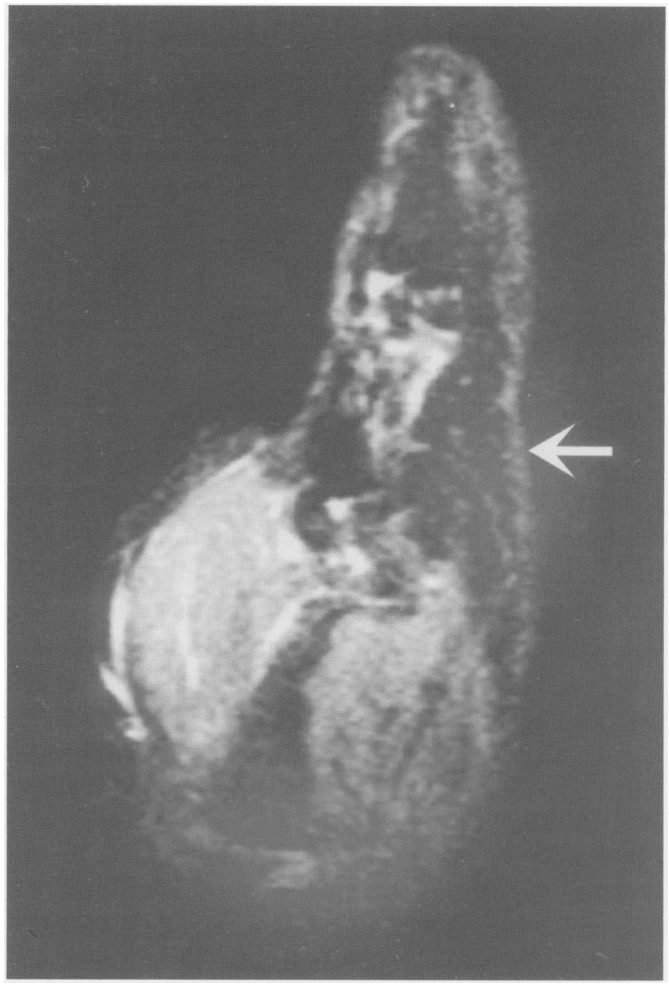

Fig 5. Coronal STIR MRI of right thumb demonstrating suppression of signal of the tissue surrounding the right thumb (white arrow) confirming that this excess tissue is fatty in nature.

DISCUSSION

Macrodystrophia lipomatosa is a non hereditary, congenital and progressive overgrowth of all of the mesenchymal elements of a digit.[3] There is disproportionate increase in the amount of fibroadipose tissue.[1] Usually the lateral aspect of the upper limb and the medial aspect of the lower limb are affected.

In 1925 this condition was first described by Feriz, who used the term macrodystrophia lipomatosa to refer to localised gigantism of the lower limb.[4] Golding extended the term, in 1960, to include involvement of the upper limb.[4]

Clinically, findings are present at birth. An equal incidence is present in males and females.[2] Involvement of an extremity is always unilateral

and adjacent digits of the extremity can be involved. The lower extremity is more often involved than the upper extremity. The 2nd and 3rd digits are the usual sites (in the distribution of the median and plantar nerves).[2]

Involvement usually causes cosmetic disfigurement and mechanical problems are encountered in adolescence due to secondary degenerative joint disease causing reduced function, as in this case. Osteophyte overgrowth may also cause compression of adjacent nerves and vessels. Syndactyly, polydactyly and clinodactyly can occur.[3]

The affected digit increases in length and girth until puberty, when growth ceases.

Aetiology is unknown and several theories exist, including lipomatosis degeneration, disturbed foetal circulation and disturbance of growth factor in utero. Pathologically there is an increase in a fine mesh of fibrous tissue that involves the bone marrow, periosteum, muscles, nerve sheaths and subcutaneous tissues.[4] Phalanges are enlarged due both to endosteal and periosteal deposition of bone.

Two subtypes of congenital macrodystrophia lipomatosa exist.[1] These are static and progressive cases. In static cases the growth of the enlarged digit(s) is at the same rate as the other digits. In progressive cases the growth of the enlarged digit(s) is more rapid than the rest of the extremity. The progressive form is the less common. Involvement of the metacarpal and metatarsal bones is more likely in the progressive group; however in both groups the changes are most pronounced at the distal end of the digit (s).

RADIOGRAPHIC FINDINGS

On conventional X-Ray images macrodactyly and soft tissue overgrowth are visible and are most marked along the volar aspect of the digit and at its distal end. This overgrowth can produce dorsal deviation of affected parts,[3] whilst in this case ulnar deviation is present (*Fig 2*). Soft tissue radiolucency, representing overgrowth of fatty tissue, is occasionally seen.[2] The phalanges are elongated, broad, and the distal ends are splayed and can have a "mushroom" shape.[4] Slanting of the articular surfaces can occur and this leads to secondary degenerative joint disease, manifesting in subchondral cyst and osteophyte formation.[5] The aetiology of the development of the secondary degenerative change, which occurs in adults, is unclear. We postulate however that it may be due to abnormal stresses across the joints due to the deformity.

MRI demonstrates an excess of fibro-fatty tissue around the affected digits.[1, 8] This will therefore have the same signal characteristics as fat on MRI; i.e. high signal on T1 and T2 weighted sequences and low signal on hit suppression sequences (STIR). Fibrous strands within the fatty tissue will be demonstrated as low signal linear strands on T1 weighted sequences. The fatty tissue may also be seen to infiltrate the adjacent muscles. Any bony abnormalities such as cortical thickening and secondary degenerative changes are also identified with MRI. Fibrous thickening of a nerve may also be seen.[6]

In our case the digit enlargement was not as gross clinically as some textbook examples of this condition; however it had been enlarged since birth. This clinical history, together with the radiographic findings of excess soft tissue swelling and advanced degenerative changes, out of keeping in a patient of this age, suggested the diagnosis of macrodystrophia lipomatosa (*Figs 1, 2*). Therefore MRI was performed to identify if the excess soft tissue was fibro-fatty in nature. This was demonstrated as the signal from this tissue suppressed on the fat suppression (STIR) sequence (*Fig 5*). Occasionally a thickened nerve can be demonstrated in the region of the soft tissue overgrowth on MR imaging. This is not visualised in all patients with macrodystrophia lipomatosa, as in our case, probably because fatty infiltration into the nerve sheath can make its detection difficult within the subcutaneous tissue.[6]

In the clinical scenario of a patient with congenital digit enlargement, MRI is a useful imaging modality to aid diagnosis. The differential diagnosis of congenital macrodactyly includes neuofibromatosis, Klippel-Trenaunay-Weber syndrome, lymphangiomatosis, haemangiomatosis and fibrolipomatosis of the nerve.[1] MR imaging, by characterising the type of soft tissue proliferation can be used to differentiate between most of these diagnoses.

In neurofibromatosis (NF) T2 weighted MR images show high signal hyperintense neurofibromas, which

will be situated close to the nerve.[8] In addition cutaneous manifestations of NF and a family history will be present.

In Klippel-Trenaunay-Weber syndrome limb hypertrophy, haemangiomas and arteriovenous fistulae are present. Plain x-ray can show soft tissue and bone enlargement together with phieboliths within the vascular anomalies. MRI is a non invasive method of identifying the presence and the extent of the vascular anomalies. These tend to be of high signal on T2 weighted images, although areas of low signal can be seen and represent haemosiderin deposition or areas of calcification.[2]

In haemangiomatosis T2 weighted MR imaging shows increased signal from the serpiginous vascular channels within the haemangiomas.[8] Bruits may be detected on clinical examination.

In lymphangiomatosis, the lymphangiomas are hyperintense to muscle on T1 weighted images and hyperintense to fat on T2 weighted images.[1] Clinically, diffuse limb swelling and pitting oedema are found.

Fibrolipomatosis of the median nerve can be seen with macrodactyly. In this condition MRI will identify fat deposits within the nerve sheath causing the marked enlargement of the nerve.[7] In comparison in cases of macrodystrophia lipomatosa the fat deposits can be within the nerve sheath, subcutaneous tissues, bone marrow, periosteum and muscles.[7]

Our patient is currently awaiting an athrodesis of the interphalangeal joint to relieve the pain caused by the secondary degenerative joint disease.

CONCLUSION

MRI is an extremely useful imaging modality in a patient who presents with congenital digit enlargement. An excess of fibro-fatty tissue, together with proportional enlargement of other mesenchymal tissues is characteristic of macrodystrophia lipomatosa. Demonstration of a hypertrophic nerve is described, but may not always be identified within the subcutaneous tissue due to fatty infiltration of the nerve.

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Case Report

Colouterine fistula mimicking pyometrium – diagnosis established with multi-detector computed tomography

GC Beattie, M Nelson, IM McMillen, AH McMurray

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Fistulae are a recognised complication of severe diverticular disease. The commonest fistulae are from sigmoid colon to bladder and vagina.[1] Colouterine fistulae, though sporadically reported in the literature, are very rare. Patients often present to gynaecologists with symptoms mimicking a pyometrium. We report a case of a colouterine fistula in a 74 year old lady. A new generation 16 slice multidetector computed tomography (MDCT) scanner with multi-planar reconstruction software was instrumental in establishing the diagnosis, obviating the need for a contrast radiology study.

CASE REPORT A 74 year old woman presented with a two week history of increasingly severe left iliac fossa pain associated with pyrexia, nausea, altered bowel habit, anorexia and a more recent history of a foul smelling green vaginal discharge (necessitating changing up to ten pads daily). A speculum examination by the general practitioner revealed pus emanating from the cervical os, and she was sent to the Accident & Emergency department. She denied any previous similar episodes. She was a non-insulin dependent diabetic of seven years' duration (metformin 850 mg tds; gliclazide 80 mg tds) and had hypertension and aloplecia totalis. Four years previously she was investigated for abdominal cramps and a change in bowel habit with a tendency to constipation. She was found to have diverticulosis on double contrast barium enema.

On admission to hospital she had a pyrexia of 38°C. There was tenderness in the left iliac fossa on abdominal palpation. Routine blood tests revealed normal renal function, a neutrophil leucocytosis and an elevated C-Reactive Protein (275 mg/l, normal <7 mg/1). Vaginal swabs cultured enteric organisms (coliforms) and proteus sp. A limited abdominal ultrasound scan revealed a diffuse pelvic inflammatory mass, and intravenous and oral contrast enhanced abdominal and pelvic multidetector CT was arranged. This revealed a thickened sigmoid colon in keeping with diverticulitis, with a pericolic abscess and surrounding inflammation. A definite communication was seen from the pericolic abscess to the fundus of the uterus, the body of which contained air and fluid (*figures 1 & 2*). The fluid had tracked into both fallopian tubes resulting in secondary bilateral pyosalpinx.

After being informed of the management options, complications and probable need for a stoma she agreed to proceed with surgery. At laparotomy a large pelvic inflammatory mass involved the sigmoid colon, small bowel mesentery, uterus, bladder and both fallopian tubes. In the centre of the mass was a moderately sized thick walled abscess containing

Antrim Area Hospital, 45 Bush Road, Antrim, BT41 2RL.
Department of Surgery:
GC Beattie, MSc (Med Ed), FRCS (Gen), Specialist Registrar Surgery.
AH McMurray, BDS, FRCS, Consultant Surgeon.
Department of Radiology:
M Nelson, FRCS, FRCR, Consultant Radiologist.
Department of Gynaecology:
RM McMillen, M Phil, MRCOG, Consultant Gynaecologist.
Correspondence to Mr Beattie, 6 Upper Braniel Road, Belfast BT5 7T5.
E-mail: garthbeattieyahoo.co.uk

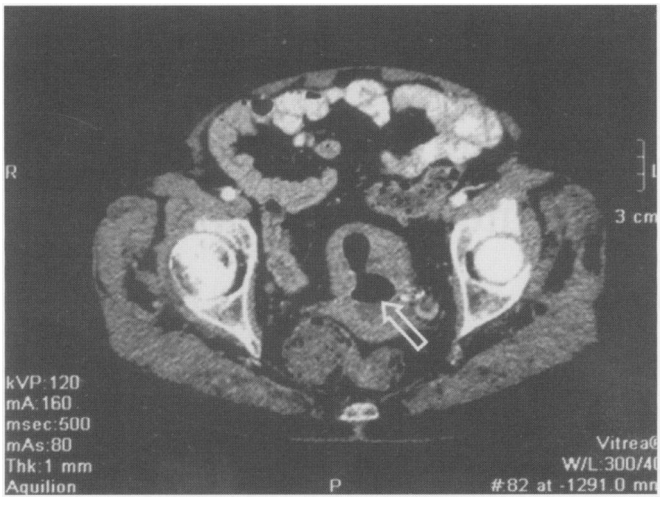

Fig 1. Transverse multidetector computed tomography section showing fundus of uterus with abscess cavity containing air, fluid and debris (white arrow).

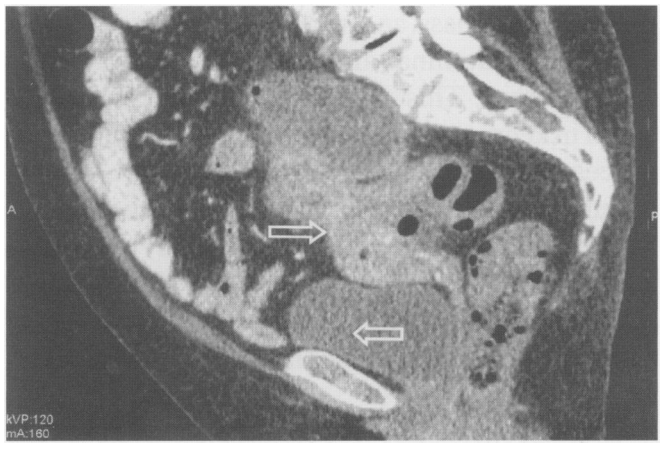

Fig 2. Multidetetctor computed tomography reconstructed in sagittal plane showing fundus of uterus communicating with abscess cavity and thickened diseased sigmoid colon (right facing arrow). The left facing arrow denotes the bladder.

around 50 ml of thick green pus. Pus from this abscess was sent to bacteriology for culture and sensitivity, which revealed similar bacteria to that isolated from the vaginal swabs. The diseased sigmoid colon was carefully separated from the pelvic organs using sharp and blunt dissection. The diseased sigmoid colon was excised, and a stoma raised at a pre-marked site in the left iliac fossa. Primary anastomosis was considered unwise in view of the extent of pelvic purulent contamination and inflammation of surrounding tissues. She made an uneventful post-operative recovery and was discharged home on the tenth postoperative day. Histopathology confirmed diverticulitis with fistula with no evidence of malignancy. She is scheduled to have a reversal of the Hartmann's procedure in due course.

DISCUSSION

The largest review of diverticular fistulae published in the literature is from the Cleveland Clinic, Ohio. Of 412 patients with surgically treated diverticular disease over a 26 year period,[1] 84 (20.4%) patients had internal fistulae. The commonest fistula was from colon to bladder (65%) followed by vagina (25%). Hysterectomies had been performed in 50% and 83% of females with colovesical and colovaginal fistulae respectively. There were three colouterine fistulae, the largest number reported in any one series. A 20 year retrospective review from Canada of 42 patients with diverticulitis complicated by fistula formation revealed the majority of fistulae were colovesical (48%), followed by colovaginal (44%) and one colotubal fistula. There were no colouterine fistulae in this series.[2] A description of 13 genital fistulae caused by diverticular disease highlights the association of colovaginal fistulae in female patients over the age of 50 who have had a previous hysterectomy.[3] The uterus acts as a physical barrier, preventing contact of the diseased sigmoid colon with the vagina. Rarely does the uterus become involved in the fistulous process. There are other sporadic case reports of colouterine fistulas in the literature.[4]

The imaging modality for diverticular fistulae has traditionally been contrast radiology, either rectally or vaginally.[3] A 'charcoal challenge test' has been reported as a diagnostic aid.[5] After a barium enema revealed no fistula tract, orally administered activated charcoal was seen emanating from the cervical os at pelvic examination the following day. Though CT has been described before in combination with vaginography to demonstrate a colouterine fistula,[6] as seen in this case, the new generation multidetector CT scanners are capable of volumetric imaging facilitating multi-planar reformations and three dimensional imaging, obviating the requirement for vaginal or rectal contrast studies. Multidetector computed tomography is synonymous with multislice CT. The isotrophic voxel nature of MDCT acquisition allows for excellent multiplanar reconstructions and improved visualisation of pathology with a shorter acquisition time. These advantages often outweigh

the fact that MDCT exposes the patient to a larger radiation dose than standard CT.

Treatment usually involves laparotomy and surgical resection with (single-stage) or without primary anastomosis, depending on the extent of tissue inflammation, localised sepsis and the surgeon's judgment. If malignancy is suspected an en-bloc resection of the uterus and colon should be carried out.[4] Percutaneous drainage of a pyometrium secondary to a colouterine fistula has been reported as a temporising measure.[7] Hysterectomy is not required if the clinicians are confident the underlying process is benign and arising from colonic diverticular disease. Excising the source of the pathology, the diseased sigmoid colon, will suffice. Interestingly, there is one report in the gynaecological literature of a conservative surgical approach to the management of a colouterine fistula. Surgeons simply primarily sutured the colon after separating the viscera to reveal the fistula, and carried out a hysterectomy with a favourable result.[8] The extent of tissue inflammation and sepsis precluded this conservative option in this case. Specialisation may well have a role in the optimal management of these challenging cases. This is supported by a paper from Quebec, looking at the value of surgical subspecialisation in the outcome for patients operated on for fistulae complicating diverticulitis.[9] When managed by colorectal surgeons (as opposed to general surgeons), there was a reduced stoma rate (5% versus 27%), less complications (27% versus 41%) and a shorter pre (three versus eight days) and post (11 versus 14 days) operative hospital stay. In order to achieve the best outcome for patients, perhaps all cases of complicated diverticular disease should be managed in regional specialist centres.

This case report highlights how a rare complication of diverticular disease can closely mimic pyometrium. The contribution to the literature in this rare disease process is to illustrate how the new generation multidetector CT scanners can focus on the pelvic organs, and with the aid of multi-planar reconstructions, demonstrate fistula morphology obviating the requirement for vaginal or rectal contrast radiology studies.

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Case Report

Retroperitoneal fibrosis: a rare cause of recurring abdominal pain

LK Solomon, P Rice, GH Hewitt

Accepted 23 March 2005

Retroperitoneal fibrosis (RPF) is a rare condition of unclear aetiology. It is believed to be immune-related. About two-thirds of cases are thought to be idiopathic.[1] We present a case of idiopathic RPF in a 37-year old male with recurring abdominal pain over a five-month period associated with features of ischaemic colitis and bilateral hydroceles. An initial CT scan of the abdomen showed a significant peri-aortic soft tissue mass .The inferior mesenteric artery (IMA) was noted to pass through the mass and to be compressed by this mass. A subsequent CT-guided biopsy confirmed retroperitoneal fibrosis. He was successfully treated with steroids only with resolution of his symptoms and radiological features.

To our knowledge no case of idiopathic RPF, presenting with features of ischaemic colitis and bilateral hydroceles, has been reported in the UK.

CASE REPORT Mr RS, a 37-year old male, first presented to the Trust via his General Practitioner with a three-week history of intermittent sharp flank and left iliac fossa (LIF) pains radiating to his left testicle. He had no significant past medical history.

Examination revealed some tenderness in the left loin and left iliac fossa areas with no other remarkable findings. CRP and ESR were significantly elevated but other baseline laboratory tests were normal. He had an Ultrasound Scan (USS) of the abdomen which was essentially normal. His symptoms settled with conservative management and he was discharged a few days later.

He was however readmitted a week later with a recurrence of the LIF pain but this time associated with bloody diarrhoea. Repeat investigations including *Clostridium difficile* were all normal except CRP, which was again significantly elevated. He

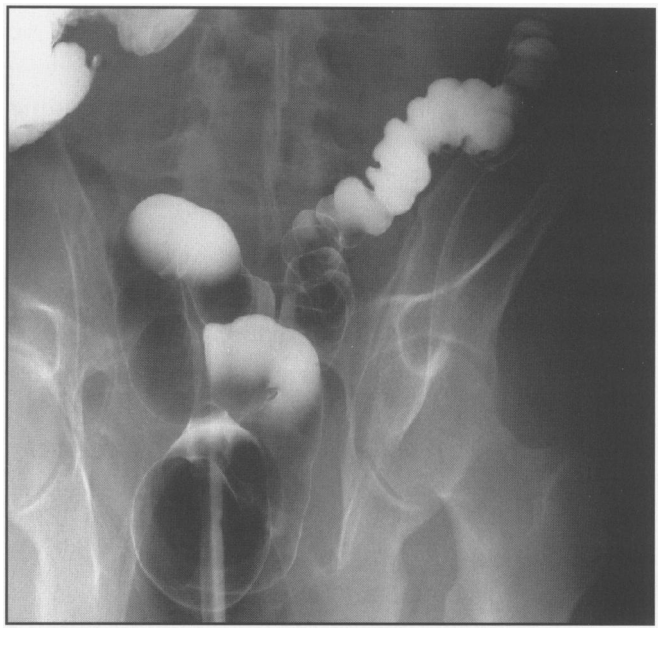

Fig 1. Initial Barium Enema: normal.

Royal Victoria Hospital, Grovenor Road, Belfast BT12 6BA.
LK Solomon, MB, BS, UPH, Senior House Officer, Colorectal Surgery.
Craigavon Area Hospital, 68 Lurgan Road, Portadown, Craigavon, BT63 5QQ.
P Rice, FRCSI, FRCR, Consultant Radiologist.
GH Hewitt, FRCSI, FRCSEd, Consultant Surgeon.
Correspondence to Dr Solomon.

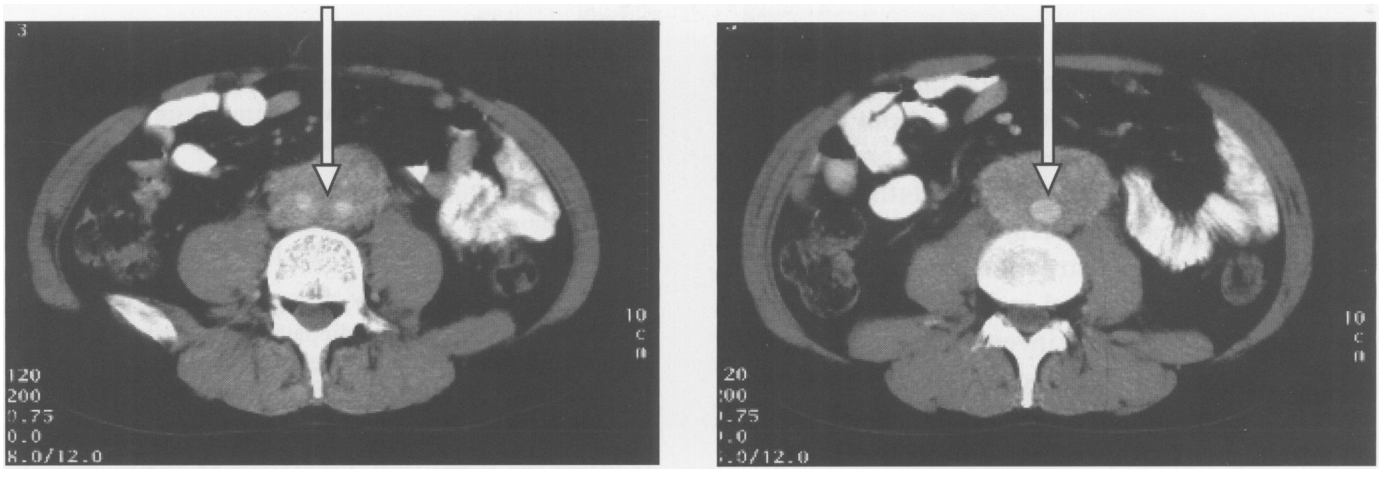

Fig 2A and 2B. CT scans showing significant soft tissue mass with IMA passing through the mass and compressing it.

next had a flexible sigmoidoscopy which revealed an inflamed friable sigmoid mucosa with contact bleeding precluding further advancement of the scope. He was, at this stage, treated with prednisolone enemas and mesalazine on the presumption that this was an inflammatory bowel condition. He was referred for a barium enema as an outpatient; this showed a normal distal descending and sigmoid colon (*Fig 1*). However, pathology results of biopsies from the sigmoidoscopy, returned later, should show features consistent with ischaemic colitis.

He subsequently re-presented two more times with LIF pain but additionally had testicular swellings which were revealed by USS to be bilateral hydroceles. Because of the recurrent nature of his symptoms he was further investigated with a CT scan of the abdomen which revealed a significant peri-aortic soft tissue mass. The IMA was noted to be compressed by this mass (*Fig2A and 2B*). By this stage his diarrhoea had settled and his colon had a normal appearance on CT.A subsequent CT-guided biopsy (*Fig 3*) confirmed histological features of RPF. The kidneys were not obstructed. An intravenous urogram showed mild bilateral hydronephrosis only.

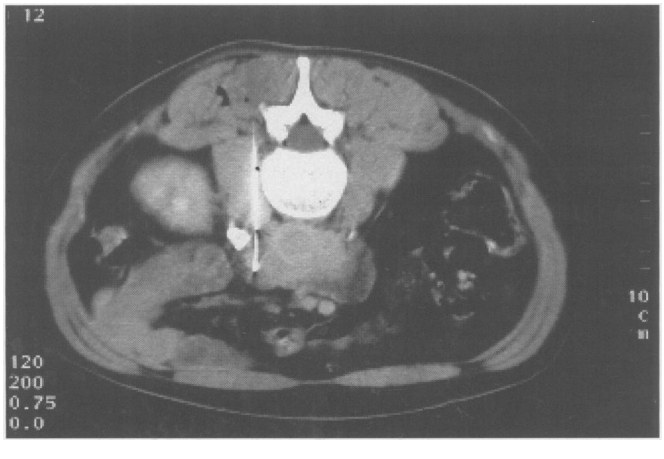

Fig 3. CT-guided biopsy with needle in mass.

TREATMENT AND FOLLOW-UP

On confirmation of the diagnosis of RPF he was started on an initial oral dose of 60mg of prednisolone daily with remarkable symptomatic improvement: he has had no further abdominal pain or bloody diarrhoea. Follow-up CT abdomen done a year later showed only minimal peri-aortic fibrotic changes (*Fig 4*). His steroids have been reduced to 10mg daily sufficient to hold his CRP at or close to normal.

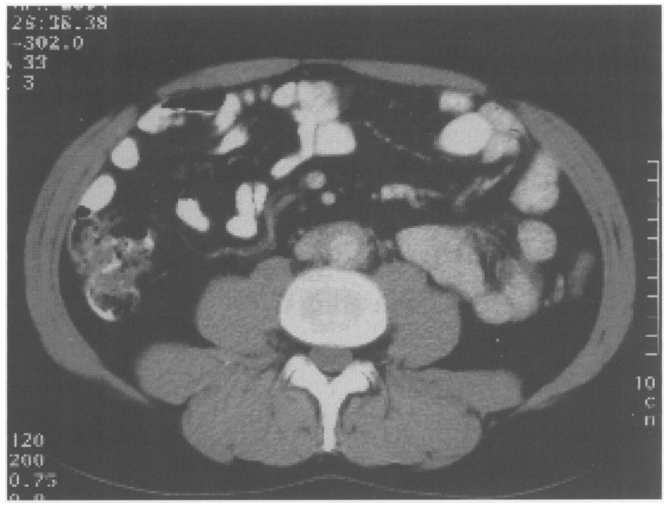

Fig 4. CT scan one year post treatment with steroids, at a similar level to fig 2, showing significant improvement.

DISCUSSION

RPF is a rare condition of uncertain aetiology but thought to be immune mediated. About two thirds of cases have no predisposing factors and hence are idiopathic. It characteristically affects the peri-aortic tissues often spreading laterally to involve the ureters leading to ureteric obstruction; the aorta and IVC are not usually displaced in RPF.[1] CT scan of the abdomen is the imaging investigation of choice.[1] It is important for the diagnosis to be confirmed either by radiological-guided or open surgical biopsy before commencement of medical treatment.[6]

Confirmed cases, even those with ureteric obstruction, can be successfully treated with steroids alone,[6] and occasionally with tamoxifen,[7] but ureterolysis may still be necessary in advanced or unresponsive cases.

This patient presented with non-specific abdominal pain later associated with bloody diarrhoea which was initially thought to be an inflammatory bowel disease from appearance of the large bowel on flexible sigmoidoscopy and the persistently high CRP and ESR. Biopsy however confirmed bowel ischaemia. Because he had further recurrences of this pain a CT scan of the abdomen was requested which then showed the mass, later confirmed to be RPF.

Although it is known that RPF usually encases the aorta, it is rare for this to significantly affect a major gut branch of the aorta and cause clinical ischaemia; there have been four reported cases worldwide [2, 3, 4] but none, to our knowledge, has been reported in previous UK literature. Although Duffy TP did report a case of RPF presenting with left hydrocele[5] this appears to be the first reported case presenting with bilateral hydroceles. This may be explained by the lymphatic drainage of the testis into the para-aortic nodes.

We suggest that RPF should be thought as a diagnosis in young persons presenting with bloody diarrhoea but with predominantly ischaemic changes in pathological biopsies.

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Case Report

Haemorrhage from small bowel ulceration complicating meningococcal septicaemia

DD McCaffrey, J Lucas, KR Gardiner

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The complication of intestinal haemorrhage in a patient with meningococcal septicaemia is described. The patient presented with haemodynamic instability associated with melaena within an intensive care unit. Upper and lower gastrointestinal endoscopy and angiography failed to localise the source of bleeding. At laparotomy, an isolated small bowel lesion was easily identified and resected. Histological examination of the small bowel revealed circumferential mucosal ulceration. The patient had no further gastrointestinal blood loss.

CASE REPORT A 49-year-old man presented with a short history of flu-like symptoms, blurred vision, nausea, vomiting, abdominal pain and general malaise. Twenty-four hours later he developed severe cardiovascular collapse and a widespread purpuric rash. Despite aggressive treatment within an intensive care unit he developed severe acidosis, renal failure, adult respiratory distress syndrome, coagulopathy, myocardial infarction and ischaemic peripheries. Type B meningococcal septicaemia was confirmed. Recovery over the following weeks was slow complicated by intolerance of enteral feeding, line sepsis and a persistently low haemoglobin concentration requiring regular transfusion. On day 29 he demonstrated haemodynamic instability, followed by frank melaena and a rapid fall in haemoglobin concentration. He required transfusion with 7 units of packed red blood cells over a 24-hour period.

He was investigated by gastroscopy, which was normal, by flexible sigmoidoscopy to 60 cm, which visualised dark red blood without a mucosal lesion and by selective mesenteric angiography, which was normal. Due to persistent haemodynamic instability laparotomy was performed and a short segment of thickened and discoloured small bowel 40 cm proximal to ileocaecal valve was resected. Inspection of the luminal surface revealed circumferential mucosal ulceration with a "punched out" edge. The surrounding mucosa looked entirely normal. Histologically the ulcer base was covered by acute inflammatory exudate and showed evidence of re-epithelialization (*Figures 1 and 2*). Aetiology of the ulceration could not be determined from histology but no evidence of a vasculitic or dysplastic process was identified.

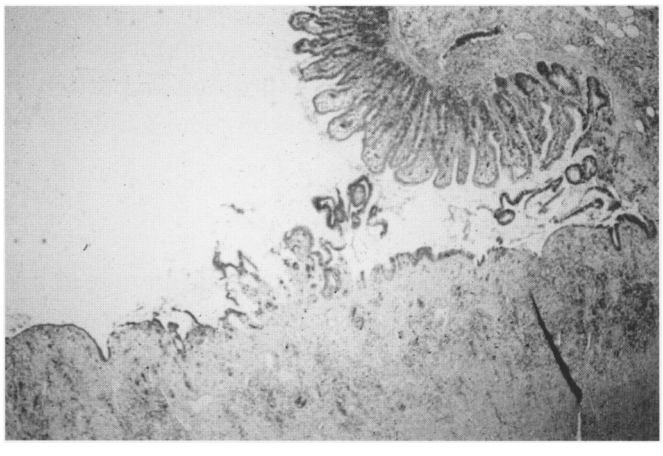

Figure 1

Colorectal Surgical Unit, Royal Victoria Hospital, Grosvenor Road, Belfast BT12 6BA.

DD McCaffrey, BSc(Hons), MRCS.

J Lucas, MB, BCh, BAO.

KR Gardiner, MD, MCh, FRCS.

Correspondence to Mr Gardiner.
E-mail: keith.gardiner@royalhospitals.n-i.nhs.uk

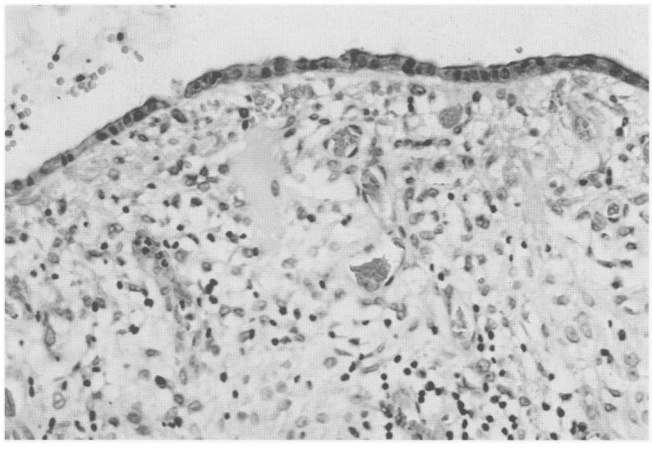

Figure 2

Following surgery the patient stabilised with no evidence of further blood loss. Although he did not develop any post-operative complications he remained in hospital for a prolonged period of rehabilitation due to the neurological sequelae of meningitis.

DISCUSSION

Meningococcal infection can occur at any age and at any time of the year but most cases occur between November and March. Over the twelve months prior to this presentation there has been an increase in the incidence of serogroup B infection among adults over 24 and in children aged 0-4 years.[1] Early diagnosis and treatment are important in view of the potential for rapid clinical deterioration of patients with meningococcal infection.

The majority of complications associated with meningococcal infection are attributable to vasculitic, suppurative, or neurological sequelae such as sensorineural deafness.[2] This patient suffered multiple organ dysfunction syndrome, myocardial infarction and gangrene of digits, pinna and lips. In addition during the recovery phase he developed severe gastrointestinal haemorrhage from an ulcerated area in the small bowel.

Haemorrhage from the small intestine, apart from the duodenum, is uncommon. Only five percent of gastrointestinal bleeding occurs between the ligament of Treitz and the ileocaecal valve.[3] The most frequent causes are tumours, such as leiomyoma, angiodysplasias, arterio-venous malformations or Crohn's disease.[4] The small bowel in particular is an area that is difficult to evaluate by standard diagnostic tests. Endoscopy is regarded as the primary investigative procedure in upper gastrointestinal haemorrhage, but has limitations, particularly when the bleeding emanates from a lesion beyond the duodenum.[5] Selective mesenteric angiography offers the potential to treat, via embolisation, as well as to localize a source of bleeding for subsequent surgical repair.[6] Gastroscopy, flexible sigmoidoscopy and selective mesenteric angiography failed to identify a source of bleeding in this patient. Unfortunately, the option of a labelled red cell scan to determine the site of haemorrhage was not available at the weekend when this bleeding occurred. Laparotomy identified the source as an isolated area of ulceration within the distal small bowel and limited resection was performed.

Small bowel ulceration may result from neoplasia, angiodysplasia, arterio-venous malformations, mesenteric ischaemia, vasculitis, Crohn's disease, Zollinger-Ellison syndrome, heterotopic gastric mucosa, or can be drug induced. This patient was not treated with any drugs associated with bowel ulceration, such as non-steroidal anti-inflammatory drugs and enteric-coated potassium supplements.[7, 8] Ulcers that cannot be explained by such specific mechanisms are included in the category of non-specific ulcers of the small intestine.

The pathological features may suggest that the ulcer was a result of an ischaemic event. Ischaemia can be focal or widespread. Causes of focal segmental ischaemia of the small bowel include atheromatous emboli, strangulated hernias, immune complex disorders and vasculitis, blunt abdominal trauma, segmental venous thrombosis, radiation therapy, and oral contraceptives.[8] Thromboembolic complications of meningococcal infection have been reported but not involving the intestines.[9] Also, there was no evidence of a vasculitic process on histological examination. Alternatively, the ulceration may have resulted from more generalised bowel ischaemia due to the effects of septicaemia. Systemic hypoperfusion can predispose to the occurrence of mesenteric artery insufficiency on the basis of reflex vasoconstriction.[10] Hypovolaemia or hypotension complicating sepsis as well as myocardial infarction have been previously described as causal factors in the development of non-occlusive mesenteric ischaemia.[8] Hypoxia and drug-induced arterial vasoconstriction are additional factors that may initiate or aggravate non-occlusive

intestinal ischaemia. Unexplained abdominal distension or gastrointestinal bleeding may be the only manifestation of non-occlusive mesenteric ischaemia. Initially the haemorrhage is evident only as occult blood, but as with any source of bleeding may become profuse.

The prognosis regarding isolated intestinal ulceration is good as it is generally self-limiting and does not recur after resection. This form of intestinal ulceration may have been caused by an ischaemic event associated with the effects of meningococcal infection. This case highlights a potential complication of meningococcal infection not previously reported and also demonstrates the difficulties of diagnosis and management of small intestinal haemorrhage. Regardless of the aetiology, the affected area was easily identifiable at laparotomy, which indicates a potential role for laparoscopy in cases of undiagnosed small intestinal haemorrhage. In addition, when non-surgical modalities cannot identify or treat small intestinal haemorrhage, exploratory laparotomy is a viable option and should not be delayed.

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Case Report

Mesenteric cysts: a rare cause of abdominal pain

C Lockhart, A Kennedy, S Ali, D McManus, SD Johnston

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Gastrointestinal stromal tumours (GIST) constitute the most important group of primary mesenchymal tumours of the gastrointestinal tract. They may be difficult to diagnose because of their non-specific presentation. We report a young man who presented with right upper quadrant pain due to a GIST, diagnosed following surgical exploration.

CASE REPORT A 27 year-old man was admitted with a history of right upper quadrant pain, occurring five days after flying home to the United Kingdom from Australia via Singapore. The pain was constant and throbbing in nature, and was exacerbated by deep inspiration. He had a poor appetite. He gave a history of passing pale stools and dark urine for one week, a number of months previously. He had been investigated two years previously for melaena and bleeding per rectum. Colonoscopy, gastroscopy, small bowel series, ultrasound of abdomen and isotope Meckel's scan were all negative. There were no risk factors for hepatitis, and he had received immunisation against Hepatitis A and B prior to his journey to Australia.

On examination, the abdomen was soft with mild tenderness in the right upper quadrant. Murphy's sign was negative. There was one finger-breadth of hepatomegaly noted. There were no other abnormal examination findings. He remained apyrexic following admission. The provisional diagnosis on admission was acute cholecystitis.

Investigations revealed a slightly raised WCC at 13.4×10^9/l with neutrophils of 10×10^9/l. Liver function tests were normal apart from an elevated γ-glutamyl transferase 253 U/l. D-dimer was elevated at 0.62 μg/nl, CRP was 67 mg/l. Serological tests for Legionella, Leptospirosis and Brucella were all negative. No malaria parasites were seen on peripheral blood smear. Complement showed a raised C3 with a normal C4. Immunoglobulins, autoimmune screen and hepatitis serology were negative.

In view of the pleuritic nature of the pain, the raised D-dimer level and the long aeroplane flight, a ventilation perfusion scan was performed, which was normal. Chest X-ray and abdominal X-ray were also normal. Ultrasound of abdomen demonstrated a contracted gallbladder with no calculi.

The patient continued to complain of persistent abdominal pain, and CT scan abdomen and pelvis was performed. This revealed two areas of decreased attenuation anteriorly within the abdominal cavity, suggestive of mesenteric cysts, the largest measuring 7.7 × 5.8 cms. and the smaller 5 × 3 cms (*Figure 1*). The lesions were surrounded by a well defined wall. There was no adjacent inflammation or lymphadenopathy and no abnormality was seen within the liver. The spleen was enlarged measuring 16.7 cms. in bipolar length. Subsequently hydatid serology was performed and was negative.

Belfast City Hospital, Lisburn Road, Belfast BT9 7AB.

Department of Gastroenterology:

C Lockhart, Senior House Officer.
S Ali, MRCP, Associate Specialist in Gastroenterology.
SD Johnston, MD, FRCP, Consultant Gastroenterologist.

Department of Surgery:

A Kennedy, FRCS, FRCS I, Consultant Surgeon.

Department of Histopathology:

D McManus, BSc, MD, FRCPath, Consultant Histopathologist.

Correspondence to Dr Johnston.

E-mail: simon.johnston@bch.n-i.nhs.uk

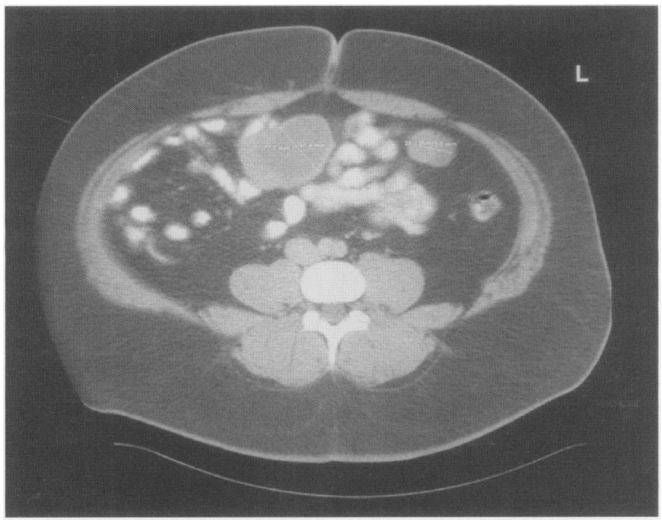

Fig 1. CT scan of abdomen demonstrating two mesenteric cysts.

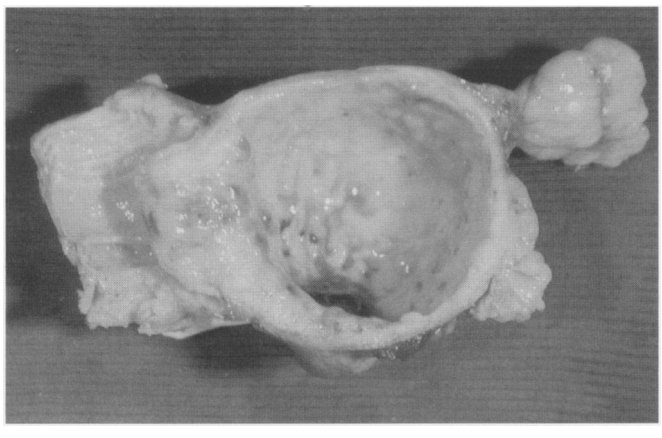

Fig 2. Resected surgical specimens.

Surgical excision of the mesenteric cysts was performed without complication (*Figure 2*). Histological examination revealed both lesions to be gastrointestinal stromal tumours (GIST). Both tumours stained strongly positive for C-kit (CD 117) and also expressed CD34. A low mitotic activity was noted. No further oncological treatment was required. He made a full recovery and remains well at 6-month follow-up.

DISCUSSION

Gastrointestinal stromal tumours (GISTs) constitute the most important group of primary mesenchymal tumours of the gastrointestinal tract. They are known for their diversity in clinical behaviour. Two problems may arise for the clinician. Firstly, the diagnosis may be difficult to establish, and secondly, it may be difficult to determine the future behaviour of the tumour and the necessary choice of further chemotherapy, if required.[1] One large study by Langer *et al*[2] aimed to identify prognostic markers of tumour progression in 48 GISTs resected from 39 patients in a single tertiary referral centre over an eleven year period. GISTs were classified as low or high risk on the basis of tumour size, mitotic rate and/or proliferation. This was confirmed by Wong *et al*[3] who recently reported a study aimed at determining whether immunohistochemical markers increase the accuracy of predicting prognosis for GISTs, and found that the mitotic count remains the best predictor of outcome following surgical resection of gastric GISTs. Ki67 immunohistochemistry and p53, Bcl-2 and cyclin Dl immunohistochemistry provide no additional prognostic features. Our patient's tumours had a low mitotic activity suggesting that the tumours were benign and no further oncological treatment was required.

Cyto-genetic and comparative genomic hybridisation (CGH) studies have indicated characteristic chromosomal patterns in GISTs.[4] This technique has been combined with immunohistochemical analysis. Bergmann *et al* reported that the most common and characteristic alteration in GISTs were loss of chromosomes 14 and 22.[4]

In our case both tumours were strongly positive for C-kit (CD 117), and also expressed CD34. Interestingly, Nishida and Yasumasa[5] report that GISTs are composed of KIT-positive mesenchymal-origin spindle - or polygonal-shaped tumour cells in the gastrointestinal tract. The gain-of-function mutations in the C-kit gene (90%) or platelet-derived growth factor receptor alpha (PDGF-R alpha) gene (5%) are now considered to be causative for GISTs. Therefore, treatments such as ST 1571 (Glivec), a molecule designed to selectively inhibit Bcr-Abl, KIT and PDGF-R activity, has recently been introduced in the management of these tumours. It shows high response-rate and efficacy for non-resectable and/or relapsed GIST (partial response 60%).[5]

In summary, we present a young man with a GIST as a rare cause of abdominal pain. His tumour had a low mitotic index and his prognosis would appear to be good following successful surgical excision.

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Case Report

Extra-pulmonary oat cell carcinoma: report of two cases

SA Badger, J Lee, H Vazir, T Diamond, KJS Panesar

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Pulmonary oat cell carcinoma was first described in 1926 and constitutes around 25% of lung malignancy.[1] Dugoid *et al* reported the first case of extrapulmonary oat cell carcinoma, without any bronchial involvement, in 1930.[2] Primary extrapulmonary oat cell tumours have since been reported originating from different organs except the liver and the central nervous system. We report two cases of primary extrapulmonary oat cell carcinoma and have reviewed the literature of this rare condition with regard to prognosis and treatment.

The history of each patient was reviewed and a relevant summary made. A literature review was performed using Medline. The key words "oat cell carcinoma", "extrapulmonary" and "small cell carcimona" were used and the results of the search correlated. The current recommendations for treatment were also reviewed.

CASE 1 A 70-year-old man, who was a non-smoker, presented with a one-year history of passing dark stools and an eight-week history of anorexia, weight loss and early satiety. Physical examination revealed a palpable epigastric mass. He was anaemic (Hb level of 7.9g/dl and mean cell volume 83.8g/1), while liver function tests and carcinoembryonic antigen were normal.

Oesophagogastroduodenoscopy (OGD) showed an ulcerated polypoid lesion in the body of the stomach. Biopsy revealed a small round blue cell tumour. Further immunohistological studies showed a strong positive reaction for neuroendocrine marker PGP 9.5. An absence of staining was noted with vimentin, lymphoid and epithelial markers, which overall was suggestive of oat cell carcinoma.

CT scan of his chest and abdomen confirmed a mass lesion measuring 3 x 2 cm arising from the posterior wall of the stomach. No lymphadenopathy, metastatic disease or bronchial involvement was demonstrated, although not confirmed by bronchoscopy. At laparotomy, the tumour was unresectable due to extensive involvement with the left lobe of the liver and pancreas. The patient received two doses of adjuvant vincristine and etoposide but his general condition deteriorated and he died three months after surgery.

CASE 2 A 39-year-old female, who also was a non-smoker, presented with symptoms of gastric outlet obstruction. OGD revealed a necrotic ulcerating tumour in the duodenum, biopsies of which suggested a small cell carcinoma. A CT scan showed a 6 cm soft tissue mass in the second part of the duodenum, displacing the pancreas

Altnagelvin Area Hospital Glenshane Road, Londonderry, BT47 1SB.
Department of Surgery:
SA Badger, MRCS(Ed), Senior House Officer in General Surgery.
J Lee, MD, FRCS(Ed), Specialist Registrar in General Surgery.
KJS Panesar, FRCS, FRCSI, FRCSEd, OBE, Consultant Surgeon in General Surgery.
Department of Pathology:
H Vazir, MBBS, FRCPath, MA, Consultant Pathologist.
Mater Hospital Trust, Crimlin Road, Belfast BT14 6AB.
Department of Surgery:
T Diamond, BSc, MD, FRCS, FRCSI, Consultant Surgeon in General Surgery.
Correspondence to Mr Panesar.
E-mail: PanesarK@alt.n-i.nhs.uk

anteriorly. No lymphadenopathy or pulmonary or hepatic lesions were noted, although not confirmed by bronchoscopy.

At laparotomy the tumour was inoperable and a palliative gastrojejunostomy was fashioned and a stent inserted into the common bile duct. Histopathology of both the OGD biopsy and a lymph node obtained at the time of the laparotomy showed a poorly differentiated tumour with a small cell appearance. It stained positive for CD56 and P53 and PGP9.5, but stained negative for insulin and somatostatin. Chemotherapy was commenced using etoposide and cisplatin, but her condition deteriorated and she died three and a half months after surgery.

DISCUSSION

Oat cell carcinoma of the lung is very aggressive, metastasises widely and is rarely curable by surgery. This form of lung cancer occurs mostly in smokers and has a higher incidence in miners with previous exposure to uranium or radium. The prognosis of pulmonary oat cell cancer is poor with a median survival of about one year and a five-year survival of about 10% in spite of aggressive treatment.[3] Extra-pulmonary oat cell cancers originating from neuroendocrine cells are biologically aggressive and associated with a poor prognosis.[4] The two cases of extra-pulmonary oat cell cancer reported here represent neuroendocrine tumours of foregut origin.[5]

Gastric small cell carcinoma was first reported in 1976 with 66 cases reported since.[6] The presentation is usually at a late stage, as demonstrated in our case.[7] The tumour is usually polypoid in appearance at the early stage, progressing to crater-like ulceration due to rapid proliferation. The aggressive nature of the tumour and relative insensitivity to chemotherapy result in few long-term survivors and surgical efforts are generally palliative.[8]

Duodenal oat cell carcinoma is rare, with nine cases previously reported in the literature. Zamboni *et al* reported three cases of small cell carcinoma in the ampullary region of the duodenum.[9] The poor prognosis of oat cell tumours was again reflected in these three cases with a median survival period of ten months.

Histologically the cells grow in clusters that exhibit neither granular nor squamous organisation. It has been shown that the argentaffin (Kultchisky) cells in the gut closely resemble cells contained in normal bronchial mucosa.[5] Electron microscopy shows that these cells contain membrane-bound dense core granules characteristic of APUD (Amine Precursor Uptake and Decarboxylation) cells. Similar granules are found in bronchial carcinoids and oat cell carcinomas suggesting that they are of APUD cell origin. The APUD cell system is a family of cells with similar cytological and ultrastructural features derived from the neuroectoderm. During embryological neuralation, when the neural folds elevate and fuse together, cells at the lateral border of the neuroectoderm begin to dissociate from their neighbouring cells. This cell population will undergo epithelial to mesenchymal transition as it leaves the neuroectoderm by active migration and displacement to enter the underlying mesoderm. Among other places they enter the gastrointestinal tract. These APUD cells are responsible for the production of polypeptide hormones and biologically active amines. The presence of the neuroendocrine granules results in the positive staining of immunohistochemical cell stains for neuroendocrine markers.

Radical surgery does not have a primary role in managing extra-pulmonary oat cell cancer, as the benefit is limited.[10] Any additional benefit of radiotherapy is not adequate to justify its potential toxicity.[11] Multi-agent chemotherapy in different combinations has some success, achieving a complete response rate (defined as 50% or greater shrinkage of measurable disease) ranging between 21-91%.[11,12] However, these are non-comparative clinical studies with small numbers of patients and the median survival still remains poor at 18-51 weeks.[12] An analysis of the different chemotherapeutic regimens used suggests best results with a combination of cisplatin and etoposide with response rates reaching 70%, while doxorubicin-based regimens appear to be less active.[13, 14, 15] Complete response has been observed with cisplatin and etoposide based treatment in a patient with widespread metastatic disease.[16] The two patients reported by van der Gaast had extensive disease with a reported survival of 11 and 16 months after combination chemotherapy with cyclophosphamide, doxorubicin and etoposide.[17] Another patient with pancreatic oat cell carcinoma

reported by Wahid survived 14 months with combination chemotherapy and radiotherapy.[18]

In summary, primary extra-pulmonary oat cell carcinoma is rare and originates from neuroendocrine APUD cells. It is essential to obtain an early accurate diagnosis so that appropriate treatment can be commenced. Oat cell carcinoma may respond to chemotherapy and stay in remission for at least a few months. Despite this the prognosis is poor with an overall median survival of one year.[3] Our case reports demonstrate and reiterate the aggressive nature of extra-pulmonary oat cell cancer and the associated poor survival. Radical surgery has little role in the management of these patients and surgery is usually limited to palliation only.

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Case Report

Pre-operative embolization for spontaneous rupture of renal cell carcinoma

S Watanabe, Y Hama, T Kaji, F Kimura, S Kosuda

Accepted 12 January 2005

Spontaneous rupture of the kidney as a presenting sign of renal cell carcinoma (RCC) is a rare but potentially lethal condition.[1-3] We report a case of spontaneous rupture of RCC successfully treated by emergency transcatheter arterial embolization (TAE) followed by radical nephrectomy. We also discuss the importance of pre-operative TAE as an emerency first aid.

CASE REPORT An 80-year-old man was referred to our hospital for treatment of spontaneous rupture of the left kidney. His past history and family history were not remarkable except for a one-year history of hypertension treated with antihypertensive agents.

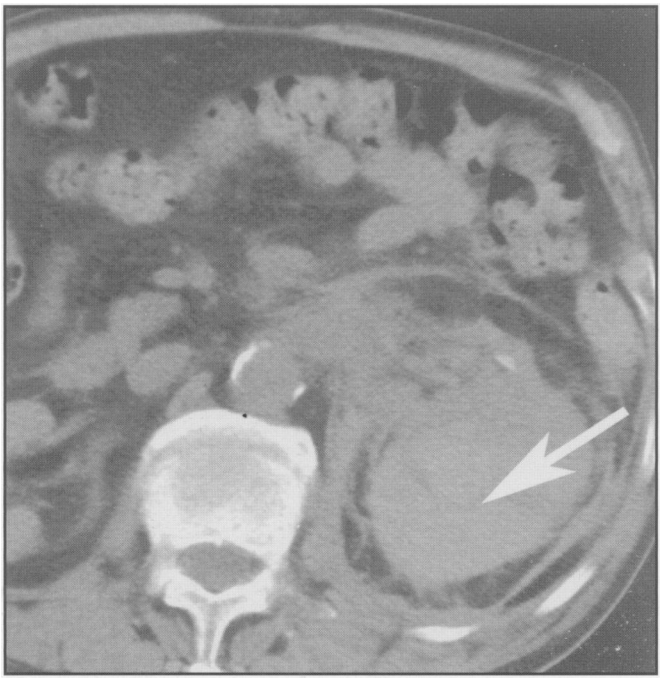

Fig 1a. Unenhanced CT scan shows a large left perinephric hemorrhage containing a fluid-blood level (arrow).

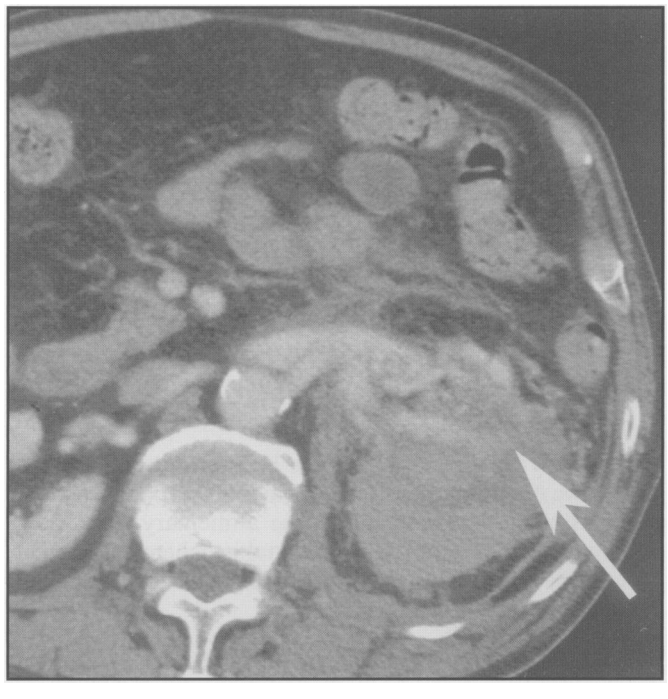

Fig 1b. Contrast-enhanced CT scan at the same level shows an irregular enhancing area (arrow) immediately ventral to the hyperdense hematoma, which is suggestive of the point of rupture.

National Defense Medical College, 3-2 Namiki, Tokorozawa, Saitama, 359-0042, Japan.

Department of Radiology:
S Watanabe, MD.
Y Hama, MD.
T Kaji, MD.
S Kosuda, MD.

Department of Urology:
F Kimura.

Correspondence to Dr Hama.

E-mail: yjhama@me.ndmc.ac.jp

On admission, blood transfusion had been continued due to the progressive anemia. Computed tomography (CT) scan showed a hyperdense non-enhancing perinephric collection adjacent to the ruptured tumor of the left kidney (*Figs. la and b*). Left renal arteriogram showed a hypervascular tumor with neovascularization (*Fig. 2*). To arrest the hemorrhage, TAE of the left renal artery was performed using gelatine sponge particles. Immediately after TAE, his hemorrhage was arrested and his condition was stabilized. Eight days after that, radical nephrectomy was performed with negligible intra-operative blood loss. The pathological examination revealed a clear cell RCC (pT3a, N0; stage II according to the Robson's classification). Chest and abdominal CT scans and a bone scan were negative for metastases. He received subcutaneous interferon alpha as adjuvant therapy, and has been free of recurrence for 6 months.

DISCUSSION

Spontaneous rupture of RCC is a rare but potentially lethal condition. The incidence of spontaneous rupture of RCC is 03-0.6%.[1, 2] Nephrectomy when possible should be performed expeditiously since conservative therapy is unsuccessful. It has been suggested that when bleeding is extensive and the patient is unstable, surgery or renal angiography with embolization is necessary to arrest the bleeding.[4] In our case, emergency embolization allowed control of the hemorrhage, a clean surgical field and reduced intra-operative blood loss.

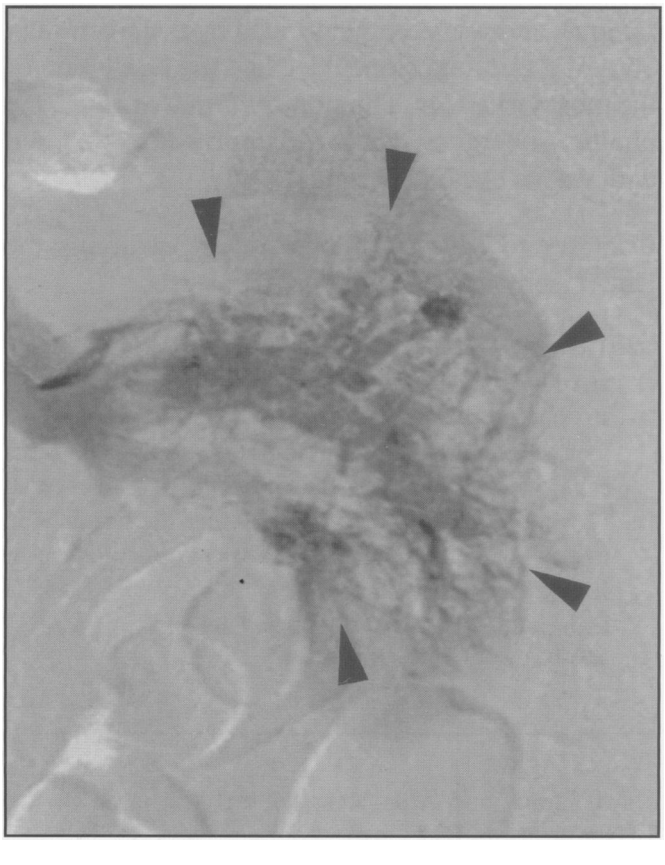

Fig 2. Left renal arteriogram shows a hypervascular tumor with neovascularization (arrowheads).

To our knowledge, only one previous case of embolization of the spontaneous rupture of RCC was found in the English reports.[3] The rupture in the previous case was attributable mainly to the uncontrolled hypertension.[3] This case had a history of hypertension; however, it had been well-controlled with antihypertensive agents. We do not consider that the hypertension was attributable to the rupture of RCC in this case.

Thus, this is the first case of non-traumatic and non-hypertensive rupture of RCC successfully treated by emergency TAE followed by radical nephrectomy. The findings in this case support the importance of pre-operative TAE for stabilizing the patient's condition and for preparing for the surgical treatment.

In conclusion, a single case cannot be generalized to others without additional scientific verifications. However, pre-operative TAE should be considered to stabilize the hemorrhagic state in a patient with spontaneous rupture of RCC and an elective surgery should be performed on a non emergency basis in a better patient condition.

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Three pregnancies in iron-age Ireland

Crying in the womb, hydramnios and caesarean section

HW Gallagher

Accepted 13 April 2005

The report of three pregnancies in Iron Age Ireland that terminated with complications is a matter of interest. Observation then was as acute and as accurate as now. They are described in the Ulster Cycle of Tales – "the oldest (non-ecclesiastical) literature of any country north of the Alps".[1] The stories are set in the closing years of the Iron Age, not earlier than the 4th century AD.[2]

CRYING IN THE WOMB

This is the story of the birth of Deirdre who became so beautiful that she caused dissension between the men of Ulster and their King – Conor. This ended with civil war. No wonder that she is known as Deirdre of the Sorrows.

> The men of Ulster were drinking in the house of Fedlimid. His wife was overseeing everything . . . She was full with child. Meat and drink were passed around, and a drunken uproar shook the place. When they were ready to sleep the woman went to her bed. As she crossed the floor of the house the child screamed in her womb and was heard all over the enclosure.[3]

The child was delivered very soon thereafter.

Crying in the Womb was a new phenomenon to me. However I found out from my obstetric colleague, Dr JHN Ferris, that the phenomenon had occurred three times in Ards Hospital, Newtownards Co. Down between the years 1961 and 1991. In no instance was the child distressed but delivery was expedited to lessen the risk of aspiration of amniotic fluid.

"Crying in the womb" is, of course, a misnomer. The head must be low enough in the vagina for the child to be able to inspire. However "crying in the womb" is much more euphonious than "crying in the birth passage".

It is comparatively rare. William Scorza of the University of Medicine and Dentistry of New Jersey has witnessed it for a few brief seconds at cesarean (sic) section just prior to delivery. Maternal-fetal(sic) medicine expert Christopher Glantz of the University of Rochester Medical Center(sic) searched the literature and found over 100 cases going back as far as 1546, but none since 1973.[4]

HYDRAMNIOS

This episode occurred during the attempted invasion of Ulster by Maeve, Queen of Connacht. Her promiscuity was well known and was no secret from her husband Conor. She told him "I never had one man without another waiting in his shadow".[5] Fergus, the Commander-in Chief of the army was equally famous, and was commemorated by the erection in Tara of a standing stone. "He had the reputation of the most virile man. The stone at Tara was called the phallus of Fergus.[6] Not surprisingly they cohabited and Maeve became pregnant.

Contrary to Maeve's hopes and expectations the Ulster army was successful.

> The army (Maeve's) was fleeing towards the River Shannon at Athlone: . . . Then Maeve got her gush of blood. "Fergus" she said, "take over the shelter of shields at the rear of the men of Ireland until I relieve myself" "By god", Fergus said, "you have picked a bad time for this." "I can't help it" Maeve said, "I'll die if I can't do it." So Fergus took over the shelter of shields . . . and Maeve relieved herself. It dug three great channels, each big enough to take a household. The place is called Fual Medba, (Maeve) Medba's Foul Place ever since.[6]

North Down and Ards Hospital Trust, Church Street, Newtownards, BT23 4AS.

HW Gallagher, MB, FRCS(Ed&I), Honorary Consultant Surgeon.

This adds up to a classic case of acute hydramnios. It can be very painful. The amount of fluid can be very great and it is frequently associated with congenital malformations.[7]

When we consider that houses at that time were wattle and daub with very shallow foundations the hyperbole is more apparent than real.

CAESAREAN SECTION

In another of the Ulster Cycle Tales there is a footnote concerning Maeve.

> They say that Maeve killed her sister, Clothru, and out of her sides her child, Furbaide (Furvaddy) son of Conor, was taken with the swords.[8]

Someone knew what to do and was not afraid to do it presumably with sword and dagger – not the most typical surgical instruments. However the operation was successful and Furvaddy lived long enough to avenge Clothru by murdering Maeve.

The descriptions of these pregnancies must have been made from life although the stories in which they occur are fictitious. The stories may have been composed in the Iron Age and transmitted orally to about the 7th century and thereafter copied from scribe to scribe till the 12th century finishing with the "books" from which the English translations were made.

Over the centuries there were ample opportunity for alterations and additions to be made to the script. Therefore it is impossible to know when each episode was composed but the author or authors intended the action to be in the Iron Age and that is where 1 would prefer to leave it.

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The Ulster Medical Journal, Volume 74, No. 1, pp. 70-71, May 2005.

Book Reviews

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Many chapters repeat the same theme. Despite this, the book provides a good insight into the history, psychosocial, mental and public health of the population in relation to Bio terrorism. It is a useful addition to Emergency Planners and professionals dealing with major disasters including bio terrorism. The accompanying CDs are a welcome addition to the book and provide an introduction to the sections by various authors.

VINOD KUMAR TOHANI
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NEIL McCLURE

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As the author relates, Sir Ian Fraser was unquestionably a man of great charm, humour and charisma but, more than this, he demonstrated warmth and generosity towards those with whom he came into contact. Above all, perhaps, he possessed unique and special communication skills which allowed him to relate to all ages and types. Richard Clarke's biography captures all of these features and more, and is a fitting testament.

COLIN RUSSELL

NOTICE

Are you missing back issues of the Ulster Medical Journal?

Spare back issues of the UMJ, which have been stored in the cloakroom, are soon to be discarded.

If you wish to obtain any of these issues, they will be available in the Ulster Medical Society Rooms after the Presidential Address on Thursday 13th October 2005.

PAUL JOHNSTON
(*Honorary Secretary*)