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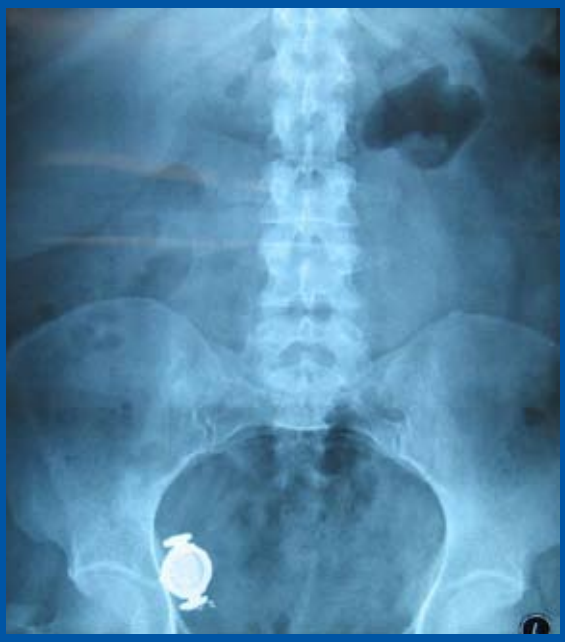

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Essay

40 Years Hard Labour

Dame Lorna EF Muirhead DBE

Accepted 18 March 2008

I'm sorry to say that there's hardly a word that is research based in this "40 years hard labour", but what surprises me is that my observation and experience is sometimes supported by subsequent research. This is an anecdotal account which I hope you will enjoy and find peppered with controversy, pearls of wisdom, and food for thought, but I expect it will not add one jot to the body of your knowledge, and most of you have probably not heard a lecture like this for some time. Not for my generation the PowerPoint lecture, but one written in longhand, which the author then performs. It is based on a chapter I was asked to write last year on essentially the same theme for a textbook for midwives.

Here goes!

The bell rang and I and three other new pupil Midwives, trying to master the art of palpation, left the antenatal clinic and rushed to labour ward to witness our first delivery.

It was 1964 when childbirth was not viewed as the normal life changing event, which it is today, but a frightening painful experience, which women had to endure in order to become mothers. It was a time when antenatal education was almost non-existent and women came to childbirth hardly knowing what to expect. Many were forced to deliver at home because there were not enough maternity beds for them to have their baby in hospital, which is what women then aspired to do. Hospital birth was becoming all the rage! Labours were longer and experienced without the support of husbands and family, who generally left them at the labour ward door, coming back later to see mother and baby.

Women laboured in Nightingale wards with only a curtain in between them. They often laboured with inadequate pain relief. 50 or 100mg of pethidine was the standard analgesia for labour, topped up by gas and air towards the second stage. However the women in Liverpool were very well treated in this respect, because they were given the Liverpool cocktail. A primigravida would be given 10mg of morphine, 100mg of pethidine, and 200mg of butobarbitone at two fingers dilated; topped up later in the labour by 100mg of pethidine and gas and air. They often woke up three days later and exclaim, "Did I have the baby!!?" So much for bonding, but at least they were spared the agony of labour, and of course, as we all know, before the idea of bonding which came on board in the latter half of the 20th century, no mother had ever bonded or formed a meaningful relationship with her baby.

1964 predated epidural analgesia, so easily dismissed today, but not by midwives of my generation, who knew the onerous and draining experience of sitting with women in agony, experiencing prolonged or painful labour for many long hours. When epidural analgesia was first used for such labours I was its most ardent supporter, and I remain so.

More women died in childbirth than they do today. The main complication which killed them was post-partum haemorrhage. The routine use of Syntometrin and the active management of the third stage of labour, which has largely eradicated this condition, certainly from normal vaginal delivery, was some way off. Physiological 3rd stage of labour was the practice of the day

The Triennial Confidential Maternal Enquiries (the fore-runner of CEMACH) contained accounts of those deaths along with the deaths of women who had inhaled vomit at caesarean section, and died of Mendelson's syndrome. As a result, women in labour were fed a liquid diet of soup, jelly and ice cream, and sucked glucose sweets, anything which quickly became liquid and passed through the stomach, so that if general anaesthesia was required the stomach had no solid food within it, and of course there was no prophylactic antacid therapy. Perhaps when reviewing whether or not women should be fed in labour today, the reasons why they were ever not fed should be borne in mind.

My practice predates the describing of supine hypotension syndrome. Prematurity was considered to be anything under thirty-six weeks gestation. Special Care baby units did not exist, though there were a few premature baby units. Can you begin to imagine managing the complications of pregnancy and labour without specialist help for the baby you deliver? The choice, which all too often had to be made, was to deliver the woman if there was an indication to do so, and the child had to take its chance.

1964 predated the contraceptive pill and the abortion act and there were many unplanned pregnancies for married and unmarried women alike. It was a huge social disgrace to be pregnant out of wedlock, so much so that girls finding themselves in this situation used to go "on holiday" to another town where they delivered their child, often having it adopted, and then conveniently arrived back home "from holiday."

It will be difficult for today's midwife and obstetrician to

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contemplate childbirth or the practice of midwifery and obstetrics within this context; just as in forty years time it will be difficult for the midwives and obstetricians of the day to contemplate the practice you do now. Professional life moves on, and goalposts and expectations constantly move.

The preoccupation of the professionals caring for pregnant women when I trained was to eliminate risk from childbirth. As professionals it was mandatory that we should do so, and women expected no less from us. After all, some women were still going to be churched following delivery (as it says in the prayer book) to "thank almighty God for vouchsafing to deliver them from the great pain and grave peril of childbirth." The attempt to eliminate risk led to the use of antenatal screening, and routine procedures for all women, to make sure that they came to labour in the best possible condition to withstand its rigours. This of course is an unchanging principle. Invariably this means that some women, those who essentially remain within agreed normal parameters, could be said to have been over-monitored and over-treated, but this blanket approach to care has undoubtedly played a significant part in making birth here as safe as it is today. However, it could also be said, that in making it so, there is a danger of our becoming victims of our own success, resulting in some of those procedures which make birth safe, now being abandoned.

This is very much like the current thinking on vaccinating all children against measles. No one believes that all children who contract measles will be damaged or die, but some will, and since it is impossible to accurately predict those children who will, vaccination of all children is advised.

If many children were dying in this country during an outbreak of measles, there would be little reluctance in modern parents about having children vaccinated. But this is not happening, and parents can be forgiven for thinking that because they never hear of such tragedy they need not accept the very minimal risk associated with measles vaccination. Likewise birth is so successful and safe here, that we are letting down our guard.

I accept the idea of low-risk and high-risk pregnancy, but it is worth reminding ourselves that there is no such thing as a no-risk pregnancy, which makes me feel justified with meticulous monitoring and appropriate intervention of those in my care. Successful though birth is here at the beginning of the twenty-first century, success cannot be guaranteed prospectively. It can only ever be classified as successful, retrospectively.

But back to my first delivery!

As I approached the labour ward I felt mounting apprehension and anxiety, but at the same time excitement at the prospect of witnessing my first delivery. However the awful screams heard in the corridor meant that anxiety was my uppermost emotion. I had rarely heard such distress. As a nurse I had witnessed people badly injured and desperately needing help sounding so agonised, but this was a woman in the height of labour about to deliver her child. We, the three new pupils, stood at the foot of the bed, silent, frightened and fearful for the woman. She pushed, screamed and shouted, and then a non-breathing blue head suddenly appeared at the vulva.

There was a temporary silence.

"Why doesn't someone do something," I thought, "the baby is surely dead," since hitherto anything I had seen that colour and not breathing had been dead. The midwife in charge however was calm, tranquil and very unworried.

Another mighty scream and it was all over. Miraculously the child shuddered into life. I stood transfixed. I had just witnessed the most awesome, terrifying, painful experience I could imagine – but the mother, child in her arms, was now smiling. I left the room totally confused, found the nearest lavatory and I wept.

Eventually my time came to work on labour ward and during the following six months I would witness, and become involved in, the most exciting, unpredictable, totally absorbing, painful process called labour. I would help eighty-four women to deliver their babies and my lifelong passion for the care of labouring women and the desire to do something to alleviate the suffering involved with it would become established.

The labours, which, in common with all midwives I like best, are those which proceed normally and allow me to practise "autonomously." However I strongly believe that midwives are there for all pregnant women, and my clinical practice over many years has embraced natural, normal, complicated, and alas fatal childbirth, the latter two of those requiring me to move into a different gear of midwifery and become an equal partner of a multidisciplinary team, working towards the optimum outcome for mother and child. Dear to me though "autonomous" midwifery is, it is secondary to doing what is necessary to secure the best outcome for mother and child.

And so, the first six months training was coming to an end. Perhaps I should tell you a bit about it. Midwifery was taught by Sister Tutors within midwifery hospitals. Each training hospital, every three months, took their required number of new pupils, who were not only guaranteed a job at the end of training – but indeed were expected, as new midwives, to work in their training hospital to give back some service. Midwifery training was divided into Part I, which covered all the theory of midwifery, and Part II, which largely involved public health and a time spent on "the district" which is now referred to as in "the community."

So I bought a very old bicycle from a pupil midwife just returning from the district, was measured for my brown mackintosh and hat, and collected my midwife's bag before cycling to the midwife's house in the middle of a council housing estate in Birmingham. The plaque on the door read "Midwife's house." Inside lived two district midwives, and every three months two new pupil midwives came to live and work with them. It was like a monastic life, totally immersed in midwifery six days and nights a week. What a wonderful experience I had with Janet Webb and Doris Eaves! They lived and worked amongst those they attended and were regarded as pillars of the community. Dressed in their green uniform they looked like the woman on the Quaker Oats packet, and yes, both drove Morris Minor cars. They knitted baby clothes, they ran antenatal clinics, and they did some fifty deliveries at home each year. So life was very gentle in spite of the long hours which they had to be on duty and available. Whilst I was with them I did twenty-one deliveries. They were mistresses in the art of midwifery and taught me so much

Daily I would be given my work, which was to attend antenatal clinics, and to visit post-natal, women which we did for ten days. Such visits included bed bathing the mother – few had

bathrooms - bathing the child, making the bed, and checking temperature, pulse, respiration, lochia and the fundal height, and sometimes included hoovering, or doing some shopping for the family.

I particularly remember one delivery I attended. A gravida four booked for home went into labour when I was in the midwives' house alone. There was a knock at the door, "Can you come to my mother" the little boy said. "She's going to have her baby." This mother, in common with most, had no telephone in her house. So I cycled carrying all the equipment I needed, and arrived at the house to hear sounds, which, had I been a little more experienced, I would have recognised as a woman approaching the second stage of labour. I ran breathless from my cycle-ride, up the stairs. Keen to do the right thing and get the procedures right, and frightened that I was on my own, I took out my razor to shave the vulva. (In 1964 it was not humanly possible to deliver without a shaved vulva!). One swift move of the razor and the head of the child appeared with the centre of its head shaved! Oh my goodness! What now! Seeing a bonnet which was laid out neatly on the dressing table ready to be put on the baby when it was born I seized it, and put it on the head still at the vulva. Was this the first child in history actually delivered wearing a hat? When Miss Webb arrived she complimented me on my putting on a bonnet, because the room was a little cold – no central heating, and only one bar of an electric fire. The mother smiled, and we kept our little secret.

The next three months taught me a lot. As I have said, women delivered their babies usually in the back bedroom of their parent's house. Few young couples had accommodation of their own. Houses usually had no bathrooms and no telephone. Midwives had to rely on the telephone box in the street to summon aid, if it was necessary.

Home birth, as ever, was wonderful when all went well, but if there was fetal distress, post-partum haemorrhage, sudden eclampsia, or a baby not breathing, all unpredictable conditions associated with labour, home birth was a nightmare. In such circumstances it was left to the husband to run to find a working telephone and ring the local hospital who would send out the flying squad.

The flying squad consisted of an ambulance, which was always available, which brought to the patient's house a team consisting of an obstetrician, an anaesthetist, a midwife and a medical student. With them they brought blood, and equipment necessary to deal with conditions like ante-partum haemorrhage, post-partum haemorrhage, retained placenta, delay in second stage, eclampsia, undiagnosed breech, or twins in the second stage. Some of these conditions were dealt with at home, but if needs be the patient's condition was stabilised before she was transferred to hospital. Flying squads were very much the predecessors of today's paramedics. The maternity services long ago knew, that to transfer a compromised pregnant, or intra-partum woman to hospital by ambulance could result in death, and so the idea of initiating treatment which would make the patient safe at the scene of their problem before taking them to hospital, was born.

Although the flying squad usually arrived within half an hour of being called, half an hour was a lifetime with a fitting woman, a woman haemorrhaging, or a second twin lying transversely. Perhaps this is why I do not share the contemporary views about the merit of home birth, or birth in freestanding maternity units.

So my time in Birmingham ended – I had passed Part II and was now a midwife. I had no thought of going back to nursing. During my midwife training, I had meet and fallen in love with a tall, dark, handsome Scot who was at university in Aberdeen. He was going to Liverpool University to do a PhD and so I looked in the midwifery journals for a post in Liverpool, and saw the advertisement for a staff nurse at Liverpool Maternity Hospital. I had never been to Liverpool – never heard the accent, and knew little about the area.

I arrived at Lime Street Station and walked up the hill to the hospital. The Matron, Emily Carter, met me. She had the face of a Madonna and was a visionary midwife, who ran a hospital with standards for women and midwifery, which were the very best of the day. I did not know then, just how lucky I was to be successful in getting a job. The local view was that you had to have a letter of recommendation from the Holy Ghost to be considered good enough to work there.

Unlike the place where I trained, Liverpool Maternity Hospital was a teaching hospital, which meant that it was attached to a medical school, and had the brightest and best doctors and midwives working at it. It was also much better staffed and had a much bigger budget. This was the workplace of Professor Sir Norman Jeffcoate, one of the most influential, if not the most influential, obstetricians in the world. Doctors used to come from all over the world simply to work with, and touch the hem of Professor Jeffcoate. James Minnit, the man who gave us "gas and air" was on the staff, and Charles Clark who did something with butterflies which resulted in our having anti-D which led to the elimination of babies stillborn, or born compromised because of rhesus incompatibility. This was a Rolls-Royce place, where excellence could be readily spotted, and I wanted to be part of that excellence.

I thought I had gone to work in paradise. Women laboured in single rooms in a state of the art labour ward. Their husbands were "allowed" to stay but only for normal deliveries. Liverpool was well ahead when it came to preparing women for labour and motherhood. It ran "mothercraft" preparation classes.

For labour, it offered women the Liverpool cocktail (or coughdrop as the locals called it). This was 100mg of Pethidine, 10mg Morphine, 200mg of Butobarbitone – given together when the cervix was 2cm dilated. It was topped up hours later with 100mg of Pethidine if required, followed by gas and air, given at the end of the first stage and into the second stage of labour.

Women slept throughout labour and often almost through delivery. Many a woman was heard to ask sometime later "Did I have my baby?" So much for bonding – but at least they were spared unwanted agony, and were very grateful for that

It is often asked "Surely all the babies were born with low APGARS after all that analgesia?" I can assure you they were not. At that time, the mid 1960s, there was no resident paediatrician in most maternity hospitals, which meant that midwives had to deal with all the babies born. Believe me, if babies had been born compromised by the analgesia which their mothers were given in labour, the analgesia would have been modified! After delivery, women were served a tray of

tea. I had never seen this. A hurried drink from a communal teapot had been the norm where I previously worked – but a tray of tea!

In the post-natal wards women rested for ten days. Their babies lived in a nursery where they were looked after by midwives and nursery nurses, and only taken to the mother to be fed. Surprisingly, against modern thinking, mothers did manage to bond with them! Post-natal wards outside feeding time were tranquil places where women spent time getting over birth. Midwives had time to devote to assisting with breast feeding and teaching mothers how to bath and generally look after their babies. Post-natal wards were not, as they are today, like Heathrow airport, full of women coming and going with very little time on the tarmac.

I was exposed to Liverpool humour almost on my first day as I asked a woman I was booking: "Name; address; religion; next of kin?" "Oh," said the woman, "I don't have a next of kin." "What about your husband?" I said. "Oh! He doesn't have one either."

The next week on labour ward, looking after a labouring woman, I said to her, "Don't you think you ought to have something for your pain?" She seemed in agony to me. She retorted, "I don't know! You're the bloody midwife!" This response tells you something about the relationship between patient and professionals at that time. That woman expected me, a qualified midwife, to advise her and to tell her what I thought would be best for her. This today is called paternalism and is grossly unfashionable, but I see some merit in women asking the professionals whom they consult, what they think is best for them individually, and the professionals giving the women the benefit of their education, knowledge and experience. Why else are we professionals?

In 1970 the Peel report, now much castigated by many midwives, recommended on the grounds of safety that all births should take place in hospital. Today's midwives are dismissive of Peel because his evidence was not "research based." But can I remind us, that most of what we did then and do now, is not research based, indeed until relatively recently we midwives had little formal research to guide us, but we still had a very successful, progressive profession. Important though it is, let us keep research in its place as only one of the disciplines, which informs us about practice. What we did have in 1970 were statistics, presented in the Triennial Confidential Enquiries into Maternal Deaths, which catalogued where and why deaths and morbidity occurred. The report supported Peel's conclusions that many of the deaths reviewed could have been avoided if the woman had been in the right place with the right equipment and the right level of expertise to hand. I share Peel's view.

Post 1970 most babies were born in hospital, and statistical evidence supports the view that maternal and perinatal deaths declined. But with hindsight there were some problems. All women, normal or complicated, now booked under obstetricians, who consequently believed that they bore ultimate responsibility for all pregnancies. In the attempt to improve labour, especially prolonged labour, which was a common problem, obstetricians, at that time, rightly intervened in intra-partum care to rectify conditions like cervical dystocia and incoordinate uterine action, so rarely seen today that modern midwives will have to resort to midwifery history books to identify it.

However, soon interventions spilled over into normal labour, doctors believing that they had a duty to do what they considered best for all women in both complicated and normal labour. The professional accountability of the midwife being a practitioner of normal childbirth was poorly understood by obstetricians and I have to say by midwives as well. Those of us in practice at the time were just too busy getting on with the job to notice this insidious intervention in normal labour, or the erosion of our role. This is not a comfortable conclusion for me to reach, since it was my generation which was responsible for it. But let us not demonise doctors. They were doing what they thought was best for women, and I deplore the current anti-doctor attitude which some display. A strong, confident profession like midwifery does not need to demonise other professions, especially our obstetric colleagues who have played a vital part in making childbirth as good and safe as it is today. Now, there's an unfashionable view! Midwives do not have the monopoly of altruism. We did not on our own, make the experience of childbirth the comparatively wonderful, safe experience which it is today in this part of the world.

For all the interventions of the 1970s and 1980s, do not for one minute think that all was bad for women then. I have no misty eyed nostalgia for childbirth at the beginning of my career or during those later years. On balance having a baby in this country gets better all the time and will continue to get better, provided we keep the best practise of yesterday and marry it with the best of today's. Let us not be tempted to throw the baby out with the bath water. As a young midwife I could only see as far as I could see, because I was standing on the shoulders of the generation of midwives who went before me. Today's midwives, and for that matter, today's obstetricians can only see as far as they can because they are standing on the shoulders of my generation. When today's midwives believe that they have found a better way of looking after pregnant women, they must avoid the temptation of rubbishing the efforts of the midwives who went before them, who like them, were giving care which conformed to the philosophy and best practise of their day.

Let me remind you about some of the advances for women in the 1970s and 1980s, since some balance needs to be given to the very negative attitudes to the management of childbirth at that time. Single rooms were provided for women to labour in privacy. The vast majority of women wanted effective pain relief during labour, and attention was paid to improving what was on offer. A marvellous innovation called epidural analgesia was introduced into labour-ward practise and midwives of the day adapted their management of labour, especially the second stage, so that the forceps rate did not rise dramatically, as one is led to believe. In my view, it is often incorrect management of the second stage of labour which leads to forceps or Ventouse delivery not epidural analgesia *per se*.

The introduction of continuous fetal monitoring meant that because the well being of the fetus could be clearly seen, relaxation of the time limits imposed especially on the second stage of labour was possible, and this was greatly welcomed. The second stage of labour was known to be a time of increased risk for the fetus, and my generation were exposed to catastrophic and unexpected intra-partum stillbirths. We welcomed continuous fetal monitoring!

Fetal scanning and choice about continuing the pregnancy in the case of abnormality became available. We are now at the time of the contraceptive pill, which gave women more control over their fertility, and the Abortion Act had been passed in 1967.

Special Care Baby Units (SCBU) were being set up everywhere, which meant that babies born spontaneously premature, had more chance of survival. It also meant that conditions in the mother, like severe pre-eclampsia, requiring very early delivery, became less of a problem. It would be good for today's midwives and obstetricians to pause and think about how difficult it was to manage those women who need early delivery without SCBU.

Organisations like the Natural Childbirth Trust, later to become the National Childbirth Trust (NCT), were born and set up classes in antenatal education and preparation for birth. However the NCT cannot, and does not take all the credit for this because many midwives ran the same sort of preparation classes.

This meant that for the first time women came to pregnancy and delivery with some idea of what to expect, and what a joy that was. What was not so desirable in this context, was that women soon began to have very fixed ideas about what they "wanted" from their childbirth experience, whether their actual childbirth performance could support this or not. This led to some disquiet amongst midwives who, until that time, were used to being consulted by pregnant women who asked for advice and usually took it. This is now called paternalism and, as I have said, is deeply unfashionable. However, in my view it is desirable for professionals to believe that they should know more than even the most well informed "consumer," and midwives know exactly what women want to achieve by the end of their pregnancy. We talk today about individualised care, but all birth plans in my experience, include most of the same things, and are not individual at all. We know that women want things to be as normal and uncomplicated as possible. They want to take home a healthy child and be proud of their achievement. They also want to be satisfied with the care they received. We want those things too! But midwives should also know that this sort of childbirth is not women's to demand, nor is it in the midwives' gift. It would be worth taking a few minutes to think about that. I hope I've managed to convince you that there were many good things which happened post-Peel.

By the late 1980s midwives could have been forgiven for believing that childbirth was very good in terms of women's and babies survival, but the price for this was the so-called over medicalisation of childbirth.

We were now at a time when fertility was largely under women's control, and when scans almost guaranteed the normality of the baby. There were major advances in the survival of neonates, and women experienced shorter labours and had choice about the method of pain relief. They laboured in private with the support of families. These advances had taken many years to achieve through the efforts of my generation of midwives. I do not accept a common view that everything which happened to women at that time was undesirable, or that women could not have been happy or fulfilled with their childbirth experience. But times change, and periodic review of the maternity services and midwives' practice is essential.

No one welcomed more than I did the recommendations of "Changing Childbirth", because it heralded the renaissance of autonomous midwifery in the care of low risk women. However I remain to be convinced that in order to achieve this, birth should be removed from hospital into the home, or into freestanding birth units. I completely support total midwifery care for low risk women, but my preference would be for it to take place in hospital with all emergency facilities to hand. The success of low risk birth in hospital lies in midwives and obstetricians "getting their act together," and having mutual respect for each other's role, as indeed they have done far more frequently than some would have us believe.

As a profession we should be concerned with equity of care. What removing birth to the home or birthing units has done is to provide a minority of women a place where a lot of attention has been paid to making a homely environment, and providing them with one-to-one midwifery support in labour. However today, the majority of women labour in hospital, where often less attention has been paid to the physical environment, and midwives frequently look after two or three women with varying risk factors at one time. Whilst congratulating midwives in birthing units and those involved in home births for the care they give, in my view, the fact that birth experience is generally so highly rated in those areas has much to do with environment and staffing ratios. If midwives worked in hospitals where similar attention was given to the physical environment, and where they were able to give one-to-one care to women with similar risk factors, I wonder what evaluations would be like. After all, one-to-one care is supposed to be available to all women. At the moment we are comparing apples and pears.

Changing Childbirth also failed to address adequately the needs of a very significant number of women for whom birth is complicated, or the practice of midwives who attend them. The experience of birth for these women is often viewed as second-rate, as is the practice of the midwife who attends them.

It seems to me that we live in a time where "good birth" and "good midwifery" is thought to be practiced at home or in birthing units, and anything else, especially birth in hospital, is "bad birth", and "not proper midwifery".

This is to be deeply regretted and does not serve mother or midwives well. I believe that midwives are there for all women, and although the practice I enjoyed most was that which I could do autonomously when everything remained normal, I had no problem at all in moving up a gear to practice midwifery within a multidisciplinary team, in the care of women experiencing difficulty. Many I know share this view.

Midwives have to guard against becoming too idealistic and too pure. As a profession we should make no apology about having a philosophy which supports non-intervention and normal birth, but we must beware that this philosophy does not become an ideology which results in our not intervening when it is necessary to do so. Having castigated obstetricians for intervening unnecessarily, midwives today must not be guilty of failing to intervene when it is essential. Herein lies the wisdom of practice.

It seems to be increasingly difficult for midwives as a profession to define, and what is meant by normal birth. We

seem to have problems in agreeing parameters of normality, especially around labour. This is probably because of the recent history of intervening unnecessarily in uncomplicated labour. It seems to me that what is seen as "good birth" today is actually "natural childbirth," not "normal childbirth." What do I mean by that? Well, natural childbirth, I would say is allowing pregnancy and birth to proceed as nature decrees, and without intervention. This means that most will be successful, some will be damaged, and some will die, very much as childbirth is in the developing world. However damage and death in childbirth is largely preventable in a developed society such as ours, and is therefore, I believe, totally unacceptable. That is why normal birth, which is the midwives' role, should take place within agreed parameters, and when those parameters have been breached, there should be timely and appropriate intervention.

Another area that I think we should be concerned about is the choice agenda, and its implications for the midwife. "Choice" is a political word of the day, and it will pass. In saying this I give my critics the opportunity to say that I do not want women to have choice, but want to nail them to the bed and do things to them. This is far from the case. I see choice as very important. What I am concerned about is the manner in which choice extends into the technical and professional aspects of what we do. Midwives, it seems to me, are often too ready to support choice, and forget that in supporting it they also have a duty of care.

This view is reinforced when I sit on the Conduct and Competence Committee at the Nursing and Midwifery Council (NMC). There I see good midwives who have not thought this through. They believe they should support women even if they choose the most inappropriate care, and they fail to safeguard themselves by understanding that they are professionals who have this duty of care. If things go wrong and the woman then brings a complaint to the NMC, the midwife may find herself ultimately being deprived of practice. There is much for the pregnant woman to have choice about, but was choice ever meant to extend into those technical and professional areas for which we have been extensively trained, and for which we hold professional accountability? What a grey and fragile area this is!

I know that the secret of women being happy to take advice from midwives, appropriate to their individual circumstances, resides in the midwife-woman relationship. Of course there are midwives and women at the extreme, but generally midwives and women within their special relationship can come to an accommodation which serves the needs of choice, accountability, and duty of care. I could go on.

I worked for some 35 years as a clinical midwife at Liverpool Women's Hospital, which sees some 8,000 deliveries a year. During that time I witnessed the joy of birth many thousands of times, sharing that moment with Liverpool families. I have also known the deep sorrow of seeing fourteen women die in the attempt. I have worked with truly outstanding, remarkable midwives and doctors, and have been inspired by their skill. I have shared with them the unparalleled experience of normal birth, but also many catastrophic situations over the years. I have seen them almost walk on water in these most dangerous and dramatic situations, and have driven home after my shift at such times almost bursting with the relief and joy of success.

I was amongst the first married midwives to work in Liverpool, and then had my own children before the days of statutory maternity leave. Those relatively few of us who had children at that time were in uncharted waters. We had to leave work, and draw out our superannuation, drawing what we thought would be a line under our professional life, since at that time almost all midwives were single and worked full-time. However, after my children went to school I was allowed the new, and rare privilege of working part-time which I did for many years, as part of the first generation of educated women to juggle home, children and a profession.

For a while I was content being part-time. Such an arrangement meant that I had the best of both worlds, at home and at work. However, it was not without its problems. A common attitude towards those who worked part-time was that they were only there for the pin money. They didn't need any professional updating, except the statutory refresher courses every five years, and indeed they were not as dedicated as their full-time counterparts, and certainly they had no aspiration or hope of promotion. For all my faults, that description did not fit me. I was professionally and politically aware and was keen, at this prestigious hospital, to engage in all the innovations in practice which midwives became involved with, and to work any shift on any day, exactly the same as my full-time colleagues. Indeed during this time I was a frequent lecturer on study days for midwives, and wrote chapters in textbooks.

I have always been an articulate woman, who dislikes controversy, but hates injustice even more, and over the years I found myself championing many local causes for midwives. I became involved in my branch of the Royal College of Midwives (RCM), variously as its chairman, secretary, treasurer, and most taxing of all as a steward. In this role I was able to support midwives through grievance and disciplinary procedures, and although I found this role very rewarding it was a times very distressing.

However Liverpool humour often sustained me. For instance, while helping a colleague one day, in middle age, I seemed to get my words mixed up, when at the delivery of his child a man said at the crucial moment "Oh, I do feel funny." "Put your hands between your legs," I said. Quick as a flash my Liverpool colleague said, "It won't make you feel any better, but it will take your mind off it!" Of course, what I thought I had said to the man was, "Put your head between your legs."

On another occasion when I was hoping to have a cup of tea with colleagues the door bell went, and a man said to me, "Good morning, Sister. I've brought my wife for inducement. I was going to bring me ma with me. She's had twelve. Me father's a Roman Catholic and has no sense of rhythm." Can you imagine what a fun day I had with him and his wife, as I looked after her in labour?

However I must not paint a saintly picture of myself. Due to constant changes, pressure of work, inadequate staffing levels, or whatever, some days I felt I had horns and a tail as I tried to be a good shift leader on a labour ward which too often resembled a war zone. On such days I didn't like myself, and I dread to think what others thought of me, as I suspect we all do when we have such days. However my experience has been that colleagues - themselves under pressure, understanding the stresses and strains which take place increasingly often - are very forgiving, and take the view that it is the pressure

of work which is largely responsible for such behaviour. Not that this excuses it, but it does explain it. This is why those cups of tea together are absolutely vital: a time to put things right with each other, and to discuss the things going on in our lives which may affect our work.

Aged 50, my family grown, and my parents' dead, I felt I might have ten years or so before retirement to do something for myself. I did not want to study for a degree. What use would that be to the profession at that age? If I were to work for a degree it would be for myself, and probably in medical ethics. My husband has always believed that I would have achieved more professionally had I not married and had children. Whilst this may be true, I actually wished to stay in the clinical arena. What I did long for was some career progression for those who wished to continue as clinical midwives. Until recently there was none.

I had always had much to say, and held strong opinions about most matters professional, and in common with most midwives I had always been good at airing those views in the tearoom. I though it might be more effective to do this where those views had some hope of being listened to, so I decided to seek election to the Council of the RCM. In order to do this I had to write a manifesto and do some serious reading. I was successfully elected, and it changed my life.

The papers for the first Council meeting dropped on my doormat in a huge bundle, which required very serious reading, and consideration. My initial reaction was that I had made a big mistake, but I told my husband I must go to Council at least once, because I had been elected.

In London, I walked into the debating chamber of the RCM Council and saw all the faces and met all the people I had hitherto only seen in our journal, "Midwives." I heard the debate, the passion, and the diverse opinions, and I was hooked. I loved every second of it. I would advise midwives to have the aspiration of being actively involved in our professional body, the oldest and largest midwifery establishment in the world, which we should cherish.

The things that I moaned about in the tearoom which seemed to me to be easy to address, in reality were not nearly so easy to resolve. I grew up politically and got so much more from my profession. I served my first term of three years, and almost on a whim put my hat into the ring for the Presidential election. I was successful, and began the most wonderful, fulfilling, exciting, and rewarding eight years as President, representing midwives nationally and internationally at branch meetings, seminars, government departments, and palaces. What a privilege it was to represent a profession so well respected and so well understood worldwide!

During this time I attended the one-hundredth birthday of our Patron, the late Queen Elizabeth the Queen Mother; had tea with her on two occasions; and sadly, some years later, I represented midwives at her funeral. I had lunch variously with the Queen and Princess Royal, and worked on the Council of The Kings Fund, whose working President is the Prince of Wales. I was also the midwife on the RCOG Council, where I met Jim and Samina Dornan, and where I was honoured to be made a Fellow *ad Eundem* of the RCOG.

Each year the Prince of Wales invites Council members of the Kings Fund, and the great and good from London who work in the health service, to the King's Fund lecture at St James's Palace. On my first visit I sat in the throne room with red damask and gold leaf on the walls, the sun shining through open windows, listening to the soldiers marching and a band playing. What a contrast I thought, to my life yesterday morning when I was trying to run a hugely busy labour ward, and was longing for a cup of coffee. Sitting next to me was the President of the Royal College of Nursing, who said "You're not staying for lunch, are you? It will only be a couple of canapés and a glass of wine. I'll treat you to lunch at Fortnum, and Mason's." "Goodness!" I thought, "I believe I could get to like this lifestyle." Returning home to Liverpool later that day I travelled first-class, which was unusual, because Virgin Railway was offering a special ticket for £14. What a remarkable day it had been! Sitting at my kitchen table, telling my husband all about it, and eating some shortbread, some crumbs fell on to my dress. Brushing them away with my hand, the dress felt very strange. I looked down and to my horror, discovered that I had been to all those places that day with my dress on inside out.

During my time as president I travelled to Vienna, the Philippines and America. I also visited some one hundred and fifty midwifery units to meet and talk with midwives in the workplace. It was an enormous privilege, and I like to believe that if a part-time clinical midwife from Toxteth in Liverpool could do this, then any midwife can.

In 2000 I was awarded a DBE (Dame Commander of the Most Excellent Order of the British Empire) for services to midwifery. I cannot begin to express the pride I feel in that award for myself and for Midwives.

In 2004 my term of office as President, and retirement from clinical practice came together, the Presidency because my term of office had expired, and my clinical work because I underwent major surgery, and running around a labour ward on night duty and day-duty at the age of sixty two years, was no longer an option.

EPILOGUE

Do I miss it? Yes, there is a huge sense of bereavement, and I find it difficult to think of my profession in which I have invested so many years marching on without me. However I do not miss the exhaustion, frustration, constant reorganisation of the health service, staff shortages, and shift work; but the essential business of midwifery, and the wonderful, talented, generous spirited professional people who are the NHS, I shall always miss.

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Review

Familial erythrocytosis arising from a gain-of-function mutation in the *HIF2A* gene of the oxygen sensing pathway

Melanie J Percy

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RED CELL HOMEOSTASIS

Red blood cell production and the supply of oxygen to the tissues is tightly controlled by a negative feedback mechanism involving the kidney. Any fall in the level of oxygen is sensed by the kidney, which then synthesizes the erythroid growth factor, erythropoietin (Epo). This growth factor acts upon bone marrow erythroid precursors to increase the number of circulating red blood cells thus correcting the oxygen deficit. The *EPO* gene, which encodes erythropoietin, is transcriptionally regulated by the Hypoxia Inducible Factor (HIF) transcription complex. The HIF complex is composed of two different subunits, alpha and beta (also known as ARNT), both constitutively expressed. The alpha subunit is continually synthesized but in the presence of oxygen it is undetectable due to degradation by the proteasome. A family of enzymes, prolyl hydroxylase domain proteins (PHD) of which there are 3 members (PHD1, PHD2 and PHD3), are able to hydroxylate key prolines in the oxygen dependent degradation (ODD) domain of HIFalpha and these enzymes are only active in the presence of oxygen (Fig 1). The von Hippel Lindau (VHL) protein is able to associate with HIFalpha once it is hydroxylated and then molecules of ubiquitin are added. This is the signal that sends HIFalpha to the proteasome for degradation. As the level of oxygen falls the PHD enzymes are no longer active resulting in less and less HIFalpha being degraded (Fig 1). Consequently, all the genes under the control of the HIF transcription complex, which includes *EPO*, are elevated. Once the oxygen deficit is corrected by the enhanced production of red blood cells the oxygen tension rises and HIFalpha is increasingly degraded.

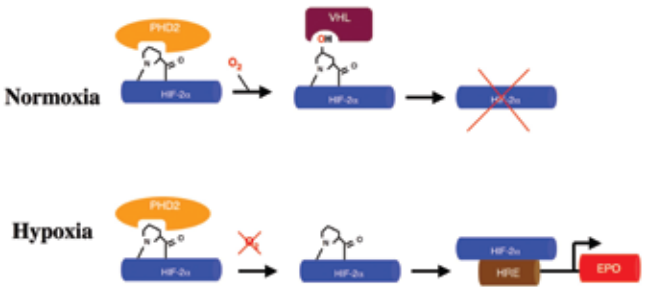

Fig 1. The control of erythropoietin synthesis by the oxygen sensing pathway.

In the presence of oxygen HIFalpha is hydroxylated by the prolyl hydroxylase PHD2 and once modified the von Hippel Lindau (VHL) protein is able to bind. HIFalpha is then targeted to the proteasome. In the absence of oxygen HIFalpha is not hydroxylated and VHL does not associate thereby allowing HIFalpha to bind to hypoxia response elements (HRE) in target genes such as *EPO*.

EYTHROCYTOSIS

Erythrocytosis is a rare red cell disorder that can arise from diverse molecular origins. It is characterised by an elevated haematocrit and haemoglobin level. There is no accompanying increase in the number of white cells or platelets. Both sporadic and familial forms exist and age of presentation is highly variable. Individuals with erythrocytosis exhibit a wide range of serum Epo levels and this reflects the heterogeneity of this disorder.

Over the last decade a registry of erythrocytosis individuals has been established at the Belfast City Hospital to which patients from the UK and Ireland been referred[1]. Interestingly, there is a preponderance of males with a ratio of 1.7 males to every female[2]. The mean age of erythrocytosis individuals present on the data base is 37 years[2]. Most individuals have inappropriately normal (46%) or raised (26%) serum Epo levels[2] indicating that a significant cause of erythrocytosis is dysregulation of Epo synthesis via the oxygen sensing pathway.

Investigation of the VHL and PHD2 proteins in erythrocytosis individuals has detected several different mutations. One VHL mutation, Arg200Trp predominates, and was first detected in a population in the Chuvash region of Russia[3]. Further studies revealed its worldwide distribution and the possibility of a common origin for most cases of this mutation[4]. In contrast, only a few different PHD2 mutations have been [5-7]. However, there remains a large cohort of erythrocytosis individuals who also possibly have an underlying defect in the oxygen sensing pathway. Previous investigation of HIF-1alpha had not revealed any causative mutations[8] but we set about investigating HIF-2alpha as murine studies indicated this isoform was the major controller of Epo synthesis[9].

THE GLY537TRP HIF-2ALPHA MUTATION

Screening the ODD region of HIF-2alpha detected a heterozygous base change of G to T at base 1609 in exon 12 (Fig 2) in a young man as reported in the New England Journal

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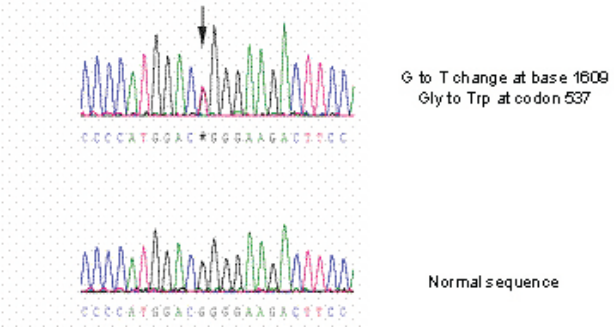
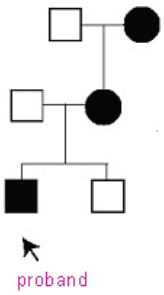


Fig 2. Detection of the c.1609G>T mutation in exon 12 of *HIF2A*.

Exon 12 was amplified by polymerase chain reaction (PCR) from DNA extracted from peripheral blood. The PCR product was sequenced and replacement of G with T at 1609 was discovered as indicated by arrow. Bases are as follows: G = black; A = green; T = red; C = blue.

of Medicine[10]. This mutation resulted in the replacement of the amino acid glycine at position 537 with tryptophan. Screening a group of health control samples did not detect this same mutation suggesting it may be associated with erythrocytosis. The propositus presented with erythrocytosis at the age of 23 years exhibiting an elevated haemoglobin level of 21.7 g/dL and a haematocrit of 0.64. Further investigation of his family revealed that both his mother and maternal grandmother also had erythrocytosis presenting at the ages of 35 and 54 years respectively (Fig 3). Mutation analyses confirmed both these individuals also possessed the Gly537Trp mutation. Measurement of serum Epo levels in the three erythrocytosis individuals revealed they were well above the normal range for the assay. The platelet and white cell counts for all three erythrocytosis family members were normal. Other non-affected family members did not possess the Gly537Trp mutation.



	Age	Hb	Hct	Epo
Affected Son	23	21.7	0.64	31.1
Unaffected Son		15.6	0.46	10.9
Mother	35	16.3	0.50	63.3
Father		13.4	0.39	16.2
Grandmother	54	19.1	0.54	118.6

Fig 3. Pedigree of family with hereditary erythrocytosis.

Three generations of one family were found to have erythrocytosis and the first noted case is indicated by an arrow. Squares and circles represent male and female family members respectively, while solid symbols indicate erythrocytosis individuals. Included in a table are salient haematological features at the time of presentation and a recent serum erythropoietin level.

GLY537TRP HIF-2ALPHA FUNCTIONAL STUDIES

To confirm whether the Gly537Trp mutation could indeed result in erythrocytosis recombinant protein was prepared from a bacterial plasmid containing a DNA copy of the mutant gene. Using this recombinant protein assays were performed to discover if the mutation affected the function of HIF-2alpha. Less association of PHD2 with HIF-2alpha was detected which would affect the ability of PHD2 to hydroxylate HIF-2alpha. The hydroxylation of HIF-2alpha is important for the association of VHL so we wanted to establish if the mutant protein was hydroxylated to the same level as the wild type protein. We found that the mutant was less hydroxylated and subsequently detected less association with its binding partner VHL. We were also able to show that the Gly537Trp HIF-2alpha protein was more stable than wild type and was able to up-regulate HIF-2alpha target genes. Thus it could be inferred that Epo synthesis would also be elevated.

The amino acid sequence of HIF-2alpha is highly conserved and Gly537 is present in this isoform from other species such as mouse, chicken and frog but is absent in the other two isoforms of HIFalpha. The replacement of the structurally small glycine with the bulkier tryptophan amino acid would cause disruption of the ODD region. This would prevent optimal binding of PHD2, thus reducing hydroxylation and the association of VHL, resulting in decreased ubiquitinylation of HIF-2alpha (Fig 4). Consequently, HIF target genes would be transcribed at a higher rate.

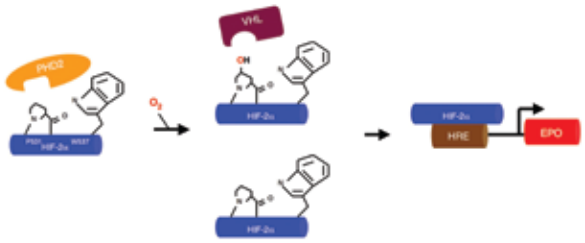


Fig 4. The impact of the Gly537Trp mutation on the function of HIF-2alpha.

The replacement of glycine with a large amino acid would prevent both the association of PHD2 and VHL to HIF-2alpha. Consequently neither hydroxylation or ubiquitinylation of HIF-2alpha would occur. HIF-2alpha is able to evade proteasomal degradation and bind to HRE of *EPO* to increase transcription.

SUMMARY

A mutation of HIF-2alpha has been detected in three generations of a family with erythrocytosis and the mutation co-segregated with the erythrocytosis phenotype. Functional studies revealed that Gly537Trp mutation would significantly impair the function of HIF-2alpha thus leading to increased synthesis of Epo. In addition to VHL and PHD2 a further member of the oxygen sensing pathway, namely HIF-2alpha, can be a cause of erythrocytosis. Furthermore, HIF-2alpha plays an important role in the regulation of Epo production. Continued study of idiopathic cases of erythrocytosis with raised serum Epo will reveal whether HIF-2alpha will be a major cause of erythrocytosis on par with VHL.

I would like to thank my collaborators Dr Frank Lee, Prof Terence RJ Lappin and Prof Mary Frances McMullin who are integral to the studies on idiopathic erythrocytosis, and thank Dr Lee for providing Figures 1 and 4.

The author has no conflict of interest.

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Paper

Predictors of excess mortality after myocardial infarction in women

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SUMMARY

Background: Research suggests that women have higher mortality after acute myocardial infarction (AMI) than men. Potential factors to explain this disparity include delay to presentation, less aggressive interventional strategies, and more severe disease at coronary angiography in women.

Methods: Consecutive patients (n=663) presenting to coronary care between Jan 2002 and Jan 2005 with ischemic type chest pain and AMI (troponin T >0.09ng/ml) were recruited. Details of the presentation and management were obtained from the medical notes. The primary endpoint was three month all cause mortality.

Results: Of these patients 31% (205/663) were female. Mean age of women was 70 (SD 11) and 63 (SD 13) for men (p<0.001). There was no difference between the sexes for delay in presentation or treatment or for ST elevation infarction site. Women had prior hypertension more than men (49% 100/205 vs. 38% 174/458, p=0.008). Women were less likely to have diagnostic catheterisation (67% 137/205 vs. 80% 365/458 p<0.001). Both genders had similar coronary artery disease extent and frequencies of LV impairment (EF<45%) and were equally likely to undergo revascularisation (79% 108/137 vs. 81% 295/365 p=NS). There was an excess 3 month mortality among women (11% 23/205 vs. 5% 24/458 in men p=0.006).

Independent predictors of 3 month mortality by logistic regression analysis were age (OR 1.06, 95% CI 1.03 -1.09, p<0.001) and LV impairment (OR 0.28, 95% CI 0.13-0.56, p<0.001).

Conclusion: As LV impairment was comparable in men and women, the excess mortality identified is due to older age at presentation of women.

INTRODUCTION

In this era of primary prevention in the cardiovascular field it is crucial that both health professionals and patients alike recognise coronary heart disease (CHD) as the leading cause of death amongst women. Cardiovascular disease is responsible for one third of female mortality worldwide[1]. Public health initiatives for women have concentrated on the "bikini cancers" with successful outcomes. It follows therefore that highlighting issues associated with CHD in women could have widespread effects on the targeting of health service provision.

Women are significantly more likely than men to die within 1 year of myocardial infarction[1-5]. Several reasons for this gender discrepancy in early mortality have been postulated. Of those patients diagnosed with myocardial infarction, the women are on average 8 years older than the men[6-9]. The diagnosis and management of CHD in women is therefore complicated by age associated comorbidities. Behavioural factors may play a role; the traditional role of the female as the care giver rather than care seeker has been implicated in their reluctance to seek medical assistance for the atypical symptoms that they often develop[10]. Women diagnosed with ischemic heart disease have greater frequencies of hypertension[5,8,9,11] and diabetes mellitus[3,6,8,9, 11,12] than their male counterparts. Also non ST elevation MIs (NSTEMI's) are more common in women than in men[10]. This clearly adds to the difficulty in diagnosing AMI in women and further compounds delay to initiation of appropriate treatment[10,13]. Several studies have demonstrated that the aggressive revascularisation strategies are less likely to be employed in women presenting with acute coronary syndromes[9,10,11,14].

The aim of this study was to clarify the differences in the presentation and management of AMI between males and females and to determine predictors of the excess mortality amongst women presenting to the Royal Victoria Hospital Belfast Coronary Care Unit.

METHODS

Study patients

The recruitment site has a doctor manned mobile coronary care unit, an Accident and Emergency department and is a tertiary facility with on site coronary angiography theatres

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TABLE I.

Baseline Characteristics of Male and Female Patients

	Males (N=458)		Females (N=205)		P value
Age (yr)*	63±13		70±11		<0.001
	No's	**%**	**No's**	**%**	
Family History	220	48	99	48	0.322
Diabetes Mellitus	74	16	42	20	0.166
Hypercholesterolaemia†	198	43	88	43	0.982
Hypertension	174	38	100	49	0.008
Smoking status-					
Never smoked	108	24	80	39	<0.001
Ex-smoker	166	36	51	25	
Current smoker	184	40	73	36	
Body-mass index >25‡	217	47	66	32	0.001
Past Medical History					
Previous angina	180	39	92	45	0.184
Previous infarction	131	29	63	31	0.644
Previous Investigation					
PCI	47	10	14	7	0.155
CABG	40	9	7	3	0.013
Total Cholesterol mmol/L*	4.8±1.2		5.2±1.2		<0.001
HDL mmol/L*	1.2±0.5		1.4±0.5		<0.001
LDL mmol/L*	2.8±1.1		3.2±1.1		0.002
Triglycerides mmol/L§	1.52		1.67		0.327
Creatinine Clearance mls/min*	82±33		63±30		<0.001

*Mean ±SD †>5mmol/L ‡The body-mass index is the weight in kilograms divided by the square of the height in meters. Blood samples are fasting taken on day 2 of admission
§ Median value – differences detected using the non parametric Mann Whitney U test. CABG = Coronary Artery Bypass Grafting, PCI = Percutaneous Coronary Intervention

and a regional cardiac surgery department. The Coronary Care Myocardial Infarction Registry was used to identify consecutive patients presenting during 01 January 2002- 01 January 2005 with a diagnosis of myocardial infarction. Myocardial infarction was defined as typical ischemic or atypical symptoms of at least 20 minutes duration with a cardiac Troponin T > 0.09ng/ml at 12 hours from symptom onset. Atypical symptoms were predefined as breathlessness, upper back pain between the shoulder blades, epigastric discomfort or jaw pain in the absence of chest pain.

Data collection

This study was a retrospective case review. Obtained from the medical notes of these patients were the following:

Demographics: Age, sex, mode of admission (the mobile coronary care unit or via the emergency room etc.)

Risk Factors: History of hypertension, diabetes mellitus, family history of coronary disease, smoking, cholesterol, and body mass index.

Delay Factors: Presentation delay was defined as longer than 2 hours from onset of symptoms to first seeking medical assistance. Treatment delay was defined as longer than 1 hour from when the patient first sought assistance to the initiation of appropriate medical therapy. Time of onset of symptoms (taken from the patient history), time of ambulance call (recorded on emergency room or mobile coronary care unit admission data) and time when seen by medical personnel were used to calculate delays.

Clinical Factors: A prior history of MI or angina, prior percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) were noted.

The site of infarction was determined from the admission ECG using standard Minnesota coding criteria. NSTEMI was diagnosed if no ST elevation was present. Echocardiography

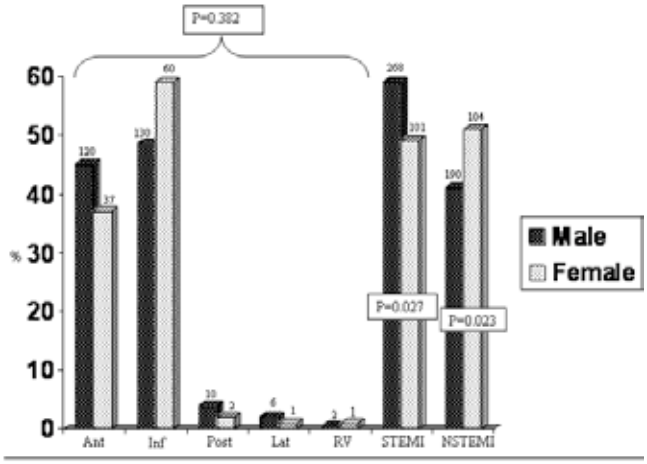

Fig 1. Comparison of infarct location from admission 12 lead ECG in males and females*.

carried out (n = 545) within 48 hours of admission was assessed. LV dysfunction was diagnosed if the Ejection Fraction was <45%.

Laboratory Data: Fasting cholesterol and triglyceride levels on day two after admission and creatinine clearance were recorded for each patient.

Medical Therapy: Antiplatelet therapies including aspirin, clopidogrel and GPIIbIIIa inhibitors were noted. Thrombolytic therapy where appropriate, beta blocking therapy, ACE inhibition and statin therapy were also recorded.

Coronary Angiography: If coronary angiography was performed during admission or within three weeks after discharge it was noted as was revascularisation by PCI or CABG. The extent of disease at angiography i.e. single, double or triple vessel disease was also documented.

Endpoint: The primary endpoint of the study was three month all cause mortality. These data were obtained from the secondary prevention clinics or where this was unavailable, from the general practitioner's records. This endpoint at 3 months post event was chosen to assess an intermediate mortality as other studies have assessed the early in hospital and 1 year mortality; it is however inclusive of in-hospital mortality.

Statistical analysis

All analyses were performed using SPSS version 11 for Windows; SPSS Inc, Chicago, Illinois, USA). Univariate comparison of dichotomous variables firstly by gender and then mortality was carried out using the Pearson's χ^2 statistic. Continuous normally distributed variables are reported as mean ± 1SD; median is quoted for data of skewed distribution. Normally distributed continuous variables were similarly evaluated in terms of gender and then mortality using the Student's t test. Mann Whitney U method was used to compare non parametric continuous variables. A p value of <0.05 was significant.

Three month mortality after myocardial infarction was compared between men and women firstly without adjustment, then with adjustment for age and then with adjustment for age and other candidate variables identified on initial univariate analysis. The models were constructed in a stepwise manner beginning with prehospital variables such as demographics and risk factors, followed by delay factors and clinical variables and finally with treatment given and interventions undertaken. In each case sex was forced into the model. In this way the influence of gender on mortality could be evaluated in conjunction with confounding factors. Results are shown as odds ratios (OR) with corresponding 95% confidence intervals (CI). The goodness of fit of the model was assessed by the Hosmer-Lemeshow statistic.

RESULTS

Baseline and presentation characteristics

Of the 663 AMI patients 31% (205) were female. Females were older (p<0.001), had a greater history of hypertension (p = 0.008) and smoked less than males (p<0.001). A BMI >25 was more frequent in the male group than in females (47% vs. 32%, p=0.001). Also the mean LDL was higher in the female group (3.2mmol/L vs. 2.8mmol/L, p = 0.002) (table I.)

Women more commonly presented with atypical features than men (24% 49/205 versus 9% 41/458, p<0.001). There were no significant differences between males and females in their modes of presentation to coronary care; 63% (288/458) of males compared to 64% (132/205) of females were admitted via the emergency department and 37% (170/458) and 36% (73/205) respectively were admitted via the mobile coronary care unit. Similar numbers of males and females sought initial assistance from their general practitioner (12% 53/458 males versus 16% 33/205 females, p = NS). Similar rates of delay were observed in both groups; 37% (170/458) males and 40% (81/205) females demonstrated a delay to present to medical services and 8% (36/458) males and 8% (16/205) females had some delay in initiation of therapy (p = 0.994). Baseline biochemical analysis for males and females is as shown in table 1. Mean creatinine clearance in the female group was significantly lower than that of the male group (p<0.001) as would be expected given that creatinine clearance is closely related to age.

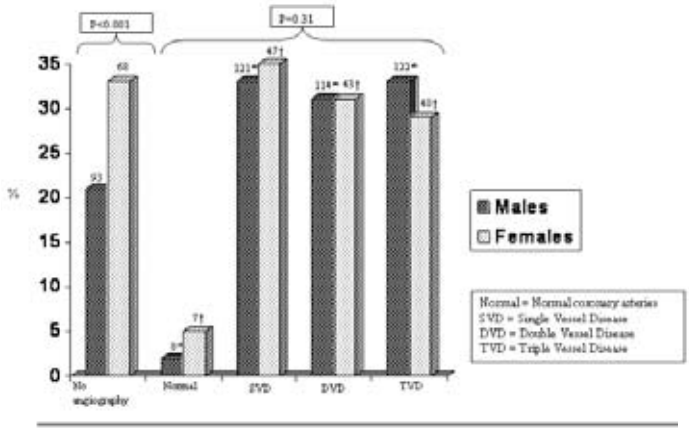

Fig 2. Coronary angiography in males and females.

Table II.

Initial Medical Therapy

Treatment	Male (N=458)		Females (N=205)		P value
	No's	%	No's	%	
Thrombolytic given*	231	94	85	97	0.197
Aspirin therapy	433	95	194	95	0.952
Clopidogrel therapy	402	88	166	81	0.014
GP IIbIIIa Inhibitor therapy	67	15	18	9	0.037
LMWH/UFH	446	97	196	96	0.282
β blocking therapy	429	94	186	91	0.118
ACE inhibitor therapy	401	88	171	83	0.115
Statin therapy	444	97	199	97	0.829

*247 Males and 88 Females met Minnesota criteria for thrombolytic therapy and had no contraindication to thrombolytic therapy. LMWH=Low Molecular Weight Heparin, UFH=Unfractionated Heparin

Clinical factors and management instituted

ST elevation infarct location was similar in males and females. There was however a preponderance of NSTEMI in females (51% 104/205 versus 41% 190/458 in males, p = 0.023) (figure 1).

Females did not receive aggressive antiplatelet therapies as often as males despite the higher prevalence of NSTEMI's in this group (table II).

Also, women did not proceed to diagnostic angiography and hence intervention as frequently as men (see figure 2). This figure also demonstrates that the extent of atherosclerotic disease at catheterisation is similar in males and females. Females who were conservatively managed were significantly older than those males who did not proceed to invasive investigation as shown in figure 3. For those 365 male and 137 female patients who did have diagnostic angiography, similar frequencies of males and females were successfully revascularised by either PCI (69% 253/365 males vs. 71% 97/137 females) or CABG (12% 42/365 males vs. 8% 11/137 females) (p = NS). LV impairment occurred with similar frequency in both genders; 28% 106/377 males compared to 30% 51/168 females, p = 0.594.

Three month mortality in females was 11% (23/205) compared to 5% (24/458) in males (p = 0.006). The age distribution of deceased patients is shown in figure 4.

Factors predictive of three month mortality

Table III summarises the results of a univariate analysis of three month mortality.

Subsequent logistic regression models analysing the influence of gender on mortality in association with pre hospital variables and also with treatment factors were constructed. Table IV demonstrates that the most significant independent predictors of early mortality amongst these models are advanced age and presence of LV impairment. ST elevation infarction site was not included in this analysis as there were no significant differences between the genders for infarction site and to do so would have reduced the numbers of patients for analysis to a much smaller number.

The influence of gender on mortality after AMI

The effect of sex on mortality loses significance when age is added in the first model. As age was such a significant confounding variable it is subsequently included in all models. The frequency of LV impairment was similar in males and females, therefore we conclude that the observed excess in mortality amongst females is due to their advanced age.

DISCUSSION

These results highlight several differences in the presenting characteristics and subsequent management of myocardial infarction in men and women. Potentially this information may be used to establish a gender specific approach to diagnosis and management of CHD, so focusing services to better meet the needs of patients regardless of their gender.

What are the gender differences in presentation and management of AMI? Women and men have different disease perception; it is known that atypical symptoms such as epigastric discomfort, breathlessness and back pain are common presentations in women[12,13]. It is hypothesised that female patients are unaware that these symptoms can represent coronary ischaemia and so may fail to present to medical services in a timely fashion[15,16]. Our results do not support this theory but do show that a large proportion of our patients delay to present for significant periods of time regardless of their gender. For those women who do present, theoretically there may be a delay in making the diagnosis and hence

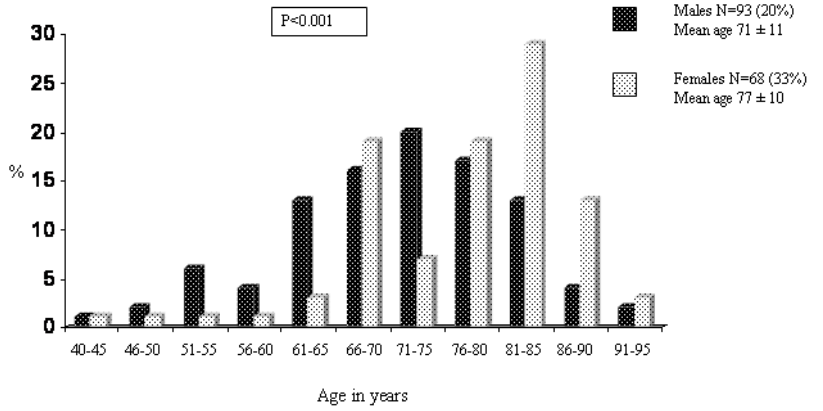

Fig 3. Age distribution of males and females who did not have coronary angiography and were managed conservatively.

TABLE III.

Univariate Analysis of three Month Mortality

	Deceased at 3 months (N=47)		Alive at 3 months (N=616)		P value
Age (yr)*	73±10		64±13		<0.001
	No's	**%**	**No's**	**%**	
Sex					
Male	24	51	434	71	0.006
Female	23	49	182	29	
Risk Factors:					
Family History	20	43	299	48	0.763
Diabetes Mellitus	10	21	106	17	0.435
History of Hypercholesterolaemia†	19	40	267	43	0.788
Hypertension	25	53	249	40	0.047
Smoking status-					
Never smoked	17	36	171	28	
Ex-smoker	19	40	198	32	0.048
Current smoker	10	21	247	40	
Body-mass index >25	14	30	269	44	0.198
Past Medical History:					
Previous angina	23	49	249	40	0.257
Previous infarction	16	34	178	29	0.463
Previous Investigation:					
PCI	3	6	58	9	0.486
CABG	5	11	42	7	0.327
Delay Total Delay	28	60	243	39	0.007
Presentation Delay	27	57	224	36	0.004
Treatment Delay	2	4	50	8	0.341
MI type:					
STEMI	25	53	344	56	0.724
NSTEMI	22	47	272	44	
ST elevation infarct site: N=369					
Anterior	8/25	32	149/344	43	
Inferior	11/25	44	179/344	52	
Posterior	5/25	20	7/344	2	<0.001
Lateral			7/344	2	
Right Ventricular	1/25	4	2/344	1	
LV impairment: N=545	21/36	58	136/509	27	<0.001
Treatment:					
Thrombolytic therapy	16	34	300	49	0.052
Aspirin therapy	43	91	584	95	0.306
Clopidogrel therapy	28	60	540	88	<0.001
LMWH/UFH therapy	44	94	598	97	0.135
GpIIbIIIa inhibition	7	15	78	13	0.659
ACE Inhibitor therapy	30	64	542	88	<0.001
B blocking therapy	35	75	580	94	<0.001
Statin therapy	41	87	602	98	<0.001
Coronary Angiography: N=502	19	4	483	96	<0.001
PCI	8/19	42	342/483	71	<0.001
CABG	4/19	21	49/483	10	0.956
Disease Extent at Angiography:					
Normal Coronaries			15/483	3	
Single Vessel Disease	1/19	5	167/483	35	0.004
Double Vessel Disease	5/19	26	152/483	31	
Triple Vessel Disease	13/19	68	149/483	31	
	N=29		**N=539**		
Total cholesterol mmol/L*	4.4±1.3		5.0±1.3		0.009
LDL mmol/L*	2.6±1.2		3.0±1.1		0.129
HDL mmol/L*	1.2±0.5		1.2±0.5		0.988
Triglycerides mmol/L§	1.2 (0.2)		1.6 (1.3)		0.001
	N=36		**N=585**		
Creatinine Clearance mls/min*	40±31		74±36		<0.001

*Mean ±SD †>5mmol/L §Median (Variance) – Differences detected by the non parametric Mann Whitney U test CABG = Coronary Artery Bypass Grafting, HDL = High Density Lipoprotein, LDL = Low Density Lipoprotein, LMWH = Low Molecular Weight Heparin, PCI = Percutaneous Coronary Intervention, UFH = Unfractionated Heparin

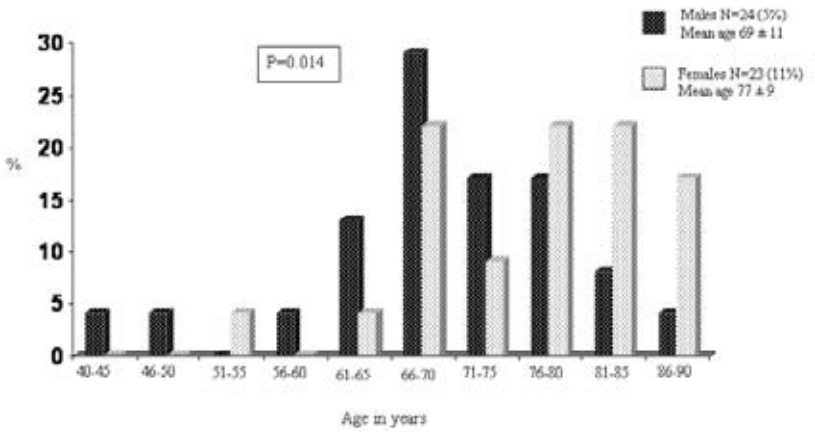

Fig 4. Age distribution of patients deceased at three months.

initiation of therapy due to a combination of atypical histories and more NSTEMI's[13]. Again our results do not support greater treatment delay in females. It is demonstrated that women have more hypertension and proportionately higher LDL and triglyceride levels than the men. Perhaps these risk factors impart more serious consequences to postmenopausal females than males of a similar age particularly when the fact that females tend to have smoked less is considered. Women are more likely to have a definite history of pre-infarct angina than men who tend to present initially with an infarct[2,4]. It is potentially in this pre-infarct stage that intervention, both revascularisation techniques and risk factor management could be optimised in females.

TABLE IV.

*The Influence of Gender on 3 Month Mortality By Logistic Regression**

	P Value	OR (95%CI)	Hosmer-Lemeshow statistic p value
Sex	0.007	2.29 (1.26-4.15)	
Model 1 - Demographics			0.702
Sex	0.121	1.64 (0.88-3.04)	
Age	<0.001	1.06 (1.03-1.09)	
Model 2 – Risk factors			0.733
Sex	0.210	1.51 (0.79-2.89)	
Age	0.001	1.05 (1.02-1.09)	
BP	0.18	1.53 (0.81-2.87)	
Smoking	0.44	0.85 (0.56-1.29)	
Model 3 - Delay			0.381
Sex	0.133	1.62 (0.86-3.02)	
Age	<0.001	1.06 (1.03-1.09)	
Presentation Delay	0.015	2.14 (1.16-3.97)	
Model 4 – Disease factors			0.219
Sex	0.100	1.83 (0.90-3.75)	
Age	0.009	1.05 (1.01-1.08)	
LV impairment	<0.001	0.28 (0.13-0.56)	
Model 5 – Treatment factors			0.410
Sex	0.197	1.54 (0.80-3.00)	
Age	0.002	1.05 (1.02-1.08)	
Clopidogrel therapy	0.010	0.40 (0.20-0.80)	
β Blocking therapy	0.006	0.31 (0.13-0.71)	
ACE Inhibitor therapy	0.005	0.35 (0.17-0.73)	
Statin therapy	0.090	0.32 (0.09-1.20)	
Model 6- Intervention			0.798
Sex	0.147	1.61 (0.85-3.06)	
Age	0.080	1.03 (1.00-1.06)	
Angiography	0.070	0.48 (0.22-1.06)	
PCI	0.030	0.35 (0.13-0.91)	

*Creatinine clearance was not included as its value is largely a function of age.

Is the "discrimination" against women in terms of investigation and management real?

ST elevation infarct site and presence of post infarct LV impairment is similar in men and women. Consistent with previous reports highlighting discrepancies in invasive investigation and management between males and females[10,11,14], this is confirmed in our patient population. This also contributes to the shortfall in the administration of aggressive antiplatelet agents in women. Figure 3 shows that those women who were managed conservatively were much older than males posing the question that perhaps there are younger males who may have benefited from invasive investigation. Contrary to the opinion that women have less intervention potential due to their smaller arteries, distribution of disease and comorbidities, we have demonstrated that those females selected for angiography have similar disease extent and revascularisation outcomes to the males. These women are however a selected group in real practice; this may prove to be the best management approach and not a reflection of "discrimination" towards the female gender.

When adjusted for confounding variables gender no longer has an influence on survival after myocardial infarction regardless of the management strategy. The advanced age of the females largely explains the excess in three month mortality observed in this group.

Implications for future policies on management of CHD in women:

As our Western population continues to age so the burden of ischemic heart disease in women is increasing. Mortality after myocardial infarction is indeed higher in women and so the challenge presents to prevent myocardial infarction where possible by targeting modifiable factors in the pre-infarct stage. Traditionally guidelines on the diagnosis and management of ischemic heart disease have made few allowances for the differences in presentation and natural history of the disease between the genders. In the light of these results and those of previous studies it follows that we as physicians are not adhering to the current guidelines[7,9,11,13,14,17]. Is this appropriate? Until recent years coronary heart disease was predominantly a male disease and the large clinical trial data have reflected this experience with only small numbers of females recruited. Our study has not specifically examined diagnostic investigations, but it is demonstrated in the WISE study[18] and others[19-21] that diagnostic strategies have different sensitivity specificity ratios in females as compared to males, further compounding the confusion in diagnosis and substantiating the myth that females are not at risk of CHD. Also whilst it is reasonable to extrapolate findings from large meta-analyses on the standard pharmacological therapies to female patients, it is important to recognise that gender related differences in metabolism and action of these medications often have important clinical effects[22]. It is also accepted that women have more complications following PCI or CABG however this opinion is based on registry observations and there are few clinical trials powered sufficiently to detect a significant outcome difference between the sexes[23-26]. Some conflicting studies determined that women have equal[5,6] if not more benefit from PCI[27]. Trial data on patients over 75 years of which women make up the majority are scarce. For this reason guidelines based on existing data should be interpreted with caution in the real life scenario, particularly with regard to elderly female patients.

It is likely that when armed with information such as is presented in this study we will appreciate that a gender specific approach to the diagnosis and management of ischemic heart disease will be more effective in the future. One such approach will take account of the diagnostic limitations of the exercise stress test in females and make better use of other more sensitive and specific investigations in this group such as dobutamine stress echocardiography and myocardial perfusion imaging. Very aggressive risk factor modification, in particular hypertension and cholesterol management, may have more marked benefits in women than men in terms of prevention of fatal myocardial infarction. Selection of female patients after myocardial infarction for intervention should take into consideration comorbidities and the risk benefit ratio of intervention in women. Disease perception and awareness is a persistent problem amongst females. The American Heart Association's "Go red for women" and the European Cardiology Society's "Women at heart" initiatives should help to raise awareness of these issues and implement appropriate changes in management strategy.

Study limitations

Several limitations should be recognised. The numbers of patients achieving the endpoint of three month mortality are relatively small in both males and females. This is clearly a reflection of the improved management strategies in recent years but may have implications on regression models for identification of independent predictors of mortality. We do however feel that the model devised is reliable in that advanced age accounted for the vast majority of the gender discrepancy. We did not take account of pre hospital mortality which is recognised to be higher in males than in females[10]. Not all of the patients had a 48 hour echo carried out (82% 545/663) therefore we do not have complete data on LV function. However identical proportions of each gender had an echo completed (82% 377/458 men vs. 82% 168/205 women). Also, the logistic regression models devised on SPSS utilise only patients with complete data for the variable under examination and so we feel the models to be accurate and reliable.

CONCLUSIONS

Three month mortality after myocardial infarction in women is higher than that of men (11% vs. 5%). Women (70 ± 11 years) were significantly older than men (63 ± 13 years). Whilst women after myocardial infarction are less likely than men to undergo invasive cardiac catheterisation (67% 137/205 vs. 80% 365/458) successful revascularisation rates were similar (71% 97/137 women had PCI vs. 69% 255/365 men and 8% 11/137 women had CABG vs. 12% 42/365 men). Independent predictors of three month mortality were age and left ventricular impairment. As left ventricular impairment was comparable in men and women, the excess mortality observed in females was mainly due to their older age at presentation.

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The authors have no conflict of interest.

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Paper

Isolated Mediastinal Adenopathy: The Case for Mediastinoscopy

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ABSTRACT

Background. We report our experience with mediastinoscopy at Auckland city hospital, a tertiary referral centre. We wished to examine correlations between clinical diagnosis and that made by histological sampling of enlarged mediastinal nodes particularly in patients with isolated mediastinal adenopathy.

Methods. We retrospectively reviewed clinical records of all patients who underwent mediastinoscopy in a five year period, mediastinoscopy was performed in the presence of enlarged lymph nodes (short axis > 1cm) found at CT. Mediastinoscopy was indicated for diagnostic staging of mediastinal adenopathy related to a parenchymal lung mass, diagnosis of isolated mediastinal adenopathy and diagnosis of mediastinal adenopathy with other CT findings. Data relating to indication, pre-test diagnosis, node stations sampled, histology, and operative complications were collected.

Results. Mediastinoscopy was performed in 137 consecutive patients. Seventy five patients had a lung mass, 47 had isolated mediastinal adenopathy and 15 had other CT findings. One operative complication occurred. In those patients with isolated adenopathy the following diagnoses were reached; sarcoidosis 23, TB 15, lymphoma 4, carcinoma 4, no diagnosis 1. Final diagnosis was significantly associated with patient's ethnicity. There was high sensitivity and specificity on comparison of clinical and histological diagnosis for both TB and sarcoidosis cases.

Conclusions. Mediastinoscopy proved to be safe and effective in nodal assessment of the mediastinum. In carefully selected cases procedural morbidity and mortality may be avoided by application of features related to patient's ethnicity and radiological findings.

Keywords: Mediastinal lymph nodes, Mediastinoscopy, Computed tomography, Mediastinum

INTRODUCTION

With the widespread availability of CT scanning, isolated mediastinal adenopathy (IMA), mediastinal adenopathy in the absence of disease elsewhere (figure 1), is increasingly found on scans performed for very different indications and clinicians are faced with the difficult clinical decisions regarding the investigation of a patient with few if any symptoms. Radiological images do not always correlate well with the pathological features of the lesions and consequently imaging diagnostics often fail to provide enough certainty to make therapeutic decisions[1]. CT does not seem to replace mediastinoscopy but rather guides its application. Differential diagnosis includes conditions for which specific therapy is unlikely to be required (sarcoidosis), for which specific therapy is required for cure and/or to prevent future disease (tuberculosis) as well as potentially life-threatening conditions the outcome from which may be considerably influenced by appropriate and timely treatment (lymphoma). The most likely clinical diagnosis of the aetiology of isolated mediastinal adenopathy is based upon patient demographics, symptoms, clinical signs and certain laboratory tests. A histological diagnosis generally requires mediastinoscopy, (which requires general anaesthesia), and an experienced cardio-thoracic surgeon, which are not available in all institutions and is not without risk[2].

In order to address these issues we undertook a study the overall aim of which was to determine the clinical utility of mediastinoscopy in the diagnosis and management of patients with IMA. Specifically to determine:

- the proportion of patients who have a malignant aetiology for their IMA
- the accuracy of physicians in their pre-operative diagnosis (benign vs. malignant)
- whether there were clinical or radiological features that correlated with a malignant aetiology

PATIENTS

The institutional review board did not require individual patient consent as this study was retrospective. The clinical records of all patients who underwent mediastinoscopy at

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Table I

Patient demographics

Variable	Patient Group		
	Mediastinal Adenopathy & Parenchymal Lung Mass	Isolated Mediastinal Adenopathy (IMA)	Mediastinal Adenopathy & Other CT Findings
Number	75	47	15
Age	61.3 ± 11	44.8 ± 16.4	44.2 ± 15.4
Sex (M / F)	45 / 30	20 / 27	9 / 6
NZ European / Other European	54	22	5
Maori / Pacific Islander	16	6	3
Indian / Asian / African / Chinese	1	18	6
Unknown Ethnicity	4	1	1
Incidental Finding	9	9	0

Auckland City Hospital over a five year period (January 2000 - December 2005) were retrospectively reviewed. Data relating to indication, pre-test clinical diagnosis, histology, length of hospital stay, and operative complications were collected. Mediastinoscopy was performed in the presence of enlarged lymph nodes (short axis > 1cm) found at CT scanning with one or more node stations involved. It is widely accepted that adenopathy of greater than 10mm diameter is indicative of significant enlargement. Mediastinoscopy was performed in 137 patients: in seventy five patients for diagnostic staging of mediastinal adenopathy related to a parenchymal lung mass or known primary lung cancer, in 15 for diagnosis of mediastinal adenopathy with other CT findings and in 47 for IMA. Those with IMA form the basis of this report.

METHODS

All procedures were performed under general anaesthesia using a single lumen endotracheal tube. Following standard preparation for mediastinoscopy a crease incision was made and dissection was performed deep down to the pre-tracheal fascia. This was then followed by blunt dissection down along the trachea to access the right lower paratracheal and pre-tracheal lymph nodes[3]. Final diagnosis was determined by a combination of histology, other test results, and correlation of all of this information with clinical findings at subsequent follow-up clinic appointments. A diagnosis of tuberculosis (TB) was made if histology showed granulomatous inflammation, and either *M. tuberculosis* was cultured from the node or other samples, TB Polymerase Chain Reaction tests was positive, acid fast bacilli were seen on histology or the patient had an unequivocal clinical and/or radiologic response to anti-tuberculosis treatment. Alteration of management was defined as a definitive diagnosis which resulted in specific therapy or alternatively avoided further investigative procedures.

Statistical analysis

Normally distributed data were presented as mean ± standard deviation, whilst non-parametric data were expressed as median and inter quartile ranges. For discrete variables frequencies and percentages were reported and groups compared using the chi squared test. A significance level of

Table II

Isolated mediastinal adenopathy, correlation of clinical diagnosis with histological diagnosis, sensitivity and specificity

Clinical Diagnosis	Histological Diagnosis	Inconsistencies	Sensitivity	Specificity
Sarcoidosis	17 of 18 (94%)	TB (1)	74%	96%
TB	13 of 16 (81%)	Sarcoidosis (2), Lymphoma (1)	93%	91%
Lymphoma	3 of 7(43%)	SCLC (1), NSCLC (1), Sarcoidosis (1), No diagnosis (1)	75%	91%
Carcinoma	2 of 5 (40%)	Sarcoidosis (2), no diagnosis (1)	50%	95%
Unknown	-	Sarcoidosis (1)	-	-

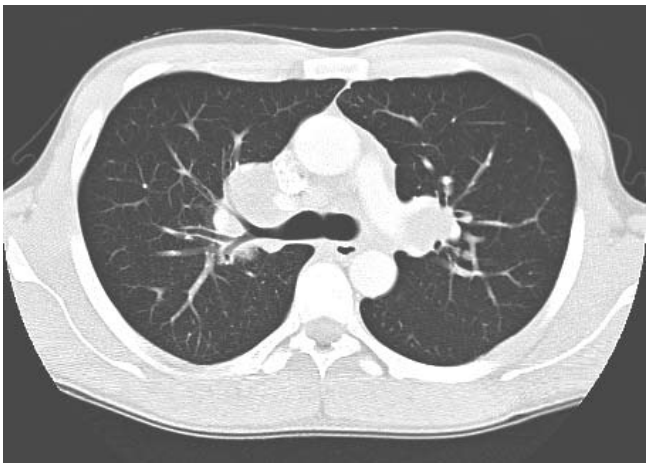

Fig 1. CT chest demonstrating bilateral hilar adenopathy.

5% was chosen. Statistical analysis was carried out using SPSS (Chicago, IL) version 10.0.

RESULTS

Mediastinoscopy was performed in 137 consecutive patients. Patient demographics are shown in table I; those patients in the IMA group were younger, more likely to be non-European and the radiologic abnormality more likely to have been an incidental finding. Median length of stay was 2 days in all groups. In all cases but one, lymph node tissue was obtained. Of the 75 patients with a lung mass, 52 were known to have a malignant underlying process (51 NSCLC, 1 metastatic germ cell tumour). Following mediastinoscopy 18 were found to have non small cell lung cancer, other diagnosis's made on nodal biopsy included TB (1), lymphoma (1) and SCLC (1). In 2 cases no final diagnosis was reached following mediastinoscopy.

Isolated Mediastinal Adenopathy

The pre-operative clinical diagnoses and the final diagnoses are shown in table II. One patient who had a pre-operative diagnosis of a benign condition (tuberculosis) was found to have malignancy (lymphoma). Five of the 12 who were suspected of having a malignant aetiology had a final diagnosis of a benign condition (sarcoidosis). Of the nine cases of IMA which were picked up as incidental findings on chest X-ray's which were carried out for other illness or for employment / immigration purposes, seven were found to have tuberculosis, 1 sarcoidosis and one lung cancer (non small cell lung cancer). In almost all of these IMA cases mediastinoscopy was followed by an alteration in management (98%). Subsequent analysis of clinical diagnosis and the definitive histological findings demonstrated high specificity for all diagnoses. Following analysis of symptom correlation with final diagnosis, a diagnosis of TB was negatively associated with a history of chest pain ($p < 0.05$). No other associations were found.

Ethnicity and Final Diagnosis

Patient's ethnicity was correlated with respect to their final diagnosis. New Zealand (NZ) European ethnicity was associated with a final diagnosis of sarcoidosis and malignancy ($p < 0.05$) but negatively correlated with a diagnosis of TB ($p < 0.0005$). The converse was found in immigrant populations (Indian, Asian, Chinese, African), with a positive association seen for TB ($p< 0.0005$) and a negative association for sarcoidosis ($p< 0.005$) or malignancy ($p< 0.05$).

Adenopathy Location and Final Diagnosis

Analysis of the location of enlarged nodes and the final diagnosis was made. Positive associations were seen between mediastinal adenopathy and diagnoses of sarcoidosis or lymphoma ($p < 0.05$). Lymphoma was also associated with paratracheal adenopathy ($p = 0.05$). An incidental finding of interest was that all_cases of aortopulmonary window adenopathy were found to be associated with lung carcinoma in those patients who had a parenchymal lung mass ($p < 0.05$). Also all patients who had mediastinal adenopathy in association with pulmonary nodules were found to have sarcoidosis.

DISCUSSION

Although the clinical pre-operative diagnosis was able to fairly reliably distinguish between benign and malignant aetiologies (sensitivity = 87 – 88%, specificity = 78 – 87%), clinical assessment was less reliable at distinguishing sarcoidosis from tuberculosis. Therefore in both benign and malignant conditions a precise histological diagnosis is required and thus a strong case can be made for mediastinoscopy in all cases of IMA.

Previous studies investigating the role of mediastinoscopy in the diagnosis of isolated mediastinal adenopathies have also shown a high sensitivity[4]. The benefits of an accurate diagnosis obtained by mediastinoscopy need to be balanced against the risks of the procedure. In the IMA group, none of the patients sustained a significant adverse outcome, although one of the other 90 patients who underwent mediastinoscopy during the period of this review developed life-threatening haemorrhage and required repair of an innominate artery rupture under cardio-pulmonary by-pass. The relatively low rates of complication (compared with published mortality rates of 0% - 0.2% and morbidity rates of 0.6% - 2.7%[4-8]) is likely due to the fact that all procedures were under-taken in a dedicated cardio-thoracic service. One large series recorded 1% of patients experiencing complications consisting of haemorrhage, vocal cord dysfunction, tracheal injury and pneumothorax[9].

Median duration of hospital stay at two days was similar to that reported in other studies[7]. A specific diagnosis with a high likelihood of altering treatment was obtained at low risk to the patient. This is consistent with a previous study examining the risk / benefits of mediastinoscopy in the investigation of asymptomatic bilateral hilar adenopathy which found that the benefits of diagnosing persons with conditions other than sarcoidosis would be offset by procedural mortality with significant cost implications[10].

There was high sensitivity and specificity for the clinical diagnosis of sarcoidosis and TB when comparison was made to histological diagnosis following mediastinoscopy. However the significance of misdiagnosing a potential case of TB as sarcoidosis infers that any cases with suspicious presentation (detection on immigration CXR) and risk factors (from a high prevalence TB region) or the presence of atypical CT findings

(infiltrates) should proceed to mediastinoscopy to obtain a diagnosis. These findings are reflected in previous publications and the point made that diagnosis can even be difficult when tissue is obtained[11]. Whilst mediastinal adenopathy in the absence of pulmonary infiltrates is an unusual but recognized presentation for TB the diagnosis can nevertheless be difficult[12]. Two cases were initially diagnosed as sarcoidosis on the basis of histology but were subsequently found to be due to TB. Both cases were non-European (Indian), in one *M. tuberculosis* was cultured from bronchial washings (presentation with atypical chest pain) and in the other there was a positive mantoux (18mm), an interval increase (x3) in node size and a clear radiological response to anti-tuberculous therapy (detected on a pre-employment CXR).

Although mediastinoscopy is a safe and accurate procedure in patients with asymptomatic stage I sarcoidosis, clinical and imaging monitoring may be more appropriate[13]. Alternate means of obtaining a histological diagnosis of sarcoidosis needs to be considered. Previous authors have suggested that in up to approximately 50% of cases a diagnosis of sarcoidosis can be obtained by conjunctival biopsy, avoiding the more expensive and invasive procedure of mediastinoscopy[14]. The authors advise that multiple tissue specimens should be examined as granulomas may be randomly distributed, and also bilateral biopsies can increase the diagnostic yield.

Similar to the results of a previous study, the commonest diagnosis of IMA was sarcoidosis[14]. The cause of IMA may vary markedly in different populations: other studies having identified lymphoma as the major pathological entity[15]. This may be related to selection bias or actual prevalence differences in different populations. Although the proportion of the major diagnoses may differ, this does not negate the findings of this study nor the conclusion that an accurate diagnosis is required in all cases.

Areas of deficiency of this study are that it was retrospective in nature thus symptom recording and clinical diagnosis were influenced by each individual physicians approach. Also the study numbers are relatively small when used for subgroup analysis. These findings should ideally be confirmed in a prospective study with data acquisition as part of set criteria. However, despite these factors the findings of this study are applicable to European populations in which the prevalence of TB is low but which do have a significant immigrant population form areas of high TB prevalence.

While mediastinoscopy is a safe and accurate procedure other potential methods of obtaining histological specimens of enlarged paratracheal lymphadenopathy include the use of CT guided bronchoscopic transtracheal needle biopsy. Sufficient material for diagnostic purposes can be obtained in the majority of cases and this technique represents an effective, less invasive methodology with a low complication rate, there was however a relatively high false negative rate of 50%[16]. CT-guided transthoracic fine needle aspiration with or without core biopsy accesses many mediastinal nodal stations with a high diagnostic yield albeit in patients with lung cancer rather than IMA[17]. Endoscopic ultrasound guided fine needle aspiration has been shown to be a safe, minimally invasive procedure for the diagnostic approach to mediastinal lymphadenopathy[18]. When used in combination with transbronchial needle aspiration the diagnostic yield approaches that of mediastinoscopy[18]. This procedure has also been applied to patients with suspected sarcoidosis resulting in a diagnosis in 82% of cases with no complications[19]. This technique is complementary to transbronchial needle aspiration and mediastinoscopy as it allows sampling of nodal stations not accessible by the other two procedures[20]. Positron emission tomography (PET) scanning when applied to the examination of mediastinal adenopathy is usually in the setting of staging non small cell lung cancer. PET has been shown to have higher sensitivity specificity and accuracy when compared to CT in staging mediastinal nodes[21]. Studies investigating the use of PET-CT compared to CT alone and videomediastinoscopy in patients with mediastinal masses demonstrated that whilst videomediastinoscopy remains the gold standard PET-CT is of value when differentiating benign from malignant lesions[22].

Mediastinoscopy is the most sensitive and specific diagnostic tool when presented with mediastinal adenopathy. There are relatively few complications and lymph node tissue was obtainable in nearly every case. Use of this procedure resulted in histological diagnosis and an alteration of management in most cases. In conclusion, patients with isolated mediastinal adenopathy who are of European ethnicity invariable have sarcoidosis, in these cases it is reasonable to observe patients only. Patients who are immigrants from regions of high TB prevalence and who have evidence of mediastinal adenopathy which is incidentally identified on chest imaging for immigration purposes usually have underlying TB. Thus in carefully selected cases procedural morbidity and mortality may be avoided by application of features related to patient's ethnicity and radiological findings.

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Paper

The Impact Of Long-Term Lithium Treatment On Renal Function In An Outpatient Population.

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SUMMARY

Aim: This study aims to compare younger and older populations of lithium-treated patients and to examine the impact of long-term lithium treatment on renal function.

Methods: A retrospective, cross-sectional survey of all patients attending a specialist clinic was carried out. Demographic, clinical and biochemical data from the two groups were compared, and stepwise regression was used to investigate an association between duration of lithium treatment and renal function.

Results: The findings reveal a positive association between duration of lithium use and mean serum creatinine levels ($t=3.369$, $p=0.001$), and so prolonged lithium treatment may be a risk factor for progressive renal impairment. However, under appropriate supervision this may not be of clinical relevance.

Conclusion: We conclude that lithium can be safely prescribed over a protracted period of time, even in elderly populations, but should be monitored closely under specialist supervision, to ensure early identification and management of adverse effects.

Key Words: lithium, depression, renal function.

INTRODUCTION

Lithium represents one of the triumphs of modern psychopharmacology. Since its introduction into the field of psychiatry, more than half a century ago, it has become established as a valuable and effective agent in the treatment of acute mania and in the prophylaxis of bipolar and unipolar affective disorders[1,2]. Its use in other conditions, such as augmentation in treatment resistant depression, has also been advocated[3]. In general it is considered as a long-term treatment strategy and therefore patients are often prescribed lithium over a period of many years.

Unfortunately the potential side effects of lithium have always been an issue, and among these the possible impact of long-term lithium treatment on renal function has given rise to considerable concern[4]. Lithium is known to affect renal concentrating ability, and lithium-induced polyuria is not uncommon, estimated to affect approximately 20% of patients, but this is rarely clinically significant[5]. It is less clear, however, whether or not the protracted use of lithium can cause progressive deterioration in renal function, culminating in renal failure. Results of several long-term studies suggest that this is not the case, and the consensus of literature has been that in the absence of lithium toxicity, long-term sequelae are rare[6,7]. On the other hand there are a number of case reports which describe instances of renal insufficiency in lithium treated patients with no other obvious cause[8,9]. At the present time regular monitoring of renal function is still recommended.

Psychiatric clinics now treat cohorts of patients who have had protracted exposure to lithium, many of whom are of advancing age. The use of lithium in older people has the potential to be even more problematic for a number of reasons. Firstly, normal age-related reductions in renal clearance and volume of distribution can result in higher plasma levels of lithium and increase susceptibility to lithium toxicity. In addition, elderly patients are more likely to have co-morbid physical health problems, and to be taking concomitant medications that may have significant interactions with lithium[10]. The prescription of ACE inhibitors and loop diuretics in particular, have been shown to dramatically increase the risk of lithium toxicity[11].

In recent years there have been significant advances in a number of effective new treatments for affective disorders, which appear to have little impact on renal function and may offer an alternative to lithium[12]. Therefore it would seem prudent at this time to review the effects of lithium in clinic populations. The aim of this study is carry out a comparison of younger and older lithium-treated patients and to examine the association between duration of lithium treatment and renal function.

METHODS

All patients under review at a specialist out-patient clinic were

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considered for inclusion in the study. This clinic serves part of the population of South Belfast (estimated 75,000) and aims to provide regular monitoring of those patients who are treated with lithium or other mood-stabilizing drugs.

In the first instance all patients currently prescribed lithium were identified. They were then interviewed to update history and information on demographic details and medical status. Following this, thorough review of the psychiatric case notes was undertaken. Data collected included information on patient's age, psychiatric (ICD-10) diagnosis, current medications, physical illnesses, duration of lithium treatment and episodes of lithium toxicity. In addition, the ten most recent serum lithium levels, urea and creatinine levels, and free thyroxine (T_4) and thyroid-stimulating hormone (TSH) levels were recorded where possible, and average values of these figures were calculated. The mean of the last ten serum creatinine levels was used as an estimate of renal function.

For comparative purposes patients were subdivided into two groups - those under the age of 65yrs and those aged 65yrs and over. To allow comparison between the groups the Mann-Whitney U test with Bonferroni correction was used (statistical significance set at $p<0.01$). The data were further subject to statistical analysis using a stepwise regression model to investigate the association between duration of lithium use and renal function. Other possible predictors of renal function were entered into the model, including age, hypertension, diabetes, concomitant medications such as non-steroidal anti-inflammatory drugs (NSAIDs) and diuretics, mean serum lithium level and episodes of lithium toxicity.

RESULTS

Fifty-nine patients currently prescribed lithium were identified.

Comparison of younger and older age groups of lithium-treated patients

(i) Demographics

Thirty-eight patients were under the age of 65yrs, and twenty-one were aged 65yrs and over. The mean age of patients in the younger age group was 45.5yrs and in the older group was 72.8yrs. Both groups had a higher proportion of female patients. Results of demographic details for both groups are displayed in Table I.

(ii) Clinical

TABLE I:

Comparison of demographic information between younger and older age groups

	Under 65yrs (n=38)	**65yrs and over (n=21)**
Age (years) (mean +/- SD)	45.5 +/- 10.6	72.8 +/- 6.8
Age range (years)	19 – 63	65 - 88
Sex M / F	15 / 23	7 / 14

TABLE II:

Comparison of clinical data between younger and older age groups

	Under 65yrs (n=38)	**65yrs and over (n=21)**
Psychiatric diagnosis (%)		
Bipolar affective disorder	32 (84.2)	10 (47.6)
Recurrent depressive disorder	5 (13.2)	10 (47.6)
Schizoaffective disorder	1 (2.6)	1 (4.8)
Duration of lithium treatment (years) * (mean +/- SD)	6.9 +/- 5.4	14.2 +/- 6.3
Range of duration of lithium treatment (years)	1 - 20	1 - 26
Average lithium dosage over past year ** (mg/day)	790.8	528.6
Episodes of lithium toxicity	0	0
Concomitant psychotropic medication (%)		
Carbamazepine	4 (10.5)	3 (14.3)
Depakote	5 (13.2)	0 (0)
Typical antipsychotic	8 (21.1)	7 (33.3)
Atypical antipsychotic	7 (18.4)	1 (4.8)
Selective serotonin reuptake inhibitor	5 (13.2)	2 (9.5)
Serotonin/noradrenaline reuptake inhibitor	4 (10.5)	2 (9.5)
Tricyclic antidepressant	4 (10.5)	5 (23.8)
Concomitant physical medication (%)		
Thyroxine	5 (13.2)	5 (23.8)
Other potentially nephrotoxic drugs (eg diuretic, NSAID etc)	2 (5.3)	4 (19.2)
Physical health (%)		
Hypertension	3 (8.0)	4 (19.2)
Diabetes mellitus	1 (2.7)	0 (0)

* Mann Whitney Z = -3.76, p = 0.0001
** Mann Whitney Z = -4.02, p = 0.001

Table II represents the clinical characteristics of both groups with regards to psychiatric diagnosis and drug treatment. It is noted that in the younger age group the vast majority of patients are prescribed lithium for a diagnosis of bipolar affective disorder (84.2%), whereas in the older group the trend is rather different, with recurrent depressive disorder (47.6%) diagnosed in almost half of these patients.

There is a statistically significant difference in the mean duration of lithium use between both groups; those in the younger age group have a mean duration of treatment of 6.9 years, whereas the mean duration in the older age group is 14.2 years (Z = -3.76, p = 0.0001 Mann-Whitney test). The average dose of lithium is also lower in the older age group (Z = -4.02, p = 0.0001). No patient in either group had had an episode of lithium toxicity. With regards to concomitant psychotropic medication, results suggest that those in the older age group are more likely to be prescribed older agents, such as typical antipsychotics and tricyclic antidepressants. This group are also more likely to require treatment with thyroxine, and to be prescribed other potentially nephrotoxic drugs. It is noted that the prevalence of thyroxine treatment in both groups far exceeds the community prevalence of hypothyroidism and possible explanations for this are discussed later.

(iii) Biochemistry

A comparison of results of biochemistry monitoring between the two groups is presented in Table III. There are no significant differences in serum lithium levels, free T_4 levels or TSH levels between both groups. The urea level is slightly higher in the older group. The creatinine level in the older age group is also higher than in the younger group, but this difference does not reach statistical significance.

Relationship between duration of lithium use and renal function

The best-fit model with stepwise regression accounted for 24% of the variance (R2 = 0.238, p = 0.0001). Stepwise regression analysis revealed that only two individual predictors were significantly associated with serum creatinine level. The duration of lithium treatment was found to be positively correlated with mean serum creatinine level (t = 3.369, p = 0.001). An association between serum creatinine level and a history of hypertension was also noted, although interestingly this was a negative correlation (t = -2.608, p = 0.012).

Table III:

Comparison of biochemistry between younger and older age groups

	Under 65yrs (n=38)	65yrs and over (n=21)
Serum lithium level (mmol/l) * (mean +/- SD)	0.64 +/- 0.12	0.68 +/- 0.14
Free T_4 levels (pmol/l) (mean +/- SD)	12.6 +/- 1.98	12.9 +/- 1.45
TSH levels (mu/l) (mean +/- SD)	2.53 +/- 1.87	3.20 +/- 3.05
Urea (mmol/l) ** (mean +/- SD)	4.31 +/- 0.96	5.72 +/- 1.46
Creatinine (µmol/l) * (mean +/- SD)**	80.24 +/- 10.59	95.15 +/- 37.60

* Mann Whitney Z = -1.60, p = 0.10
** Mann Whitney Z = -3.95, p = 0.0001
*** Mann Whitney Z = -2.04, p = 0.04

DISCUSSION

To the best of our knowledge this has been the largest study of its nature in the UK. It benefits from inclusion of a mixed age population and demonstrates what is happening in actual clinical practice. Importantly, it attempts to reflect differences in the use of lithium in younger and older populations, and to address particular concerns about the prescription of lithium over a prolonged period of time, often in patients of advanced age.

Any retrospective cross-sectional study of this nature will inevitably be limited by inherent methodological weaknesses. We acknowledge that this study may not capture all those prescribed lithium within the catchment area, but we are confident that the vast majority will have been included. It is also possible that this sample may not be representative of lithium-treated patients in other areas, but again our experience would suggest that similar practices exist across other parts of Northern Ireland. The relatively small sample size has potential to increase the likelihood of error and with a larger dataset further statistically significant differences between the groups may have become apparent. One particular drawback in the design of this study is that it does not identify those people who may have already developed renal impairment and had lithium treatment withdrawn. However, our findings would indicate that even if this is the case, close monitoring has led to identification of such patients and appropriate action taken. It is encouraging to note that indeed only one patient in the entire sample was found to have an average serum creatinine level in excess 130 µmol/l.

Despite the potential limitations of this study we feel that the findings are of value. Results of the comparative study indicate that although there is a statistically significant difference in urea level, the difference in creatinine levels is not statistically significant. Particularly of note, there are no clinically relevant differences between the two groups on any of the biochemical markers. Regression analysis does show that longer duration of lithium use is associated with higher creatinine levels, independent of age and other confounding factors. However, given the findings of the comparative study, this is not necessarily associated with clinically relevant abnormalities in renal function. Therefore, although progressive renal impairment should be considered a risk, this may not be of major clinical significance. The importance of monitoring glomerular filtration rate in patients receiving long-term lithium therapy is now increasingly

emphasised, and future studies should aim to use this as a marker of renal function[13].

Several other findings from the study are also worth highlighting. It is interesting to note that much of the use of lithium in the elderly population is aimed at treatment of depressive illness, in contrast with the younger population where it is most frequently used in bipolar disorder. This is particularly relevant as alternative treatment options may be more limited in these cases. The high level of thyroxine prescribing has already been noted but we feel that this is in keeping with other studies in similar poulations[14]. Hypothyroidism is a well-recognised side-effect of lithium, and in addition the use of thyroxine in treatment of subclinical hypothyroidism can sometimes be of value in management of affective disorders. These factors almost certainly account for the differences observed. There is also a rather unexpected finding of a negative correlation between serum creatinine level and history of hypertension. This is clearly counterintuitive. However closer inspection of the data reveals that only three patients in the study had a history of hypertension, and it is unlikely that results from such a small sample would be meaningful.

The results of this study are in keeping with other research which concludes that, in the vast majority of patients, lithium does not contribute to progressive renal impairment[15]. Although lithium may adversely affect several aspects of renal function, it can be used safely over many years provided episodes of acute intoxication are avoided and renal function is carefully monitored. This view has been expressed by others who have studied the use of lithium in older patients[16,17]. However, if a serial decline in glomerular filtration rate is identified, that is more rapid than age-related decrease in renal function, then alternatives to lithium treatment should be considered.

In recent years there has been progress in our understanding of affective disorders and their management. Various alternatives to lithium prophylactic treatment have been advocated. These drugs may have different tolerability and safety profiles, and certainly are a welcome development given the potential side effects of lithium.

Unfortunately however their efficacy in long-term prophylaxis over years is not conclusive. As yet no other proposed mood-stabilizing treatment has such substantial research evidence of long-term efficacy in bipolar disorder, as well as yielding a significant reduction in mortality risk from suicide[18]. It is also worth noting that most evidence to date relates to the general adult population, with limited research into their use in the elderly[19]. Therefore we would caution against an unnecessary trend to use modern alternatives until this is backed up by firm evidence. While we continue to await evidence of more effective and safer treatment, lithium should not be abandoned or feared.

The authors have no conflict of interest.

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Paper

Myocardial Revascularization By Off Pump Coronary Bypass Surgery (OPCABG): A Ten Year Review

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ABSTRACT

Background: The use of cardiopulmonary bypass (CPB) may contribute to post-operative complications and organ dysfunction. Off pump coronary artery bypass grafting (OPCABG) avoids the use of CPB and hence is proposed to reduce these complications. We present the results of OPCABG in Northern Ireland over ten years.

Methods: Data was collected retrospectively from 1995 to 2005. Follow-up was done by telephonic questionnaire and from medical records within a closing interval of two months.

Results: 324 patients (224 male) underwent OPCABG with a median age of 62 years (range 35 to 79 years). There were 149 patients with CCS class III/IV angina and 48 with NYHA class III/IV. 148 patients had suffered a myocardial infarction in the past. 36 patients had a pre-operative predictive mortality score (EuroSCORE) of >5 and 48 patients had a preoperative LVEF of <30%. 585 bypass grafts were constructed (LAD=260, Diagonal=27, LCX/OM=123, RCA/PDA=103, RCA/PLV=72). Four patients needed to be converted from OPCABG to CPB on table. Another four patients needed re-operation due to graft related problems in the post-operative period and 6 needed post-operative Intra-aortic Balloon Pump (IABP) support. Post-operative complications included 3 TIAs, 1 complete stroke, 9 patients with renal failure and 51 patients developed atrial fibrillation post operatively. There was one peri-operative death due to pulmonary edema. Ninety percent of patients were in CCS angina class I/II and NYHA class I/II post-operatively. Forty one patients developed significant recurrence of angina requiring medical management, with 7 patients needing PCI/stenting. At the time of follow-up (median 5 years, range 3 months to 10 years) 9 patients had died.

Conclusions: Off pump coronary artery bypass (OPCABG) can be achieved with a low mortality and good medium to long term survival. OPCABG is associated with fewer post-op complications and comparable late coronary interventions.

Keywords: Off-pump, coronary artery bypass grafting, cardiopulmonary bypass, coronary artery disease, CABG, OPCABG

INTRODUCTION

Coronary artery bypass grafting (CABG) or direct myocardial revascularisation involves the use of a vascular conduit to bypass atheromatous lesions in coronary arteries. The first recorded bypass operations were in the sixties when Goetz et al[1] and Kolessov[2] grafted pedicled internal mammary arteries to the right coronary artery and left anterior descending arteries respectively. These operations were performed without the use of cardiopulmonary bypass also known as Off-pump coronary artery bypass grafting (OPCABG).

Development of Cardiopulmonary bypass (CPB) and myocardial protection led to the development of myocardial revascularisation with cardioplegic arrest. This enabled cardiac surgeons to operate in a motionless and bloodless field; and so OPCABG was relatively abandoned for the technical advantage that CPB and cardioplegic arrest offered.

CPB is associated with activation of the complement system and the coagulation cascades which may contribute to the varying degrees of organ damage reported in the literature[3 4]. Blood contact with the artificial surfaces of the CPB circuit produces a well-documented diffuse inflammatory response that affects multiple organ systems. Specific deleterious effects of the inflammatory response have been found in the heart, lungs, central nervous system, kidneys, and gastrointestinal tract[3]. These unavoidable side effects of CPB have led to the renewal of interest in OPCABG. Significant technological advances made in the last decade have allowed OPCABG to be performed with good success rates without the risks of CPB. This paper presents a retrospective review of our results over a ten-year period.

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METHODS

All Patients who underwent OPCABG between September 1995 and March 2005 were identified from theatre records (n=324). Demographic data was obtained from medical case notes and the computerised patient data system (PATS). Formal EuroSCORE[5], a validated predictor of operative mortality for cardiac surgical procedures, was calculated for each patient pre-operatively to predict the mortality. This scoring was introduced in 1999, and hence we included those patients who had the EuroSCORE computed pre-operatively and those who were operated by the senior authors (GC and PB) and excluded the rest of the patients (n=266). Operative variables recorded included: number of bypass grafts; type of conduit used; number of distal anastomoses; number of patients converted to CPB and the reasons for conversion. All the demographic, EuroSCORE and the procedure specific data were collected prospectively in this cohort of patients included for analysis, the post-discharge follow-up was done retrospectively.

All patients underwent an operation through a standard median sternotomy with the Left internal mammary artery (LIMA) harvested where indicated under direct vision. Heparin was administered at 2mg/kg prior to division of the mammary artery with supplemental doses to maintain adequate heparinisation (ACT, activated clotting time>250seconds); and reversed with protamine (1:1) after completion of the last proximal anastomosis. Aspirin or antiplatelet therapy was stopped five days before operation and recommenced immediately after the operation. Subcutaneous Enoxaparin was administered at 40mg twice daily post-operatively till the patients were mobile for deep venous thrombosis prophylaxis.

Commercially available mechanical stabilization devices such as the Octopus 2 (Medtronic Inc, Minneapolis, MN), CTS stabilizer (Guidant Inc) were used to stabilise the coronary targets on the beating heart; and pericardial traction sutures were used to position the heart where appropriate. The target coronary arteries were occluded proximally with a temporary snare using a pledgeted 4-0 polypropylene suture. Retrograde bleeding was controlled with a sterile, humidified carbon dioxide blower (Medtronic DLP, Grand Rapids, MI). Intraluminal coronary shunts (Bio-Vascular, Inc, St. Paul, MN) were used infrequently (< 10% of patients) when retrograde bleeding was excessive or when it was anticipated that occlusion of a coronary target would be poorly tolerated because of critical ischaemia.

Distal anastomoses were constructed with a continuous running 7-0 polypropylene suture. Proximal anastomoses were sewn to the aorta under a partial occlusion clamp with a continuous 6-0 polypropylene suture. All patients received postoperative care in the same Cardiac Surgery Intensive Care Unit (CSICU) with early extubation where appropriate, the aim being discharge by day 6.

Definitions of co-morbidities/complications:

Postoperative variables recorded included creatine kinase isoenzyme MB (CK-MB) (as an indicator of peri-operative myocardial injury, with absolute increase of more than 10% compared to creatine kinase levels); changes in the morphology of ST segment indicating ischaemia or infarction; incidence of ishaemic ventricular arrhythmias; Intra-Aortic Balloon pump (IABP) use and inotropic requirement as an indicator of myocardial dysfunction. Pulmonary dysfunction is defined as the long term use of bronchodilators or steroids for lung disease or prolonged ventilatory dependence due to pneumonia or ARDS. Neurological dysfunction is defined as neurological disease severely affecting ambulation or day-to-day functioning. Transient Ischaemic Attacks (TIAs) are neurological events with the signs and symptoms of a stroke which resolve completely within 24 hours. Renal failure is defined as anuria or oliguria (<10ml/hr) (with an adequate mean BP) and renal impairment is a serum creatinine >200 micromol/l or need for renal replacement therapy. Follow-up was done by telephonic questionnaire (within a closing interval of 2 months) and from medical records.

Statistical analysis:

For normally distributed data the mean and standard deviations are expressed. Fisher exact test was used to determine significance between categorical variables and Mann Whitney U test for continuous variables. Binary logistic regression with confirmation by forward method was used for the multivariate analysis.

RESULTS

Analyses revealed 324 patients (224 male) to have had OPCABG in the Royal Victoria Hospital between Sept 1995 and March 2005. Mean age was 62 (range 35 – 79). The study population consisted of 266 patients as outlined above, with a EuroSCORE median of 3 (range 1 – 8). Thirty six patients had a EuroScore[5] of more than five. There were 149 patients with CCS class III/IV angina (angina with mild exertion/ angina at rest) and 48 with NYHA class III/IV (marked limitation of physical activity/unable to carry out any physical activity without discomfort). 148 patients had suffered previous myocardial infarction (MI) and 48 patients had a preoperative left ventricular ejection fraction (LVEF) of <30% on echocardiography or as estimated by ventriculogram.

A total of 585 bypass grafts were performed (Left anterior descending branch (LAD) = 260, Diagonal branch = 27, Obtuse marginal branch = 123, Posterior descending artery branch = 103, Posterior left ventricular branch = 72). The average number of grafts per patient was 2 (range 1 – 4) with a LIMA to LAD graft in 242(75%) of patients. Four patients had their operations converted to CPB; three for unstable haemodynamics and one for myocardial optimisation following a myocardial infarction intra-operatively. There were 2 peri-operative myocardial infarctions, 1 discovered on the operating table as above, the other detected post-operatively from CK-MB measurements. Four patients needed re-operation due to graft related problems in the peri-operative period, 6 patients required an intra-aortic balloon pump peri-operatively for haemodynamic instability including 1 post-operative death due to pulmonary oedema.

The median chest drainage was 781ml (range 130 to 2483ml). Median ventilatory time was 18 hours (range 2 to 168 hours). Four patients suffered cerebrovascular accidents (CVAs) peri-operatively; 3 were confirmed as TIAs and recovered fully prior to discharge and 1 patient had a complete stroke.

Table I:

Comparison of the outcomes in a high risk group versus low risk group

Variable	Low-risk (n=73)	High Risk (n=58)	*P* value
Pre-op Neurological disease	1	5	0.08
Pre-op Renal impairment	1	7	<0.05
Pre-op Pulmonary disease	1	6	0.069
No of grafts	2.08(1-4)	2.24(1-3)	NS
Post-op CKMB	25(3-460)	30(3-187)	0.44
Ventilation (hours)	16.24(3-240)	15.87(4-24)	0.042
Blood loss (mls)	730(200-2430)	750(240-2000)	0.57
Hospital stay (days)	7.4(4-46)	7(4-19)	0.58
Adverse events	1	5	0.08
Late re-intervention	2	4	0.19

Fifty one patients developed transient atrial fibrillation post-operatively one of which was from chronic pre-operative atrial fibrillation. Nine patients developed post-operative renal failure one of which was known to have renal impairment pre-operatively and had a nephrectomy 7 years earlier. There were 6 wound infections post-operatively, one of which had a sternotomy wound dehiscence with mediastinitis and was successfully treated with debridement and rewiring.

At follow-up most patients (90%) were in CCS class I/II and NYHA class I/II post-operatively. A total of 41 patients developed a recurrence of angina, with seven needing PCI/stenting, the rest were well controlled medically. At the time of follow-up (median 5 years, range 3 months to 10 years) 9 patients had died.

Surgery in high risk patients:

The high risk group is defined as having one or more of the following: Age>75(n=8), LVEF<30% (n=48), MI within 6 weeks (n=7), pre-operative neurological dysfunction (n=5), pre-operative pulmonary dysfunction (n=6) and pre-operative renal impairment (n=7). We excluded (n=6) patients who had a non-cardiac procedure carried out together with OPCABG. We compared our results of OPCABG between the high-risk and low risk patients to see if there was any difference in the frequency of adverse events.

There were five patients who had more than two selection criteria for high-risk. Amongst high-risk patients, one developed CVA, two patients had pneumonia and two had transient renal failure not necessitating dialysis (adverse events) but none of the patients died in the perioperative period. One patient in low risk suddenly collapsed 3months after surgery, two patients in the high-risk group died, one due to a ruptured aortic aneurysm within 6months of surgery (which was known prior to his operation) and other due to a CVA and subsequent development of septicemia 10 months post-surgery. (Table I)

DISCUSSION

This retrospective review presents the first report of the results of OPCABG in the province over ten years. Various modifications and technological advances over this period now allow the safe performance of OPCABG in more groups of patients that previously would have been considered unsuitable. Numerous studies have demonstrated the safety and efficacy of OPCABG with favourable early outcomes and a recent meta-analysis revealed that OPCABG is a safe alternative to conventional CABG with respect to mortality, and is recommended to reduce perioperative morbidity[6]. We have demonstrated that using this technique, success rates (mortality) are comparable to conventional CABG using CPB.

OPCABG is unsuitable for patients with a severely dilated or hypertrophied heart; patients in cardiogenic shock; patients with mechanical complications of myocardial infarction like post-infarct ventricular septal defects (post-infarct VSD) and patients who may need concomitant valve procedures. In these cases the preferred method would be CABG with CPB. There is always the option to convert an OPCABG to conventional CABG for a number of reasons which include myocardial instability intra-operatively, intra-myocardial coronary arteries or difficult access to target vessels; but with modern technology and techniques this rarely happens.

A consensus is now emerging as to the appropriate application of OPCABG to benefit patients with a pre-operative risk of developing neurological dysfunction. These included patients with extensive carotid artery disease who have a high risk of developing a perioperative stroke[4]. OPCABG is ideally suited for patients who have an atherosclerotic aorta where manipulation of the aorta can be avoided by using bilateral internal mammary arteries with T configuration grafts to avoid the proximal anastomosis of the aorta. Patients with documented renal impairment who may be at increased risk of developing further renal damage, secondary to hypotension due to CPB, also benefit from OPCABG. The literature observes a trend towards a reduced need for blood transfusions, earlier weaning from ventilation and earlier discharge with the use of OPCABG even when it is employed in the elderly patient and in patients with several co-morbid conditions[4 6 7]. Currently, about 20% of surgical coronary revascularization at the national level is performed using OPCABG[8]. OPCABG is a useful strategy in the armamentarium of a modern cardiac surgeon and in carefully selected patients has proven benefit

with improved outcomes.

The outcomes of low risk patients and high risk patients were comparable (Table I). These high risk patients would have been expected to have a higher degree of complications and adverse events if they underwent conventional CABG with CPB.

This was a retrospective review and was not randomised so there is a selection bias for OPCABG. We cannot conclude from this study that OPCABG is a better alternative to CABG with CBP but we show that it is a successful and comparative option in surgical revascularisation of diseased coronary arteries. Due to advances in medical therapy older and sicker patients with other co-morbid conditions are referred for coronary bypass operations. This means an increasing proportion of patients may present with relative contraindications to CPB such as renal impairment and an increased risk of cerebrovascular accidents. For such patients a successful alternative is OPCABG.

The authors have no conflict of interest.

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Paper

Foreign Body Ingestion in Prisoners – The Belfast Experience

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Keywords: Gastrointestinal, Foreign Body, Ingestion, Prison.

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SUMMARY:

Deliberate ingestion of foreign bodies is common amongst prison inmates. The motives behind the ingestion are variable. As the only designated hospital in Northern Ireland treating acute surgical pathologies in the prison population, we reviewed our experience of foreign body ingestion between March 1998 and June 2007. Types of foreign objects, symptomatology, haematological analyses, radiological findings, operative intervention and complications were retrieved from case notes. A literature search was performed using Medline to correlate this clinical data with published evidence to produce therapeutic guidelines to assist the surgical multi-disciplinary team.

Eleven prisoners presented with foreign body ingestion over the study period (M=8 and F=3, mean age: 28.1 years, range 21-48). Mean follow-up was 597 days (range 335-3325 days). Although the literature states that most foreign bodies usually pass spontaneously without the need for intervention, this study demonstrates a higher intervention rate of 36% within the Northern Irish prison population in comparison with other prisoners.

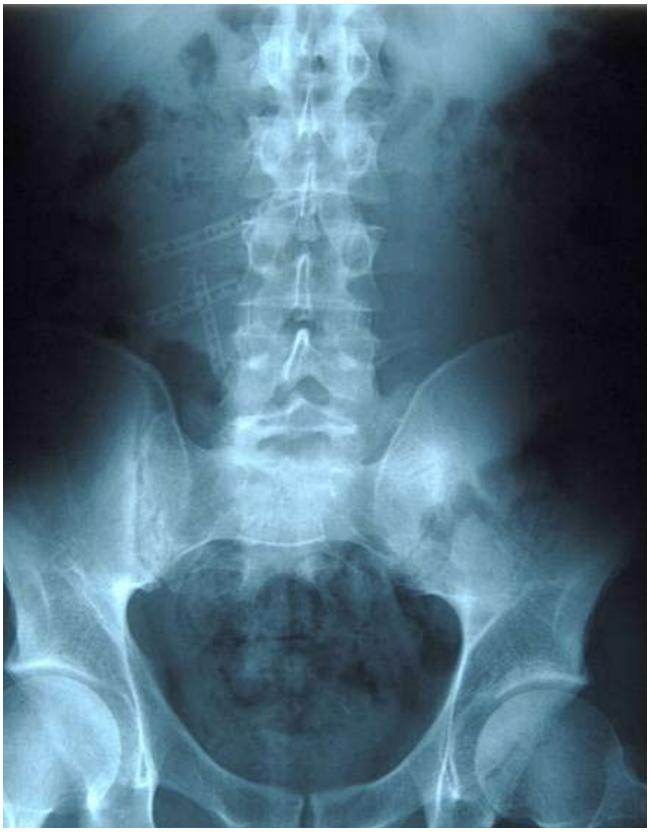

Fig 1. Razor blades in the small bowel.

INTRODUCTION

Ingestion of foreign bodies is a common clinical problem. Difficulties can often occur in both diagnostic and management protocols. Approximately 80% of cases occur in the paediatric population with ingestion frequently occurring accidentally[1]. In adults, the unintentional swallowing of objects occurs mainly in the elderly population and those patients with learning disabilities and alcohol dependence, whereas intentional episodes occur commonly in psychiatric patients and prisoners[2]. In the latter group razor blades, batteries and other sharp metallic items are most commonly encountered[1].

In the general population, 80-90% of foreign bodies will pass spontaneously[3]. However, endoscopic intervention is required in 10-20% of patients with less than 1% of patients requiring surgery[3]. The prison population is a unique environment with different emotional and physical constraints where both the nature and motives behind ingestion are ambiguous with further difficulties encountered in the diagnosis and management of such patients.

OBJECTIVE

To perform a clinical epidemiological review of all patients from the prison population in Belfast who presented to the Belfast City Hospital for management of ingested foreign bodies and to correlate these clinical data with published evidence to produce therapeutic guidelines to assist the surgical multi-disciplinary team.

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TABLE I

Clinical data for all 11 patients

(RIF=Right iliac fossa, RUQ=Right upper quadrant, SB=Small bowel, SBO=Small bowel obstruction).

No	Age	Sex	Type of FOREIGN BODY	Intentional	Repeated ingestion	AXR	CT Scan	Endoscopy: attempted retrieval	Surgery	Hospital Stay (days)	Outcome
1	29	M	Razors	Yes		3 Razors in SB		No	No	1	Alive
2	23	M	Razors	Yes		1 Razor in SB		No	No	1	Alive
3	31	M	20p coin	Yes		20p coin in RIF, SBO	Complete SBO	Yes – colonoscopy: failed	Laparotomy: Resection of terminal ileum and Right hemicolectomy	6	Alive : diagnosed with Crohn's disease
4	25	F	Razors	Yes		Razor in RUQ		No	No	1	Alive
5	26	M	Razors	Yes		1 Razor in SB		No	No	1	Alive
6	21	M	Batteries	Yes	Yes – Razors	3 Batteries in SB		No	No	1	Alive
7	23	M	Razors	Yes		5 Razors in SB, 1 in rectum		No	No	1	Alive
8	24	M	Razors	Yes	Yes – Razors and Metallic Rod	2 Razors in SB and rectum		No	No	1	Alive
9	37	F	Batteries	Yes	Yes – Batteries	6 Batteries in SB, SBO		No	Laparotomy: enterotomy	6	Alive
10	22	M	Batteries	Yes	Yes - Batteries	2 Batteries in SB, SBO		No	Laparotomy : enterotomy	8	Alive
11	48	F	Watch	Yes		Watch in RIF		Yes – successful extraction	No	4	Alive

METHODS

A nine-year retrospective review of all prisoners presenting with foreign body ingestion to the Belfast City Hospital Surgical Unit was completed. Clinical records were then reviewed for data regarding patient demographics, type of foreign body ingested, intention of ingestion, clinical presentation, past medical and social history, haematological analyses, radiological findings, management details including the need for operative intervention and complications. A further assessment of any previous admissions with similar complaints was completed from review of the hospital patient administration system. Follow up was completed for all patients by the prison medical teams with specialist review in the Belfast City Hospital as required.

RESULTS

Demographics: Eleven prisoners (8 males, 3 females) presented with gastrointestinal foreign bodies over the study period. Mean age was 28.1 years (range 21 - 48). Mean admission duration was 2.3 days. Ingested foreign bodies identified included razor blades (n=6), batteries (n = 3), a 20-pence coin (n = 1) and a wrist watch (n = 1), (Figs 1 - 3). Presenting symptoms included reduced appetite (n = 4), vomiting (n = 8), abdominal pain (n = 8) and constipation (n = 5). None of the patients had a significant gastrointestinal past medical history. Most smoked tobacco (n = 8) and consumed alcohol (n = 6) on a regular basis. See Table I for clinical data for all 11 patients.

Investigations: Haematological analyses were normal on admission except for a mean raised C-reactive protein of 47.2 mg/l (range 2 - 221). A plain abdominal X-ray confirmed the presence of a metallic foreign body in all patients. An erect chest X-ray was normal in all patients. Computerised Tomography (CT) imaging was required in patient 3, which confirmed small bowel obstruction secondary to an impacted 20-pence coin at the terminal ileum.

Management: Seven patients were managed conservatively. Patients 3 and 11 underwent attempted endoscopic retrieval of the foreign body. Patient 3 admitted to swallowing a 20-pence coin. The coin had impacted in the terminal ileum and attempts at endoscopic retrieval were unsuccessful. He proceeded to laparotomy where the terminal ileum and right

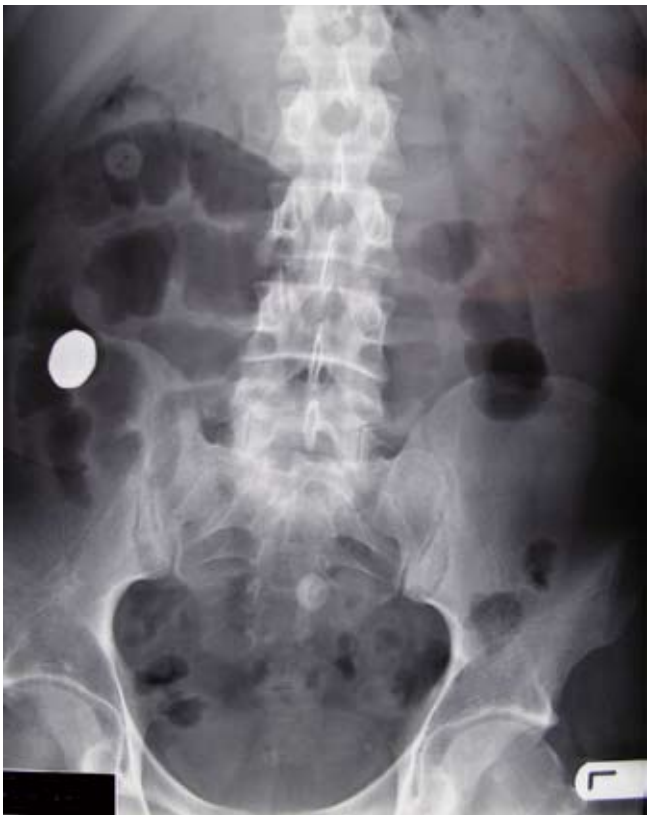

Fig 2. 20-pence coin in the right iliac fossa. Dilated loops of small bowel proximal to coin. Reproduced with permission from the Irish Journal of Medical Science - Reference 4

colon were resected with a primary anastomosis performed. Histopathological analysis revealed Crohn's Disease with stricturing distal to the impacted 20-pence coin[4]. Patient 11 was admitted after intentionally swallowing a wrist-watch 6-weeks prior to presentation. Endoscopic retrieval from the ileo-caecal junction was successful (Figs 3, 4). Two further patients (9 & 10) required operative intervention for continuing obstructive symptomatology. An enterotomy was performed with extraction of the metallic foreign body followed by primary closure in both instances.

Outcome: Mean follow-up was 597 days (range 335-3325 days) and was complete for all patients. There were no significant post-operative or long-term complications. All (n = 11) cases of foreign body ingestion were intentional. Almost half of the patients (n = 4) repeated the ingestion of foreign objects (Fig 5).

DISCUSSION:

Ingestion of metallic foreign bodies remains a common problem amongst prison inmates. Swallowing multiple objects at once or repeating the ingestion is a frequent occurrence[2]. The motives behind the ingestions vary. Underlying psychiatric conditions such as schizophrenia, depression, self-mutilation, masochism and suicidal tendencies, attempts to escape incarceration by transfer to a hospital or psychiatric unit, genuine accidental ingestions and attempts at drug trafficking are common motives[1,3,5-6]. Blaho *et al* demonstrated a very high incidence of foreign body ingestion from 2 different prison populations during a 5-week study period where 14 ingestions were noted in 8 male prisoners[6]. The foreign bodies ingested and the methods of ingestion were similar. Communication between the inmates of both prisons was well established[6]. This study suggested imitative behaviour as an underlying cause.

There is no published epidemiological data describing the true prevalence of foreign body ingestion in the prison population. From review of published case series, patients affected range from 22 to167 cases in the United States series to 261 cases from larger European studies[3, 7-8].

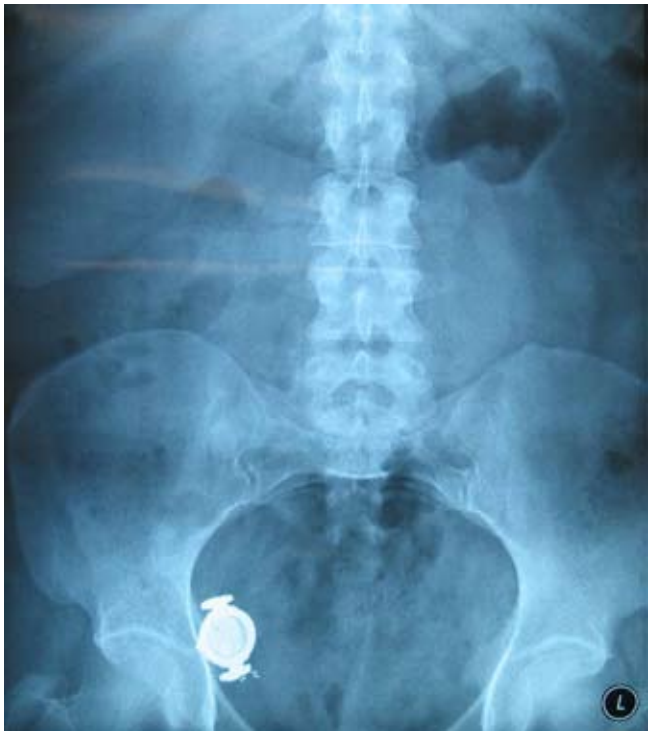

Fig 3. Wrist-watch in right iliac fossa. Failure to progress beyond terminal ileum.

The majority of foreign bodies that reach the gastrointestinal tract will pass spontaneously. Foreign body impaction may occur at areas of anatomical narrowing (the cricopharyngeus, the lower oesophageal sphincter, the pylorus, the ileocaecal valve and the anus), physiological angulation (the curvature of the duodenum) or areas of pathological strictures (terminal ileum in Crohn's disease)[1,2,4,6,9]. The most common sites for perforation are the lower oesophagus and terminal ileum[2,9]. Bleeding occurs when injury to the gastrointestinal mucosa occurs.[5] Generally, foreign bodies greater than 2-2.5 cm in size will not enter the pyloric canal and those exceeding 6-10 cm in length will not progress through the curvature of the duodenum[1-2,10].

Treatment depends on the patient's age and symptomatology, nature and type of ingested foreign body and the anatomical location especially if impacted. Foreign bodies may be managed conservatively or therapeutically with endoscopic, laparoscopic or open surgical methodologies. Blunt objects such as coins can impact in the oesophagus resulting in partial or complete obstruction. Endoscopic retrieval should be attempted in all instances, as prolonged lodgment can lead to pressure necrosis, perforation or fistula formation[1-2]. A prospective *in vivo* study by Feigel *et al* demonstrated that a

retrieval net was superior to the basket or forceps technique[11]. If the blunt object has passed in to the stomach and is less than 2cm in diameter, a conservative outpatient management protocol with weekly radiographs should be adopted. If the blunt object remains in the stomach, it has been recommended to delay endoscopic retrieval for 1-2 months to facilitate any opportunity for spontaneous passage[2,5,11,12]. Blaho *et al* also recommend a 3–4 week waiting period to allow passage before attempts at endoscopic retrieval are made[5]. Zuloaga *et al* suggest a two month waiting period[12]. One of the patients in our study presented with a five week history of colicky right iliac fossa pain. The abdominal X-ray on presentation revealed a wrist-watch in the right iliac fossa suggestive of probable impaction at the terminal ileum (Fig 3). Repeat X-rays showed

Fig 4. Endoscopic retrieval of wrist-watch was successful. The watch was still functioning.

failure of progression of the object. Colonoscopic retrieval of the wrist-watch was successful on day-3 post-admission (Fig 4).

Endoscopic retrieval of sharp objects, such a razor blades, straightened paperclips and needles that are lodged in the oesophagus should be performed urgently[1,2]. If the object progresses into the stomach or duodenum, immediate attempts at endoscopic retrieval should be undertaken, as the risk of perforation at the ileocaecal valve is approximately 35%[1,2,9]. If the sharp object has passed beyond the duodenum, the patient should be monitored with daily radiographs and remain under strict observation. Surgical intervention may be required if a sharp object fails to progress radiologically after 72-hours. Emergency laparotomy is required if the patient develops acute clinical signs[1,2]. All six patients that swallowed razor blades in our study presented after the blades had passed into the small bowel. None of them developed symptoms of obstruction or perforation and consequently were successfully managed conservatively.

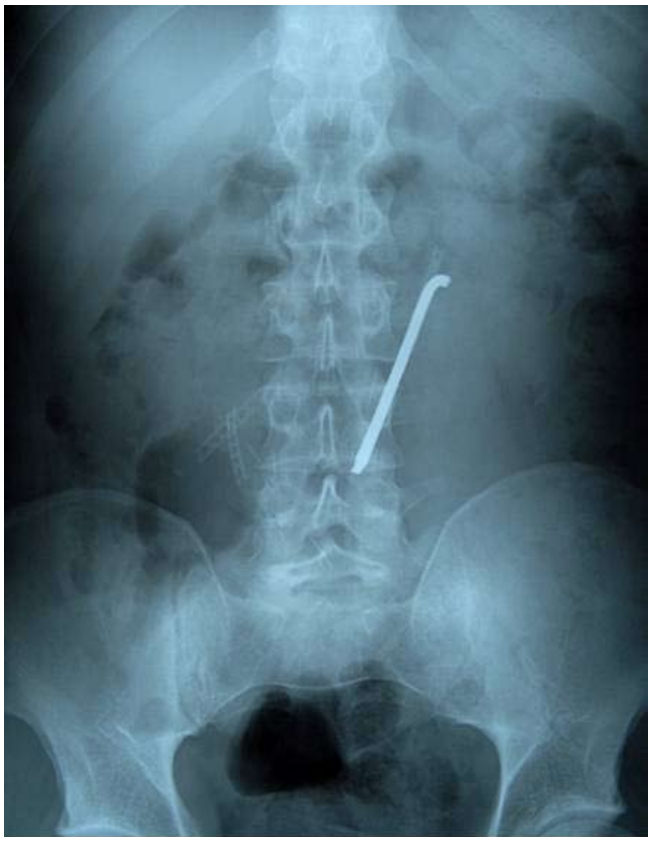

Fig 5. Re-ingestion of metallic rod combined with previous ingestion of razor blades as shown in Figure 1.

Batteries (disc or button) require urgent endoscopic retrieval if lodged in the oesophagus due to the possible risk of chemical burns, electrical discharge and liquefaction necrosis which can lead to subsequent perforation[1,2]. Once the battery has passed into the stomach, retrieval is only indicated if it remains in the stomach beyond 48 hours, or if it is a larger battery measuring more than 2cm in diameter[2]. Once beyond the duodeno-jejunal flexure, 85.4% are passed within 72-hours[13]. A follow-up radiograph twice per week is sufficient[2]. Laxatives and anti acids have no proven benefit in management, however gastric lavage has been described to facilitate removal[14]. Our study showed that 67% of patients that swallowed batteries developed small bowel obstruction requiring a laparotomy with enterotomy. Murshid *et al* also describe the successful laparoscopic extraction of a sewing needle from the terminal ileum of a 17-year-old female after failure of the endoscopic approach[9]. Packages of narcotics should not be removed endoscopically as the risk of rupture and leak of the toxic substance is high[1,2]. Surgical intervention is reserved for those cases where signs of obstruction or leakage of substance occurs[2]. A management protocol is outlined in Table II.

Many prisoners who deliberately swallow foreign bodies ingest multiple objects or repeat the ingestion in a further episode[5,7]. Weiland *et al* demonstrated that amongst 22 male prisoners there were 75 separate hospitalisations, with a total of 256 objects swallowed[7]. In our study 36% of prisoners repeated the ingestion. Patient 8 was managed conservatively following ingestion of razor blades. He represented a few weeks later with ingestion of further razor blades and a metallic rod (Fig 5).

TABLE II

Recommended management protocol for ingested foreign bodies.

Type of Object	Site of Object	Management Protocol
Batteries	Oesophagus	Urgent endoscopic retrieval
	Stomach and Duodenum	If > 48 hrs → endoscopic retrieval
		If > 2 cm → endoscopic retrieval
	DJ Flexure	Twice weekly X-rays
		If signs of Obstruction/Bleeding/ Perforation → urgent endoscopic retrieval +/- laparotomy
Sharp Metallic Objects	Oesophagus	Urgent endoscopic retrieval
	Stomach and Duodenum	Urgent endoscopic retrieval
	DJ Flexure	Daily x-rays/ strict observation
		If fails to progress > 72 hrs → laparotomy
		If signs of Obstruction/Bleeding/ Perforation → laparotomy
Blunt Metallic Objects	Oesophagus	Endoscopic retrieval
	Stomach and Duodenum	If < 2cm → weekly X-rays/ conservative management
		If > 2 cm → observe with weekly X-rays for 1-2 months. If failure to progress → endoscopic retrieval
	DJ Flexure	Weekly X-rays/ conservative management
		If signs of Obstruction/Bleeding/ Perforation → urgent endoscopic retrieval +/- laparotomy

CONCLUSION:

Although the literature states that most foreign bodies in the general population usually pass spontaneously without the need for intervention, this study demonstrates a major difference within the prison population where surgical or endoscopic intervention was required in 36% of these patients (18% required a laparotomy, 9% required endoscopic intervention, and a further 9% required both endoscopic and open removal), in contrast to 1% in the general population[1,2]. Weiland *et al* conducted a 10 year study (Wisconsin, USA) on 22 male prisoners with a total of 256 ingested foreign bodies; 40% of the objects passed spontaneously, 30% were managed endoscopically whereas 30% required surgery[7]. Similarly Barros *et al* conducted a 6-year study (Madrid, Spain) where 167 patients (including 70 prisoners) were reviewed. Surgery was required in 30% of the patients[3].

Identification of prisoners who have a pre-incarceration tendency to swallow foreign objects or those who repeatedly ingest objects, and subjecting them to psychiatric and behaviour modification therapy may prove efficacious. However, this was not assessed in this study.

The authors have no conflict of interest.

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Paper

Minimally invasive parathyroid exploration for solitary adenoma. Initial experience with an open, 'short incision' approach.

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SUMMARY

Background: In the vast majority of patients with primary hyperparathyroidism (HPT) the causative pathology is a benign solitary adenoma. The conventional surgical approach for HPT has involved bilateral cervical exploration with attempted identification of all four parathyroids and resection of enlarged glands. However, in recent years new techniques have permitted accurate preoperative localisation of the single parathyroid tumour in many patients. This has facilitated a focused unilateral operation to be performed in patients with a solitary parathyroid adenoma. More recently we have progressed to a minimally invasive surgical approach for such individuals in whom the tumour has been localised preoperatively.

Patients & Methods: Between September 2004 and July 2006, 24 patients with proven HPT, underwent focused, unilateral cervical exploration through a short (2.5-3 cm) incision placed low on the appropriate side of the neck. Preoperatively, each patient had been shown to have a single focus of activity after parathyroid isotope scanning.

Results: There were 21 females and 3 males in the study group with a mean age of 61.5 years (range 25 - 84 years) at the time of operation. The approach was successful in 22 patients with a mean operating time of 49 minutes (range 22-85 minutes). Postoperatively, the serum calcium level returned to normal in every patient and has remained so during a mean follow up period of 11.5 months (range 1-22 months). No individual developed postoperative hypocalcaemia although one patient developed a temporary unilateral vocal cord paralysis.

Conclusion: A short incision cervical approach for HPT due to solitary adenoma is a viable alternative for appropriately selected patients.

INTRODUCTION

Primary hyperparathyroidism (HPT) is a common disease and in the vast majority of patients, the underlying pathology is a solitary benign adenoma[1-3]. Historically, the conventional surgical approach for the patient with HPT has involved routine bilateral cervical exploration with attempted identification of all four parathyroids and surgical resection of enlarged glands.

However, with the availability of new techniques which permit accurate preoperative localisation of the single tumour in a significant proportion of patients, we have, for some time, practised a surgical strategy of focused unilateral operation for individuals with HPT due to solitary adenoma and in whom the tumour has been localised preoperatively.

Our experience with this innovative approach indicates clearly that, provided a set of exclusion criteria for unilateral neck exploration is strictly applied, a focused unilateral operation leaves the patient no more vulnerable to persistent or recurrent hypercalcaemia than a standard bilateral procedure [4,5].

Against this background a number of less invasive surgical procedures have begun to emerge, all of which involve a focused operation for solitary parathyroid adenoma after preoperative localisation of the tumour and using either an endoscopic or a limited open surgical approach [6-8].

We have been attracted to one such approach utilising a short incision placed low in the neck on the side of the tumour, and which has the potential for achieving a pleasing cosmetic outcome for the patient. We report our early experience with this new type of surgical exploration.

PATIENTS AND METHODS

Between September 2004 and July 2006, 24 patients with proven HPT were selected to undergo a focused, unilateral parathyroid exploration through a short (2.5-3 cm) incision placed low on the appropriate side of the neck (Fig.1). Preoperatively, each patient had undergone dual isotope subtraction scintigraphy[9-12] and had been shown on scan to have a single focus of activity following subtraction.

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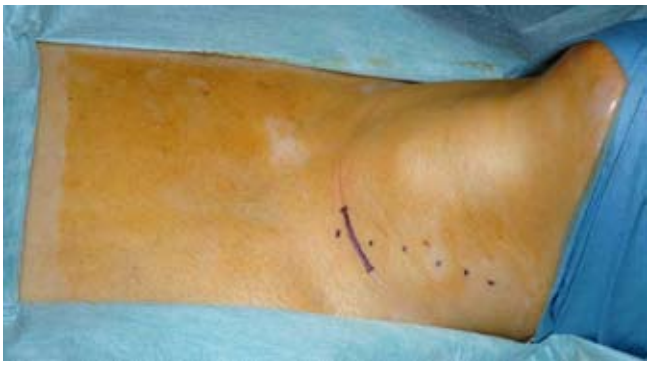

Fig 1. 2.5cm skin crease incision low in left neck over scan detected solitary parathyroid adenoma

Prior to operation the proposed procedure was discussed in detail with every patient selected, with particular reference to the small possibility of injury to the recurrent laryngeal nerve and the potential for the requirement to convert to a standard neck exploration through a full 'collar' incision.

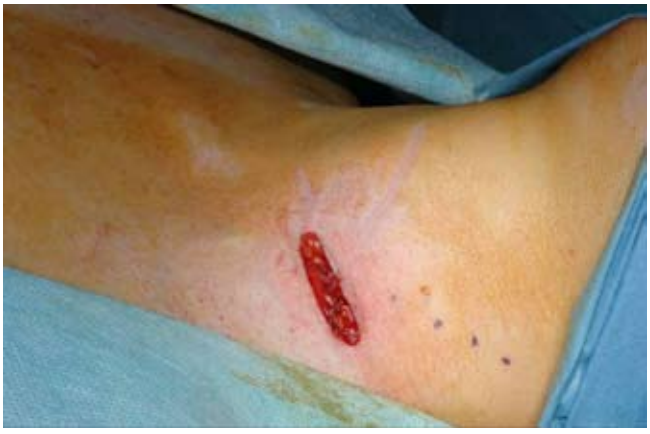

Fig 2. Incision deepened through subcutaneous tissue and platysma muscle.

All the operations were carried out under general anaesthesia with full muscle relaxation. Following incision of the skin the platysma muscle is divided in the line of the incision (Fig 2). The anterior border of the sternocleidomastoid muscle is then identified and freed in both cranial and caudal directions. The space between the carotid sheath structures laterally and the strap muscles medially is now opened and developed and the lateral lobe of the thyroid gland is identified and, if necessary, delivered into the wound (Fig 3). A careful search is now made for the parathyroid tumour, which is identified, mobilised and removed (Fig 3). Individual small vascular clips are employed to secure the vascular pedicle associated with the tumour. The thyroid lobe is then replaced and the wound closed with an absorbable subcuticular suture (Fig 4).

RESULTS

Of the 24 patients included in this pilot study 21 were female and 3 male with a mean age at operation of 61.5 years (range 25 - 84 years). All patients had a proven biochemical diagnosis of HPT with persistent hypercalcaemia and concomitant elevated or inappropriate plasma level of parathyroid hormone (PTH, intact molecule assay). Individual patient details are recorded in Table I.

In two individuals, the parathyroid adenoma could not be convincingly identified via the small incision and the procedures were therefore converted to full neck exploration by extending the skin incision into a standard collar wound and exploring the relevant side in regular fashion from the midline. In both patients, the tumour was subsequently located at the site suggested by the isotope scan. The mean operating time for the remaining 22 patients was 49 minutes (range 22 – 85min).

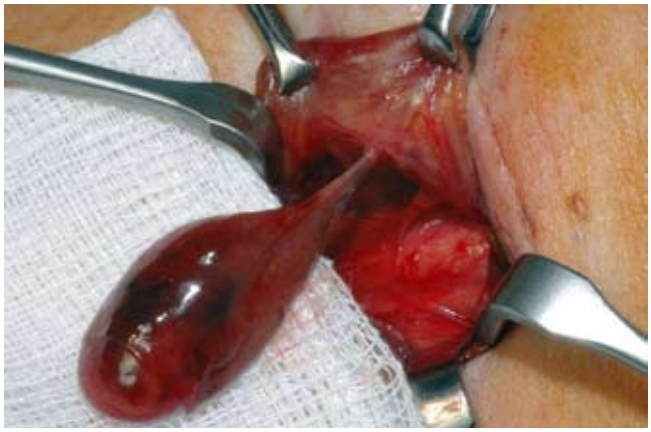

Fig 3. Parathyroid tumour mobilised and delivered into wound.

Postoperatively, the serum calcium level returned to within the normal range in every patient operated by the minimally invasive technique and has subsequently remained so during a mean follow up period of 11.5 months (range 1-22 months), Table I. There were no symptoms of hypocalcaemia in any individual following operation. One patient was found to have a unilateral vocal cord paralysis on routine postoperative indirect laryngoscopy but demonstrated a normal voice and explosive cough at review a few months later.

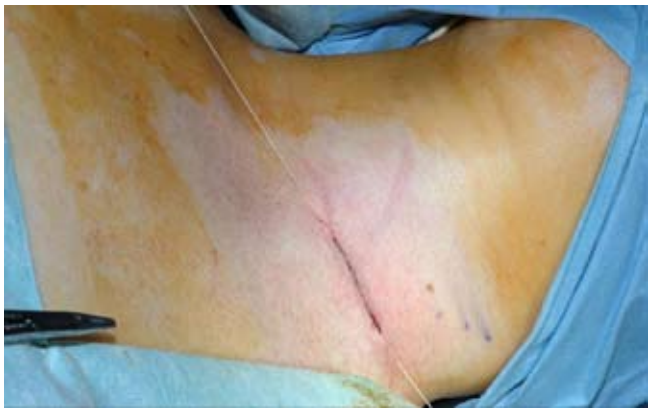

Fig 4. Skin incision closed using subcuticular absorbable suture.

DISCUSSION

There is now ample and unequivocal evidence that focused, unilateral parathyroid exploration can be carried out in appropriately selected patients with HPT, without increased incidence of persistent or recurrent hypercalcaemia following operation[4,5] .Although we have been long time advocates of this type of surgical approach, we have consistently and repeatedly emphasised the importance of applying a strict set of exclusion criteria for unilateral neck exploration

TABLE I

Serial No.	Age (Years)	Sex	Serum Calcium(mmol/l) (Preoperative)	Serum Calcium(mmol/l) Postoperative	Operation Time (Minutes)	Complications	Follow-Up (Months)
1	69	M	2.79	2. 38	36	Nil	22
2	48	F	3.11	2. 30	43	Nil	18
3	48	F	3.19	2.28	45	Nil	18
4	84	F	2.76	2. 39	22	Nil	17
5	59b	F	2. 72	2. 46	60	Nil	16
6	63	F	3. 09	2. 48	50	Nil	15
7	35	F	3. 21	2. 31	50	Nil	15
8	46	F	3.00	2. 43	66	V.C Palsy	15
9	78	F	3.02	2.48	50	Nil	15
10	81	F	2. 76	2. 46	44	Nil	14
11	60	F	2.75	2.20	38	Nil	12
12	67	F	2. 97	2. 31	52	Nil	11
13	79	F	3.18	2. 33	51	Nil	11
14	54	F	3.02	2.32	85	Nil	10
15	54	F	3.07	2.15	32	Nil	9
16	74	F	3.02	2.26	30	Nil	7
17	61	F	2.70	2.40	70	Nil	7
18	62	F	2.88	2.29	47	Nil	7
19	83	F	2.98	2.24	32	Nil	6
20	69	F	2.86	2.32	75	Nil	6
21	25	M	2.96	2..12	51	Conversion to standard procedure	2
22	53	M	3.10	2.14	77	Conversion to standard procedure Nil Nil	2
23	66	F	2.98	2.31	60		1
24	58	F	2.94	2.12	40		1

when patients are being considered for a limited, focused operation. If any such criterion exists then the individual in question should have a standard bilateral cervical exploration performed.

Previously, we have carried out scan-directed unilateral neck exploration for HPT using a standard collar incision placed low and centrally in the neck. Results from our earlier studies have provided a sound evidence base and have given others and us the confidence to progress to less invasive and cosmetically more favourable surgical approaches for patients with HPT due to solitary adenoma. These new procedures include full endoscopic parathyroidectomy[6,13], video-assisted open parathyroidectomy[7] and open 'short incision' parathyroidectomy with[14] or without[8] the use of intraoperative measurement of PTH. Having considered the various 'minimally invasive' procedures available, and influenced to some extent by the important report by Gauger and colleagues on the feasibility of the endoscopically assisted technique[15], we have chosen to pursue, in the first instance, a strategy of open parathyroidectomy via a carefully placed short incision, in appropriately selected individuals. Initial reports from other centres employing this approach have been encouraging[8,14] and our initial experience with it, recorded in this report, justifies we believe, a continuation of the use of this technique.

Of the 24 patients reported here and on whom we operated on an 'intention to treat' basis via a short lateral cervical incision, two required conversion to a full open exploration through a collar incision because we were unable to convincingly identify the parathyroid tumour via the initial approach. We feel that this initial 8.3% conversion rate to full open operation probably reflects our current position on the learning curve for this new procedure. We have, however, been surprised and impressed by the extent of the exposure of the thyroid lobe and the parathyroid glands that can be achieved via a very limited skin incision (Figs 3, 4). Our patients and we have also been pleased with the relatively short-term cosmetic results of this type of approach. It is of course an absolute requirement for this type of surgical procedure that the parathyroid tumour is accurately and unequivocally localised prior to operation.

For many years we have routinely utilised double isotope subtraction scintigraphy as a preoperative localisation investigation in patients diagnosed with HPT[10,16] and we continue to employ this type of scan as the only routine localisation study prior to operation. It has been suggested that before undergoing a minimally invasive focused unilateral

operation for HPT a patient should have concordant positive localisation results from two independent techniques, for example, Sestamibi isotope scanning and ultrasonography. However on the basis of our experience to date, and in the absence of any convincing, objective evidence that there is such requirement (specifically no prospective randomised studies) we would question the necessity for localisation concordance using two different investigations.

Finally, we would reiterate our view that the type of surgical procedure described in this paper should not be regarded as an 'easy option' to be undertaken by any surgeon working in the neck. If the high levels of successful outcomes together with concomitant low complication rates for patients undergoing parathyroid exploration are to be maintained, then parathyroid surgery should continue to be performed only by specialist endocrine surgeons who are familiar with the embryology and anatomy of the glands and who are fully trained in the spectrum of parathyroid surgical procedures.

The authors have no conflict of interest.

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Medical History

Paratyphoid Blamed On Ulster: A Nursing Odyssey

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SUMMARY

The aim of the Modicum mission from the United States was to determine the fate of the Western World, the Second Front and the Manhattan Project plans for development of atomic weapons. The Modicum mission was appointed in March 1942 by Franklin Delano Roosevelt as President and Commander-in-Chief of the US forces. The journey via the Anglican Cathedral in Bermuda, to Gander, to London, to Ulster was eventful. There was a clay-pigeon shooting contest in Gander. Generals Marshall, Eisenhower, Clark and Averell Harriman were outshot by their pilot. In Ulster, an escorting US sergeant killed a Londonderry bus driver with three shots. At a house party requested by King George VI and General Marshall, at Ashbrook, Ardmore, near Londonderry, it is alleged Averell Harriman was poisoned with *Salmonella schottmülleri*. He was delirious and 'gravely ill' for three weeks at 3 Grosvenor Square next to the American Embassy. He subsequently married his "other nurse", Pamela. Ambassador Pamela Churchill Harriman, a long-time ardent supporter of the Clintons, died in February 1997 following a stroke.

Key words: Enteric Fever, Paratyphoid

INTRODUCTION

In order to try to determine the origin of the paratyphoid B, enteric fever infection of W Averell Harriman, Franklin Delano Roosevelt's expediter, we need to follow itineraries. Harriman writes in his autobiography that Hopkins and himself "were billeted at the country house of a retired army officer who lived in elegant discomfort not many miles from Balyrena [sic], the base General Marshall was visiting". "Harriman," he writes of himself, "was forced to spend three weeks in bed", "gravely ill", "feverish and at times delirious, with what doctors believed to be a form of paratyphoid, probably traceable to drinking water from the Irishman's old well"[1]. "The incubation period of enteric fever (typhoid and paratyphoid) is typically eight to fourteen days, sometimes twenty-three"[2]. Christie cites incubation of twenty-one to twenty-three days, but four to five days may suffice when *S paratyphoid B* is the infecting agent, and the vehicle a highly favourable one, such as milk or cream[3]. Acute onset of symptoms is common[2]. The course of paratyphoid B infection may be identical to typhoid, producing a clinically indistinguishable enteric fever. The incubation period of enteric fever due to water-borne contamination is almost invariably longer than infection from other sources[2,3]. The pathology of enteric fever due to paratyphoid B is well described by Gadeholt and Madsen who report on 1,324 cases occurring in Norway between 1912 and 1961. Thirty-four of these patients with paratyphoid B died. All but eight of the surveyed 2,647 cases of typhoid and paratyphoid B were autopsied[4].

WAR-TIME JOURNEYS

On the 20th March 1942, Averell Harriman checked out of the Dorchester Hotel in London and flew with Lord Beaverbrook to Bermuda. From there, Beaverbrook flew to Miami and Harriman to Washington, DC[5]. A fortnight later General George C Marshall and Harry Hopkins and part of the Modicum mission left Baltimore early on the 4th April 1942 in a Pan-Am Clipper for Bermuda, having been given aliases in Washington[6]. In Bermuda the opposite approach to the secrecy was taken. The next day in the cathedral, Marshall read the second lesson at Easter Matins, Revelation 1:4-18*, ending "have the keys of hell and of death"[7-11]. According to Mrs. Marshall's account, her husband read "Philadelphia" with particular emphasis, leading one Philadelphian worshipper to enthusiastically express her pride in her native city[8]. Marshall and Hopkins were wished God-speed direct to London, but they flew non-stop to Gander, Newfoundland to join the rest of the Modicum group. At Gander were Dwight D Eisenhower, Mark Clark and Averell Harriman. The combined party was then put on a Boeing 307 Stratoliner piloted by Otis Bryan[12]. The Stratoliner had to return to Gander, Newfoundland, because of atrocious weather conditions over Greenland. Pilot Bryan won a "high brass Gander skeet (clay-pigeon) shoot out (24 of 25)". Marshall was an excellent and experienced quail hunter[13], but was outshot. Bryan then flew them on to Prestwick; thence to London[12]. Upon their arrival, Winston Churchill told Marshall he knew of his Easter lectern performance[8].

* Marshall and Hopkins knew of plans for the Manhattan Project. On 11th October 1939, in conversation about atomic bombs with Alex Sachs, an economist, President Franklin D Roosevelt said "What you are after is to see that the Nazis don't blow us up." To General Edwin M Watson, US Army, "This requires action"[9]. Watson and Sachs left together and action there was, and already had been. Enrico Fermi and Leó Szilárd, both then at Columbia University, and others were duplicating the German feat of splitting the uranium atom. On 11th October 1941, Roosevelt wrote to Winston Churchill proposing Anglo-American full-cooperation, and the following December, Churchill thanked Roosevelt for his letter of 11th October 1941[10,11].

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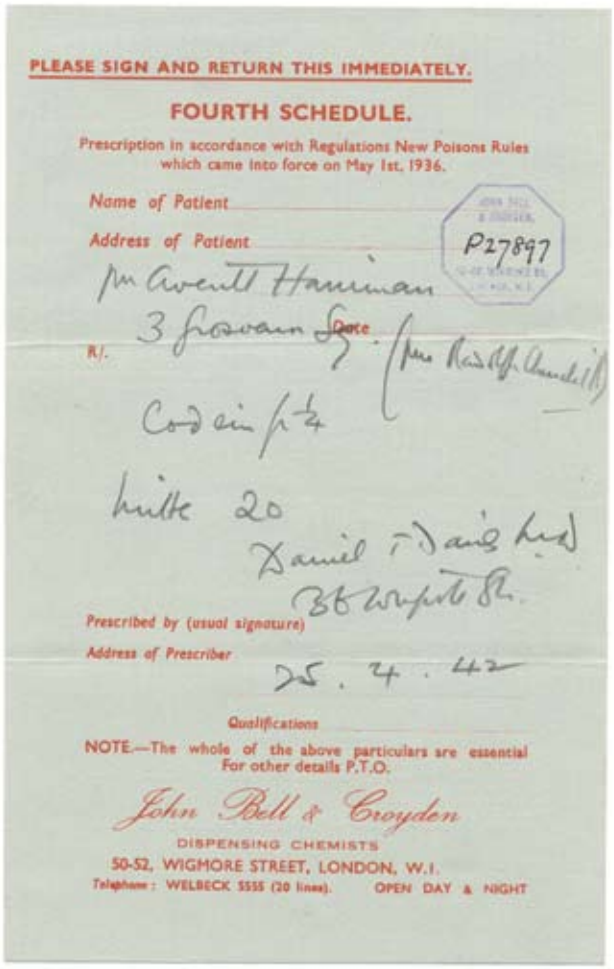
PLEASE SIGN AND RETURN THIS IMMEDIATELY.

FOURTH SCHEDULE.

Prescription in accordance with Regulations New Poisons Rules which came into force on May 1st, 1936.

Name of Patient

Address of Patient

P27897

Mr Averell Harriman

3 Grosvenor Sq.

W.1.

Codein ½

Mitte 20

Daniel Davis Ltd

Prescribed by (usual signature)

Address of Prescriber

25. 4. 42

Qualifications

NOTE—The whole of the above particulars are essential For other details P.T.O.

John Bell & Croyden

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Fig 1a. Davies followed the therapeutic regimen specified by Osler and Christian[2]. This prescription for codeine is the only prescription in the Harriman archives written during April and May 1942.

Fig 1b. A vomit-bowl had to be sent to Mrs Randolph Churchill by Special Messenger.

BOEING 307 STRATOLINER ACROSS THE ATLANTIC

A total of only ten Stratoliners were ever built, all by Boeing. Three were for Pan Am, five for TWA and a ninth for Howard Hughes. The tenth, the prototype, had crashed, but TWA put the Stratoliner into service on July 8, 1940: the first fully-pressurised aircraft to enter aviation service. With 33 passengers and five crew, a 12-foot wide cabin and overnight berths, it could fly 20,000 feet higher than all other airliners. A galley-kitchen was provided, staffed by two registered nurses[12].

The Stratoliner's deployment for the Marshall, Hopkins, Harriman trip to London and then Ulster had national and international implications for the United States. The US War Department of which Marshall was effectively professional head, wanted control of all the Stratoliners and many other civilian airliners and helicopters: this they achieved on May 7, 1942[14] by Franklin D Roosevelt's presidential memorandum to the Secretary of War and the Chief of Staff[15]. Undoubtedly the US military realised that the flight across the Atlantic at 14-20,000 feet would be manifest to the Axis and would impress US allies.

LONDON, APRIL 1-15, 1942

On the 3rd April 1942, FDR had written "Dear Winston, Best of luck. Make Harry (Hopkins) go to bed early, and let him obey Dr. Fulton, US Navy, whom I am sending with him as super-nurse with full authority"[16]. Hopkins was a long-term live-in White House advisor to the Roosevelts. In 1939 he had undergone surgery for cancer of the stomach[17].

From the 9th to the 16th of April, the US Delegation, having arrived on the 8th, had long formal meetings in Whitehall with Winston Churchill and the British Chiefs of Staff. General Hastings "Pug" Ismay took the minutes[18]. Having been ill and in pain after his arrival, Hopkins on April 15, 1942 addressed Westminster MP's. He suggested, records Harold Nicolson, "That we should be mad to get rid of Winston". "Somebody asks him whether America can advise us on the sort of propaganda we ought to conduct". Hopkins replied, "We are the worst propagandists in the world and you are the next worst. Why not consult someone better?"[19] Averell Harriman was present. Marshall had asked King George VI at luncheon earlier that day if, because of Hopkins' delicate health, while in Ulster they could stay in a private home[20].

Averell Harriman, meanwhile, had moved into 3 Grosvenor Square, London, with his daughter Kathleen. Aged twenty-four, she had been educated at Foxcroft, a fashionable girls' boarding school, and Bennington College, Vermont. Number 3 was adjacent to the American Embassy on the square's south side. The bottom two floors contained embassy offices. The Harrimans, father and daughter, were joined by Pamela Churchill, the wife of Randolph who had just left London to join the Special Air Service (SAS). Harriman, Pamela and Kathleen all had separate rooms and could order food from the American Embassy[21].

Six hours earlier than the US Army itinerary, for 17th April 1942, Marshall, Harriman and Hopkins flew to Limavady, near Londonderry, to inspect newly-deployed US troops[22]. They were met at the airport by their designated host, Major Douglas Beresford Ash DSO, DL, who had been a Royal Fusilier Captain at the Somme. He survived that blood-bath of Ulster manhood to become squire of the family estate, Ashbrook[21]. Pamela continued as Winston's sometime hostess. He appreciated his daughter-in-law, saying "Aren't I lucky to have such a pretty daughter-in-law?"[23]

Fig. 2. William Averell Harriman by Gardner Cox, oil on canvas, 1975, National Portrait Gallery, Smithsonian Institution.

The Washington Post of 19th April 1942 states, "Hurrying about in an American staff car guarded by machine-gunners and riflemen of the United States Scout Corps, General Marshall and the others were busy." Marshall visited the US Field Hospital of 250 beds outside Londonderry and spoke to "at least one patient in each ward - Americans and British alike"[24]. On their way to Ashbrook from Limavady on April 17th, near Ballykelly, a bus driver was shot dead. US Sergeant WV Clipsham fired the three shots. At his court-martial for manslaughter Clipsham was acquitted, partly on the grounds that the bus driver had deliberately delayed Marshall, Hopkins and Harriman by driving in the middle of the road[25].

A VISIT TO ASHBROOK

Marshall, Harriman and Hopkins arrived at Ashbrook, Ardmore, before lunch on 17th April 1942 to be received by their host and hostess, Major Douglas and Lady Helena Beresford Ash[26]. According to Harriman, Hopkins developed "An immediate aversion for the place, resenting not only the lack of creature comforts but also his host"[1]. Ashbrook was no White House and Fusilier Ash was less captivating than Hopkins' longtime host President Roosevelt. Marshall, on the other hand, was charming. John Beresford Ash, the son, has said "When I was being bathed, General Marshall thought I was a little girl." General Marshall atoned by letter and a "box of candy" for the little "tow-haired gentleman." John Beresford Ash ate the chocolates and the letter still exists[26].

Dinner on the 17th of April was not an entire success. Marshall ate a disproportionate share of the main course - thin slices of liverwurst, slivers of carrots on a few lettuce leaves and strips of bread. There was a small dessert. Hopkins and Harriman "suffered the pangs of hunger all that evening". Early the next morning Hopkins wrote a note to Marshall suggesting porridge, pork and beans for breakfast. Marshall from his bed wrote on a blank radiogram in pencil, "the Chief of Staff …feels compelled to observe that the hour hardly justifies Mr. Hopkins in disturbing the rest of so high a military official. The Chief of Staff suggests that instead of a crude meal of pork and beans, Mr Hopkins would be better off, with a small circle of liverwurst, the ragged edge of a piece of lettuce and the false hopes of more to come"[27]. On their leaving the next day, 18th April, the escorting convoy was held up while Marshall, Hopkins and Harriman inspected the rhododendrons, on which Harriman was an expert. "The war can wait," said Marshall[26]. Rhododendrons covered many of Harriman's 40,000 acres of Arden, New York. Arden also had thirty-odd bedrooms and its food was of "genuine mediocrity or worse"[28].

According to the proposed itinerary,[22] luncheon on the 18th of April was provided for the Modicum party at the headquarters of Major General Russell P Hartle, commander of both US Army Northern Ireland and V Corps. Since late March of 1942 his mess had served mainly American rations[29], Averell Harriman, Hopkins and Marshall flew from Limavady to the RAF station at West Freugh. Thence by ground to Portpatrick, from where Hopkins and Marshall flew by Pan Am Clipper Flying Boat to Washington, DC, arriving in time for dinner the next day, 19th April 1942[22,27]. From the Portpatrick Hotel Harriman arrived on the 19th April 1942 at 3 Grosvenor Square, thence to report to Winston S Churchill.

ILLNESS

On the 21st April, Averell Harriman became violently ill. High pyrexia was accompanied by delirium. He was cooled, fed and nursed by his daughter Kathleen and friend Pamela Churchill[21]. The patient and nurses were friendly with Lord Beaverbrook, who summoned Dr Daniel Thomas Davies - later knighted[30,31]. Davies, University of Wales and the Middlesex, FRCP 1932, had been Assistant Chemical Pathologist at the Middlesex[30]. Davies used a Widal test and microscopy to diagnose Paratyphoid B due to *Salmonella schottmülleri*[31-33]. Dr Davies' narcotic prescription for Averell was delivered to nurse Pamela on the 25th of April (Fig 1)[34]. Dr Davies then prescribed eighteen days worth of strict 'modified ulcer diet'[35] based on the Osler textbook as revised by HA Christian[36]. Next day, 26th April, at 2:00 pm, Eastern Daylight Time, Davies telephoned the Harriman family physician, Dr Alvan L Barach, of 929 Park Avenue, New York City. Davies reported on his consultation with Viscount Dawson of Penn about Averell Harriman[36]. The following day, the 27th, daughter Kathleen wired Lord Beaverbrook, now translocated from Miami to the Waldorf-Astoria in Manhattan, "Averell picked up a bug in North Ireland hob nobbing with the indigent aristocrats. Character obscure but has caused high fever…Explain to Marie (her step-mother). Pam joins with love"[37].

Two days later, Pam's mother-in-law wrote in her own hand from 10, Downing Street, Whitehall:

> April the 29th 1942
> My dear Averill [sic],

> Winston and I are grieved that you are ill.
>
> Please please be very patient and lie very still. Winston had paratyphoid. It is a horrid and tedious illness, but when at last it is over one truly is absolutely well again. In fact the very capable Austrian doctor who looked after Winston (who fell ill at Salzburg) told me that after paratyphoid one has a completely new inside to one's stomach like a new born baby. In fact one is rejuvenated!
>
> I'm afraid when the temperature goes down one becomes terribly hungry and of course one can't eat anything solid. Winston was very naughty and ate roast mutton too soon and had a relapse. We both send you our love and thoughts and wishes.
>
> Yours ever,
>
> Clementine S Churchill
>
> We all feel you have contracted this illness in the service of both our countries[38].

Dr. Davies brought in three American Red-Cross nurses, but Pamela Churchill stayed on as "the other nurse"- Averell Harriman's oft-repeated description of her war-time service to him[21] (Fig 2).

Daniel Davies, after his chemical pathology role at the Middlesex, had at the age of thirty been appointed as a physician to the Royal Free. His service as Physician to the Royal Household culminated in his Appointment as Physician to King George VI and later to the Queen. A more exacting patient of his was Beaverbrook. Davies, having made the diagnosis of paratyphoid B in Averell Harriman, would obviously realise the importance of suggesting a source of infection that did not betray inter-allied war planning or transportation secrets. Whether or not Ashbrook was the source, it was a convenient attribution. News of all this never reached the British 31st General Hospital or the advance body of the US 5th General Hospital at Musgrave Park,[39] who by late March 1942 were, like the other US forces in Ulster, supplied with food and water tested and approved by the US military[29].

THE NURSING OF HARRIMAN

The nurses wore rubber aprons. These were washed frequently with bichloride of mercury solution. After handwashing, the nurses soaked their hands thoroughly in 1:1,000 bichloride solution before and after each contact with Averell Harriman, and before they ate[40]. Pamela Churchill was vaccinated against paratyphoid B, and the other caregivers had already been vaccinated[40].

The Davies modified Christian-Osler regimen included food obtained by the US Army and Navy as well as "beef bouillon made nearby by the chef at Claridges"[41]. "Delirious with fever and chills he required constant care"[21] which Pamela and Kathleen provided.

ORIGIN OF PARATYPHOID

"The portal of entry of the paratyphoid bacillus is through the intestinal lymphatics and during the incubation period they multiply in the liver, spleen and mesenteric lymph glands"[42]. In Sir William Savage's 40 different series reported in 1942[43], water was rarely a vehicle of infection: four-fifths of the cases were due to infected food. Half of the time the infected food was cream or cream cakes.

Fig 3. Averell Harriman (right) and Harvard University President Nathan M Pusey escorting Mrs. Jacqueline Kennedy to dinner at the meeting inaugurating the Institute of Politics at the John F Kennedy School of Government, Harvard University, 17th October 1966. Associated Press wirephoto from the *New York World Telegram* and *Sun* Newspaper Photograph Collection, in the Library of Congress.

Bedell Smith writes that Averell Harriman "while on a trip to Northern Ireland with Harry Hopkins and General Marshall… contracted paratyphoid from drinking contaminated water"[21]. No one else at Ashbrook reported contracting paratyphoid in 1942. When or where, then, did Harriman contract the disease? In the previous twenty-three days he had been in the United States, on the Stratoliner with its two sojourns in Gander, Newfoundland, London and then Ashbrook. There were no reported cases in Washington, DC[44], or London[45] at that time, so that makes cream and cakes at Gander or cheese from the galley of the Stratoliner suspect.

Gander would, in 1942, get cheese from Quebec. The Province of Quebec was experiencing enteric fever outbreaks traced eventually to its cheeses[46]. Harriman was present at Hopkins' talk to the Westminster MPs, but no one else was recorded as having been sickened at either the House of Commons, the US Embassy or the Dorchester Hotel. *The New York Times* reported that Harriman had had influenza[47], most likely as instructed by the US Embassy. Paratyphoid B was extremely uncommon in Ulster in 1942, and almost non-existent in March and April 1942 (Table I). The Medical

Department, US Army, reported for 1942 only one admission to hospital for paratyphoid in its entire European theatre of operations[48] and a total of forty-one admissions to hospital for paratyphoid world-wide for that year[49]. Newfoundland was administratively a part of Great Britain from 1934 to 1949 and we are unable to locate data on its incidence of enteric fever in 1942. The source of Harriman's enteric fever will probably never be conclusively ascertained, but it is extremely unlikely that it was Ashbrook water. The incubation period was too short.

TYPHOID VACCINATION POLICY

All US Army and AAF (US Airforce) personnel were vaccinated with typhoid, paratyphoid A and B bacilli heated to a temperature of 53-55ºC. The US vaccine contained 1,000 million typhoid bacilli and 250 million *Salmonella paratyphi* (a) and the same number of *Salmonella schottmülleri* in each cc. Doses were 0.5cc followed by 1cc administered subcutaneously approximately a week and then a fortnight later. Complication rates were about twenty percent[50]. Since Hopkins was under naval medical supervision, he had presumably been similarly inoculated against paratyphoid. The efficacy of enteric fever vaccination is complex and still presents a challenge to world health policy[51].

THE HARRIMANS

Patient Harriman's father, Edward Henry, was described as "a malefactor of great wealth" and an "enemy of the republic" by President Theodore Roosevelt. Edward H Harriman's wife Mary was a New York banker's daughter of impeccable probity. Their first-born son Harry died of diphtheria. William Averell, the next son, was born in November 1891. Averell's upbringing was arduous: work, then strenuous sport, then more work[52]. Groton, a spartan but leading private boarding school, was followed by Yale, where Harriman was elected to the semi-secret, but prestigious club, Skull and Bones[53]. In 1909 Edward H Harriman died, leaving a fortune equal to £500,000,000 in today's money and instructions to sons Averell and Roland to increase that capital. Steamships, Soviet manganese mines and an airline were not lucrative but Averell became chairman of Union Pacific and ordered complete modernization of its railroad system, which was most successful; he fussed like "a professional housekeeper"[54].

Fig 4. General Secretary of the Communist Party of the Soviet Union Yuri Andropov (right) greets Mr and Mrs Harriman on the 2nd June 1983 in the Kremlin. Photograph by Vladimir Musaelyan for Tass, copyright 1983, Sovfoto. From print in the W Averell Harriman Papers in the US Library of Congress, container 895.

Harriman scored the final winning goal for the United States in the 1928 Pan-American Championship Polo Series. The United States won two out of three games against Argentina before a combined final series attendance of 85,000 spectators[55]. His first wife Kitty contracted tuberculosis. They were divorced in 1929 after Harriman had become attracted to Marie Norton Whitney, the wife of Cornelius Vanderbilt "Sonny" Whitney. Averell and Marie were to remain married from 1929 until Marie's death in 1970 (Fig 3).

Averell Harriman married 'the other nurse' the Hon. Pamela Digby Churchill Hayward, on Monday 27th September 1971 at Our Lady's Chapel at St. Thomas More Roman Catholic Church on East 89th Street, New York City. Marie Harriman had died in September 1970 and Leland Hayward on 18th March 1971. Hayward's producers' rights to *South Pacific, Mister Roberts* and *Sound of*

TABLE I:

The Reported Incidence of Enteric Fever (Paratyphoid and Typhoid) in different areas of Averell Harriman's travels, Spring 1942

REPORTED CASES

Week ending	London District, Typhoid	London District, Paratyphoid	Ulster, Typhoid	Ulster, Paratyphoid	Washington DC*	New York City*
28/02/42	2	0	2†	--	0	2
07/03/42	1	1	0	NR‡	1	3
14/03/42	3	0	3	0	0	3
21/03/42	0	1	1	NR	0	1
28/03/42	0	0	2	NR	0	2
04/04/42	1	0	0	NR	1	1
11/04/42	0	0	2	NR	0	6
18/04/42	1	1	0	NR	0	4
25/04/42	0	0	0	0	0	4
02/05/42	3	1	0	0	1	5
09/05/42	3	0	1	0	0	2
16/05/42	2	0	1	NR	0	2
23/05/42	0	NR	1	NR	0	2
30/05/42	1	0	0	NR	0	3

*Reported incident cases typhoid and paratyphoid combined
†Includes paratyphoid-a and -b
‡NR = No return available for that period

Music continued. Ex-Governor (of New York State) Averell appeared happily married until his death on 27th July 1986[56] (Fig 4).

Aged sixty-six, Pamela Harriman was in late 1986 worth approximately $115 million[57]. Pam-PAC (Pamela's Political Action Committee) was a leading funder of Democratic candidates. On the 18th October 1991, Pamela donated $1,000 to Bill Clinton. In April 1992 she invited him to dinner at her N Street Washington, DC house. By July, she was fully involved in his campaign as co-chairperson. Pamela acknowledged that Hillary Rodham Clinton "has analytical capability and intellectual self-confidence - Hillary is not irritated or put off by stylistic differences"[58]. Pamela gave a cocktail reception and dinner for the Clintons on the 12th September 1992 at her Willow Oaks, Virginia, farm, which raised over two million dollars[59].

On the 4th May 1993, Pamela undertook her Senate Confirmation Hearings to become the 64th U.S. Ambassador to France[60]. All went smoothly, except Senator Helms exhibited some confusion. Pamela's membership in the Monet society, he opined, was support for Jean Monnet.

"Senator, it is the painter. His home is in France. It is called Giverny". "Are you prepared to supplement with personal funds?" Helms asked. "Yes, Senator, whatever is necessary." "It will be necessary," said Helms[61]. Ambassador Harriman complied but only up to a point (Fig 5). All did not go well financially. A senior legal adviser and former US Secretary of Defense, Clark Clifford, was disbarred because of his involvement in the Bank of Credit and Commerce International (BCCI) financial scandal, and her chief financial officer, inherited from Averell, was fired for investing millions of Harriman dollars unwisely and without due authorization[62].

The Trustees of Averell Harriman's daughters and grandchildren filed suit against Pamela on 15th September 1994. In a lengthy 100-plus page complaint, they accused Pamela of being a "faithless fiduciary". This Manhattan Federal Court action was supplemented by requesting the commissioner of accounts in Loudoun County Court, Virginia to remove Pamela as executor of Averell's estates and as trustee of three trusts established in his will[62]. In June 1995, Averell's offspring filed another suit against Pamela for rejecting a settlement agreed by attorneys. Pamela no longer spoke to Kathleen. In October 1995, Pamela sued her former advisers, including Clark Clifford and Brown, Brothers Harriman & Co. Just after Christmas 1995, the Harriman heirs and Pamela shook hands and discussed the Republican-induced US Federal Government shutdown. They then settled their legal suits that day – 29th December 1995. On the 6th January 1996, Mary Harriman Fisk dropped dead of a heart attack. Pamela, now back in Paris, sent Kathleen a gracious note of condolence on the death of her sister. The next day, Sunday 7th January 1996, a member of Ambassador Harriman's staff phoned the Hedley-Whytes' Paris hotel room to say that the Tuesday 9th of January Embassy dinner party to which they had been invited in connection with trade and standards negotiations had been cancelled due to the Congressional action. John Hedley-Whyte had previously chaired a meeting on medical equipment standardisation and the US acceptance of CE (Conformité Européene) markings[63] in the US Embassy on the Champs Elysées. Ambassador Harriman was, like her late husband Averell, an expediter, for the President of the US. William Jefferson Clinton had a few months earlier, in 1995, signed a treaty with European Union President Jacques Santer[64].

Ambassador Harriman, the 'other nurse', died on the 5th February 1997, following a stroke suffered the previous day

Fig 5. "Portrait, oil on canvas, 1996, of the 64th US Ambassador to France, following Benjamin Franklin, 1996, by Anthony Palliser (1949-). The Honorable Pamela Digby Churchill Hayward Harriman was confirmed by the Senate in May 1993 and died in office on February 5, 1997. This photographic reproduction was provided courtesy of the Embassy of the United States of America in Paris, solely for use in association with this Medical History."

while at the Ritz Hotel, Place Vendôme, where she had been swimming[65]. She was posthumously awarded France's Grand Cross of the Legion of Honour by President Jacques Chirac[66]. President Clinton delivered the eulogy during her memorial service at Washington's National Cathedral, before her burial at the Harriman family estate in Arden, New York[67].

POSTSCRIPT

If anyone has evidence that Ashbrook was or was not the source of Harriman's serious paratyphoid infection they should clarify the unproven, indeed unlikely aspersion that currently exists. On the positive side, all present at Ashbrook for the regally requested house-party agreed that the wine stored in a "large, brass-bound mahogany bucket"[27] was excellent.

ACKNOWLEDGEMENT

This Medical History is dedicated to the memory of General Lord Ismay, KG, GCB, CH, DSO. (1887-1965), who in 1958-1959 inspired a modicum of history into a Medical House Officer at St. Bartholomew's Hospital, London (JH-W). Pug was a wonderful patient and raconteur.

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Case Report

A classic diagnosis with a new 'spin'

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Key Words: Pericarditis, Constrictive, Magnetic Resonance Imaging

SUMMARY

We describe a case of pericardial constriction following viral pericarditis and illustrate the use of cardiac magnetic resonance imaging in the diagnostic process. The advantages of cardiac magnetic resonance in the investigation of pericardial disease are briefly explained.

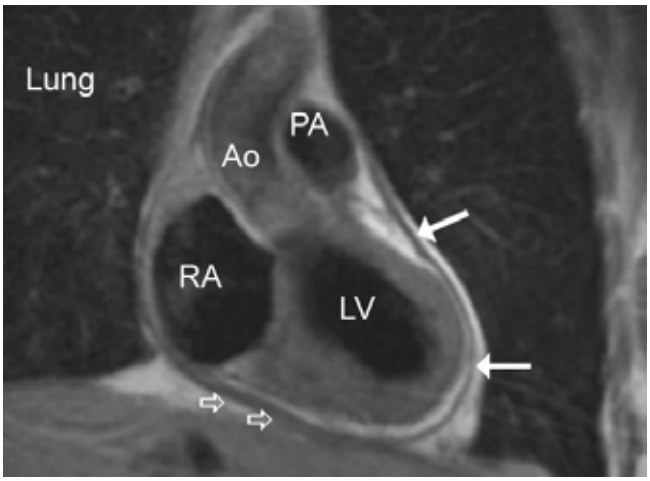

Fig 1. Coronal MRI through the left ventricular outflow tract showing normal (solid arrows) and thickened pericardium (open arrow), visible as the black layer in between bright layers of pericardial and epicardial fat.

AO=Aorta; LV=Left ventricle; PA=Pulmonary Artery; RA=Right Atrium

INTRODUCTION

Constrictive pericarditis and restrictive cardiomyopathy are characterized by similar clinical features, and similar findings at echocardiography and cardiac catheterisation. It is important to discriminate between these two entities as the former can be cured by the procedure of pericardiectomy, whereas those patients with restrictive cardiomyopathy do not benefit from surgery. The emerging technique of cardiac magnetic resonance imaging (CMR), which compensates for cardiac motion by gating the acquisition to the cardiac cycle, may prove particularly useful in differentiating these conditions.

CASE REPORT

A 45-year-old female presented to her general practitioner (GP) with a two month history of increasing dyspnoea. The GP noted bilateral pleural effusions and referred the patient to respiratory outpatients. Five months previously the patient had been admitted with chest pain. Troponin levels were normal, and she had been discharged with the diagnosis of atypical chest pain.

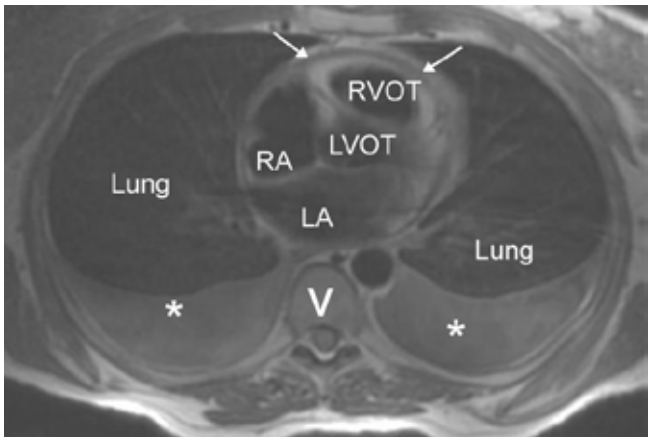

Fig 2. Axial MRI at the level of the right ventricular outflow tract demonstrating large bilateral pleural effusions (*) and thickened pericardium (arrows).

LA=Left Atrium; LVOT=Left ventricular outflow tract; RA=Right Atrium; RVOT=Right ventricular outflow tract; V=Vertebral Body;

After review at outpatients a CT chest was performed that showed no abnormality other than the effusions. Investigations for underlying infective, autoimmune or neoplastic causes were negative. Pleural aspiration indicated that the fluid was a transudate, and when the effusions recurred, the patient was referred to cardiology for further investigation.

At cardiology outpatients, physical examination revealed an elevated jugular venous pressure, mild peripheral oedema and a left sided pleural effusion. Pulsus paradoxus, an exaggeration of the normal decrease in systolic blood pressure during inspiration, was not present. However Kussmaul's sign[1,2],

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an increase in jugular venous pressure during inspiration (it should normally fall with negative intrathoracic pressure) was demonstrated. The electrocardiogram showed sinus rhythm with small QRS complexes, and constrictive pericarditis was suspected clinically. An echocardiogram revealed normal left and right ventricular sizes, with normal ventricular systolic function and no significant valvular abnormality.

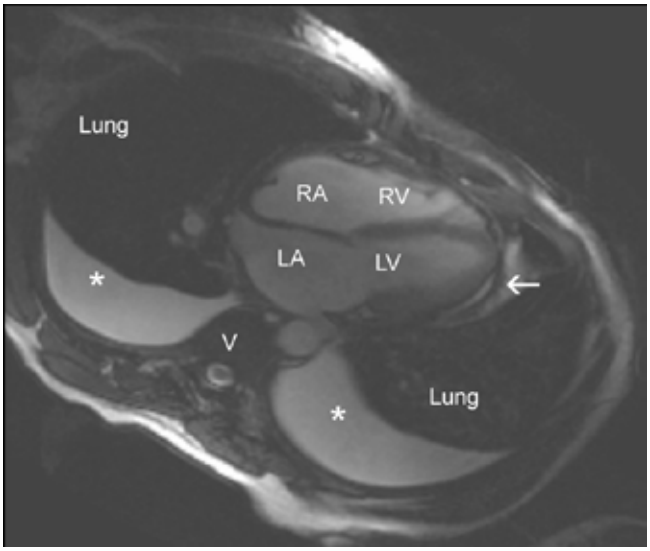

Fig 3. The four chamber view of the heart below is a still frame taken from cine sequence. The moving images show abnormal septal motion ('septal bounce') which is more commonly demonstrated by echo in patients with pericardial constriction. In addition there are bilateral pleural effusions and evidence of pericardial thickening (arrow).

*LA= Left Atrium; LV= Left Ventricle; RA=Right Atrium; RV= Right Ventricle; V=Vertebral Body; *=Pleural Effusion*

A cardiac MRI scan (CMR) was performed using a 1.5 Tesla Signa scanner (General Electric Medical Systems, Amersham, UK) and images are shown in Figures 1-3. The thickened pericardial layer is demonstrated as a black line between the brighter fat layers[3]. Note that the width of the pericardium is variable, being thicker in some parts than others. Additional MRI sequences produced moving cine images, which showed abnormal septal motion, with the characteristic 'septal bounce', resulting from inter-dependence of ventricular pressures.

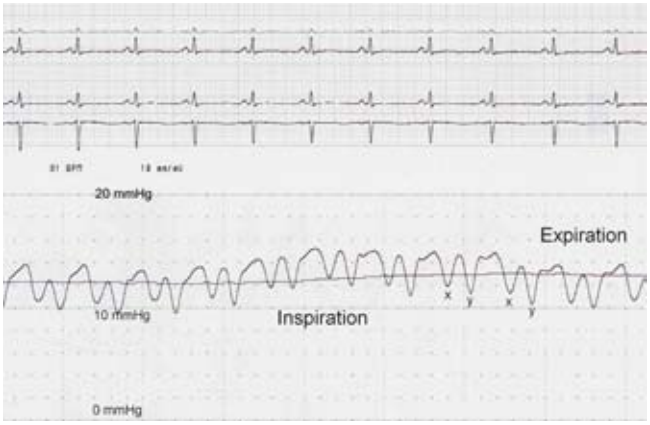

Fig 4. Right atrial pressure tracing. Right atrial pressure is elevated (mean 12 mmHg) and a prominent y descent is visible. The mean right atrial pressure rises with inspiration, the physiological basis for Kussmaul's sign.

The patient was taken to the catheter laboratory for further investigation. Coronary angiography demonstrated normal coronary arteries. Pressure wave tracings from cardiac catheterisation are shown in Figures 4 and 5. Right atrial pressure is elevated, and then rises further with inspiration (fig.4). The 'y' descent is steep and prominent, consistent with early rapid filling of the right ventricle. Figure 5 shows simultaneous pressure tracings from the left and right ventricles with classic diastolic 'dip and plateau' configuration (the square root sign). This results from rapid early diastolic filling of the ventricles (dip), which is then halted by pericardial restraint (plateau). This tracing also demonstrates equalisation of right and left ventricular pressures during diastole. The patient was referred to the cardiac surgeons and both constriction and a thickened pericardium were confirmed at the time of pericardiectomy. The patient remains well following her definitive cardiac surgical procedure.

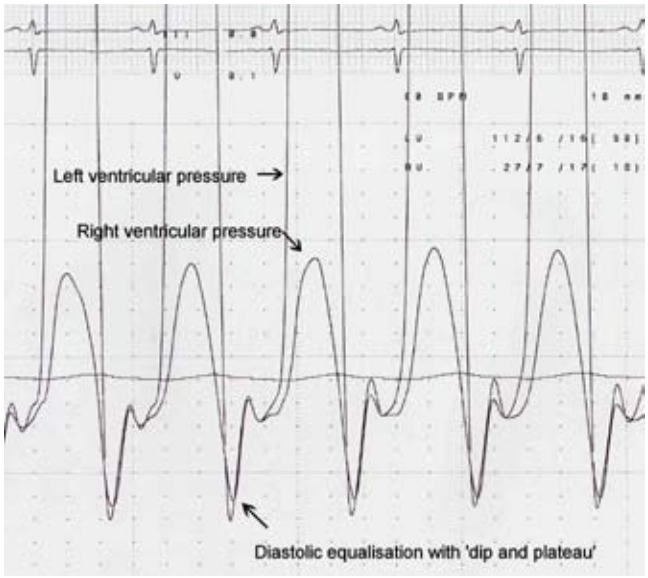

Fig 5. Simultaneous left and right ventricular pressure recordings. The classical diastolic equalisation with the dip and plateau pattern (square root sign) is seen in both pressures tracings.

DISCUSSION

Trans-thoracic echocardiography (TTE) is usually the initial investigation when pericardial disease is suspected. It is widely available, portable, and provides both functional and anatomical information. However, pericardial tissue has a low signal to noise ratio with ultrasound and cannot be easily identified by TTE. Additionally, the small field of view during both transthoracic and transoesophageal echocardiography means that some sections of the pericardium may not be visualised, and the full extent of the pericardium cannot be seen in any one imaging plane. Therefore the echocardiographic diagnosis of pericardial disease is usually made from functional assessment by Doppler criteria, and many of these features overlap with those of restrictive cardiomyopathy.

In recent years cardiac MRI has become a routine imaging

procedure to demonstrate anatomy, function, and even myocardial perfusion and coronary arteries. Applying standard MRI protocols to the heart would result in uninterpretable images due to motion artefacts from cardiac contraction. The development of cardiac gating, which permits the acquired MRI data to be synchronized with the electrical activity of the heart, allows cardiac motion to be effectively 'frozen' and high quality images to be obtained. Although pacemakers, claustrophobia, and intracerebral aneurysm clips remain contraindications to MRI, coronary artery stents and many prosthetic heart valves can be imaged safely.

A variety of MRI sequences may be applied to cardiac imaging. The scanner may be used to produce still, anatomic, images, in which the apparent intensity of tissues may be manipulated by the type of sequence used so that, for example, signal from fat can be suppressed. This is useful in the diagnosis of arrhythmogenic right ventricular dysplasia, where fatty tissue infiltrates the myocardium, and in the diagnosis of cardiac tumours such as lipomas. In fact the principle of different tissues exhibiting particular intensities with certain types of pulse sequences can used to non-invasively characterise cardiac tissue as viable or irreversibly scarred after myocardial infarction. In addition, MRI can produce moving, 'cine', images allowing assessment of wall motion (analogous to B-mode echocardiography) and allow quantification of flowing blood (analogous to Doppler echocardiography).

MRI provides excellent delineation of the pericardium without the use of contrast media or ionising radiation. Unlike echocardiography, the large field of view has the potential to demonstrate associated abnormalities in the chest or mediastinum such as lymphadenopathy or local invasion, although the absence of such pathology by MRI is not definitive.

The pericardium is relatively easy to distinguish. It has a fibrous nature and low water content, which causes it to appear as a band of low signal intensity between the relatively bright, high signal, epi- and pericardial fat layers. Normal pericardial thickness on these images is less than 2mm.

A pericardial thickness of greater than 4mm indicates abnormal thickening, and if accompanied by signs or symptoms of heart failure, is strongly suggestive of constriction. CMR is very useful in differentiating constrictive pericarditis from restrictive cardiomyopathy in symptomatic patients, a distinction which is often difficult to obtain by other methods. The reported sensitivity, specificity, and accuracy for the diagnosis of constrictive pericarditis by CMR is 88%, 100%, and 93% respectively[4].

Pericardial thickening alone is not diagnostic of constriction, and other signs such as dilated inferior vena cava, or dilated atria, should be sought. Cine CMR imaging provides functional data such as the abnormal motion of the interventricular septum, and phase contrast CMR can, like Doppler TTE, demonstrate the abnormal ventricular filling patterns. While TTE will remain the primary cardiac imaging modality in the immediate future, CMR provides a powerful tool in cases of diagnostic uncertainty, and can provide a comprehensive non-invasive evaluation of pericardial disease.

The authors have no conflict of interest.

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Letters

GIANT CELL TUMOUR OF THE TENDON SHEATH - AN UNUSUAL CAUSE FOR LOCKING OF THE KNEE JOINT.

Editor,

Locking of the knee is a common presentation at orthopaedic outpatient departments. These patients normally require magnetic resonance imaging (MRI) where there is a clinical suspicion of a soft tissue lesion. The most common lesions are meniscal tears and typically present with associated pain. We present an unusual case of a giant cell tumour arising from the tendon sheath causing painless locking of the knee joint.

Case report: A 39-year-old male presented with a twelve-month history of painless locking in his left knee. He worked as a roofer and found his symptoms worse when climbing ladders. He was referred by his general practitioner who suspected a meniscal tear. There was no history of any trauma to the knee. Clinical examination revealed no swelling, effusion or joint line tenderness around the knee, and a full range of movement. A mass arising from the medial aspect of his patella, which was mobile within the knee joint, was palpable. The lesion was firm but not bony in nature, and was not visible on X-ray. The mass was presumed to be a soft tissue lesion and, because of the hazards associated with his occupation, the patient proceeded directly to arthroscopy rather than MRI. At arthroscopy a large intra-articular lesion was identified originating posterior to the medial patella. The size of the lesion prohibited removal during arthroscopy, and was therefore excised in its entirety via a medial parapatellar incision. Histology showed the specimen to be a giant cell tumour of the tendon sheath measuring 40 x 35 x 15mm (Fig 1). Postoperative recovery was uneventful and at two-month review the patients symptoms had resolved.

Discussion: Giant cell tumours of the tendon sheath (GCTTS) are benign soft tissue masses, typically found on the flexor surface of the hand and wrist[1]. They are more common in males with an average age of presentation of 30-50 years[2]. These tumours are classified in two types; the common localized type and the rare diffuse type. The more localised form accounts for 88% of cases effecting the hands and feet arising from the synovium of the tendon sheath[2]. It is unusual for giant cell tumours to involve larger joints and to be intra-articular. In large joints diagnosis is difficult because the signs and symptoms can be non-specific[3]. The rare diffuse form, occurring in joints such as the knee and ankle, is considered to be an extra-articular extension of a primary intra-articular pigmented villonodular synovitis (PVNS). PVNS and GCTTS share similar histological characteristics and are regarded as different manifestations of synovial proliferations[2].

As in this case, plain X-rays are often of limited benefit. MRI is an important diagnostic modality. T1 and T2 weighted images show a low intensity homogenous signal for a GCTTS due to the presence of dense fibrous tissue[3].

Ideally GCTTS should be completely excised, but may have to be incomplete due to the nature of spread into the surrounding synovium[4]. Zhang *et al.* reviewed 12 cases of intra-articular GCTTS within the knee, and reported that nine cases were misdiagnosed with meniscal injuries or chronic synovitis. Only three cases had the diagnosis confirmed by MRI prior to surgery[5]. They found no incidence of recurrence in any of the cases. Further studies have looked at recurrence and quote figures around 10-20% rising to 44% if excision was inadequate[2].

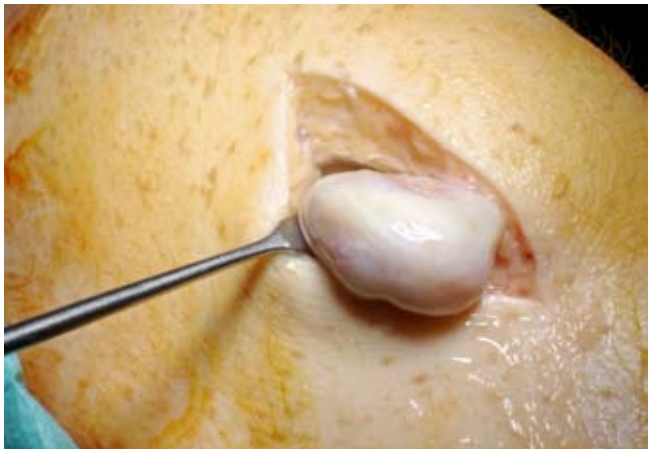

Fig 1. Giant cell tumour of the tendon sheath measuring 40 x 35 x 15mm being excised through a medial parapatellar incision.

Conclusion: This case highlights that GCTTS, although rare, can be an unusual cause for locking of the knee joint. Its presentation may mimic a meniscal tear, but a history of no previous trauma to the knee and painless locking are important discriminating symptoms.

Conflicts of Interest: None declared.

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CLIMATE CHANGE AND ITS IMPACT ON HEALTH

Editor,

On the 29th January 2008, a landmark conference entitled 'Climate Change and its Impact on Health' took place at the Royal College of Physicians in London. Although the

audience was from a medical background, most of the speakers were not – the former Government Chief Scientist, a City financier, a climatologist, Professors of Palaeontology and Peace Studies, and the former Director General of the Confederation of British Industry all talked about different aspects and they were joined by the Editors of the Lancet and British Medical Journal, and a Professor of Public Health.

There were some very clear messages. None of the speakers had any doubt that climate change – a rise in average temperature and a rise in atmospheric carbon dioxide levels – first was real, second was due to the activities of humans and third was likely to have serious consequences for human health because of an increase in infectious diseases, heat-related diseases and malnutrition. There was also no doubt that the only solution in town was to reduce carbon emissions and that this needed to be done by concerted government and inter-governmental action. There was also agreement that currently-available technologies were able to do this. Those cited were fuel-efficient vehicles, reduced vehicle use, more nuclear energy, substitution of coal by gas for electricity generation, carbon capture and storage and more use of wind, sun, hydrogen and biomass to generate power. Used together these could stop any rise in carbon emission. The cost arguments were set out in the Stern Report published in 2006[1]. The cost of failing to deal with climate change would be at least 20% of global gross domestic product (GDP) whereas it would cost only 1% of GDP to act now on global warming.

There was also general agreement that the medical profession could act both personally and politically. Personal contributions included using energy-saving light bulbs, reducing travel by car, using public transport and cycling or walking to work. Politically the medical profession should be at the forefront of lobbying for effective government action on climate change and to this end the Climate and Health Council has been established (www.climateandhealth.org). The obvious analogy here is the leading role of the profession against cigarette smoking.

The closing address of the conference was given by Dr James Hanson, Director of the NASA Goddard Institute of Space Studies who suggested a moratorium on further coal-fired power stations and urged individuals to influence those who are elected to Governments. This address was delivered by videolink so Dr Hanson did not have to increase his carbon footprint by flying to London. (The possibility of reducing the NHS carbon footprint by practising more medicine this way was barely mentioned at the conference.)

Although this conference may have scared many in attendance about the future of our planet it also conveyed a message of optimism. This optimism though, was tempered by the proviso that corrective action needs to be taken now rather than later, and that to do that we all need to emerge from our states of denial.

No conflict of interest declared

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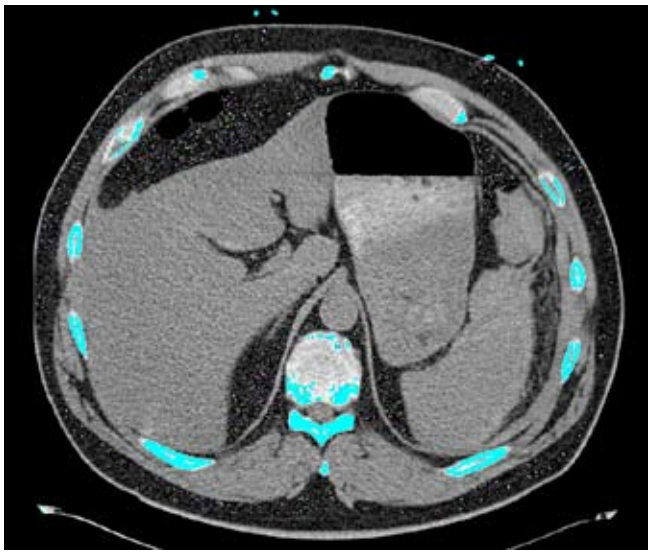
IATROGENIC SPLENIC INJURY IN PERCUTANEOUS PROCEDURES

The potential for splenic injury during left sided thoracentesis or percutaneous renal biopsy is well known, its occurrence has been rarely reported[1]. In a series of 244 incidental splenectomies, only one was secondary to left thoracentesis[2]. Each year about 600 new cases of extrinsic allergic alveolitis are diagnosed in the UK[3]. Lung biopsy is an important diagnostic tool for diffuse lung disease. Others include bronchoalveolar lavage and high resolution computed tomography[3]. We present a case of delayed splenic rupture following percutaneous lung biopsy, which required urgent laparotomy.

Case Report: A 48-year-old gentleman presented with left upper quadrant pain and shortness of breath for eight hours prior to admission. There was no history of trauma, haematological or storage diseases. The patient underwent a left lung biopsy two months earlier which had led to the diagnosis of extrinsic allergic alveolitis.

On examination, he was comfortable and haemodynamically stable. Respiratory and cardiovascular examinations were unremarkable, abdomen was soft and non-tender. Initial haematological investigations, cardiac enzymes and electrocardiogram were normal. A provisional diagnosis of inferior wall myocardial infarction was made.

He became progressively hypotensive and developed abdominal distension with left upper quadrant tenderness. Two scars were noted, one over 6th and the other over 8th intercostal spaces.



Urgent computed tomography of abdomen and pelvis revealed complex fluid collection around the spleen and free intraperitoneal fluid (fig 1). At emergency laparotomy, 2.5 litres of intraperitoneal blood was removed. A large clot was identified under left dome of diaphragm. A small-healed wound over the lateral surface of the spleen was identified. No

active bleeding was evident and the findings were consistent with those of a ruptured subcapsular splenic haematoma. Postoperative recovery was uneventful and the patient was discharged on day seven.

Discussion: This case highlights the delay with which an iatrogenic splenic injury can present. The most important indicator in this case, which could relate to splenic injury, was a scar near the splenic region following lung biopsy. Clinical problems after splenic rupture have been classified into three groups characterized by the delay in presentation and type of symptoms[4]. Group one: acute ruptured spleen, Group two: delayed ruptured spleen, and Group three: occult ruptured spleen. Our case was group two, with delayed presentation two months after injury.

Computed tomography is the gold standard for investigating splenic injuries. Grading scales based on computed tomography findings can predict the likelihood of successful non-operative management, which is often possible if the splenic hilum is intact (even when capsular disruption is present)[5] .However, due to haemodynamic instability in this case, percutaneous drainage was not performed. As new cases of diffuse lung disease are being investigated, physicians should be increasingly aware of the possibility of splenic injury after lung biopsy. Splenic injury should be considered if haemodynamic instability occurs even after two months of lung biopsy.

No conflict of interest declared.

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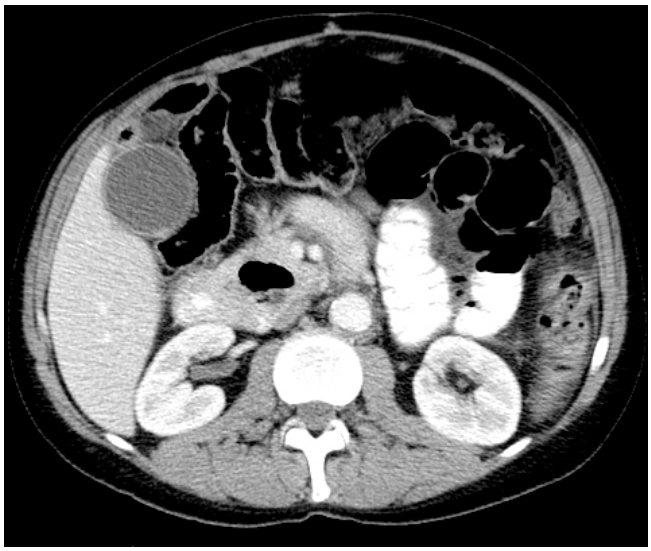
CHYLOUS PERITONITIS WITH SMALL BOWEL OBSTRUCTION

Chylous ascites may present with a number of abdominal complications[1,2]. We present a case of chylous peritonitis presenting as small bowel obstruction.

Case Report: A 44 year old male presented to the accident and emergency unit with crampy abdominal pain of a two days duration, worse over the previous day. He had a background history of a partial oesophago-gastric resection for Boerhaave's syndrome some months earlier. On examination there was marked abdominal distension with epigastric tenderness. Plain abdominal X-ray showed a large fluid filled loop suggestive of a volvulus. CT scan (fig 1) confirmed a volvulus of the small bowel with a twist of mesentry root and likely venous obstruction.



At laparotomy there was a volvulus around a band from the apex of the anti-mesenteric border of the small bowel to the fourth part of the duodenum. The entire small bowel was dusky with venous engorgement but viable. There was striking engorgement of the lymphatics in the wall of the small bowel and 400ml of milky chylous fluid free in the peritoneal cavity. The patient made an uneventful recovery after surgery.

TABLE I

Causes of Chylous fluid
1. Abdominal surgery
2. Blunt abdominal trauma
3. Malignant neoplasm's - Hepatoma, small bowel lymphoma, Small bowel angiosarcoma, and retroperitoneal lymphoma
4. Spontaneous bacterial peritonitis
5. Cirrhosis - Up to 0.5% of patients with ascites from cirrhosis may have chylous ascites.
6. Pelvic irradiation
7. Peritoneal dialysis
8. Abdominal tuberculosis
9. Carcinoid syndrome
10. Congenital defects of lacteal formation

Discussion: Chylous peritonitis is the extravasation of milky chyle into the peritoneal cavity. This can occur de novo as a result of trauma or obstruction of the lymphatic system. An existing clear ascitic fluid can turn chylous as a secondary event. A true chylous effusion is defined as the presence of

ascitic fluid with high fat (triglyceride) content, usually higher than 110 mg/dL.

Chylous fluid in the peritoneal cavity is a rare clinical condition that occurs as a result of disruption of the abdominal lymphatics. Multiple causes have been described (table I). Congenital chylous ascites is the commonest cause of chyloperitoneum in young children. Other causes in children include idiopathic or obstructive lesions caused by malrotation, intussusception, incarcerated hernia, lymphangioma, blunt trauma, liver disease, and tuberculosis. In children, malrotation and volvulus contribute to chylous ascites[3]. Volvulus of the midgut may result in several manifestations. Venous and lymphatic obstructions occur first because of lower intravascular pressures. Vascular congestion leads to bowel oedema and possible oozing of blood, causing melaena. Lymphatic congestion causes the formation of a mesenteric cyst and chylous ascites.

Milky ascites is subdivided into three groups: True chylous ascites - Fluid with high triglyceride content, Chyliform ascites - Fluid with a lecithin-globulin complex due to fatty degeneration of cells, and Pseudochylous ascites - Fluid that is milky in appearance due to the presence of pus. Dietary chylomicrons are absorbed in the small intestines and gradually pass along larger omental lymphatics to the cisterna chyli located anterior to the second lumbar vertebra. The cisterna is joined by the descending thoracic, right and left lumbar, and liver lymphatic trunks, and, collectively, these form the thoracic duct, which passes through the aortic hiatus and courses through the right posterior mediastinum and eventually enters the venous system. The thoracic duct carries lymphatic drainage from the entire body, except for the right side of the head and neck, right arm, and right side of thorax. Chylous effusions develop when these channels are injured or obstructed. Abdominal distension is the most common symptom, and rarely, it may present as acute peritonitis.

As chylous peritonitis is a manifestation rather than a disease, the prognosis depends on the treatment of the underlying disease or cause. Few cases presenting as chylous peritonitis are reported in literature

Three cases presenting as acute appendicitis have been reported[4,5].

The authors have no conflict of interest.

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MESOTHELIOMA – "NOT JUST IN THE CHEST"

Editor,

Malignant deciduoid mesothelioma (MDM) is a rare phenotype of epithelioid mesothelioma, which most commonly occurs in the peritoneal cavity of young females. MDM remains a challenge even to the most astute diagnostician with the differential diagnosis being benign pseudotumoral deciduosis. It carries a dismal prognosis.

Case Report: A previously healthy 31-year-old woman presented with a short history of increasing abdominal girth and shortness of breath without weight loss. She smoked 15 cigarettes per day and had no risk factors for chronic liver disease or prior history of asbestos exposure. There was no family history of neurofibromatosis. Clinical examination revealed ascites in the absence of signs of chronic liver disease, café au lait spots or lymphadenopathy. Diagnostic paracentesis revealed no evidence of bacterial or mycobacterial infection. The serum ascites albumin gradient was 1.1g/dL. Cytology was consistent with benign reactive mesothelial cells although no leucocyte reaction was noted.

Haematological, tumour markers, inflammatory markers and biochemical parameters were in the normal range. A chest radiograph showed no signs of pericarditis, pleural plaques or effusions. Ultrasonographical and CT scanning demonstrated ascites with normal hepatic echotexture and anterograde flow in the portal vein. No thoracic lesions were seen. A diagnostic laparoscopy drained 9L of ascites and numerous small nodules were observed concentrated around the small bowel.

Histological examination of these nodules with conventional stains was consistent with a mesothelial process although it was impossible to differentiate between a benign reactive or neoplastic aetiology. Typical features of epitheliod mesothelioma were not observed. Further expert opinions were sought and immunostaining is shown in Figure 1.

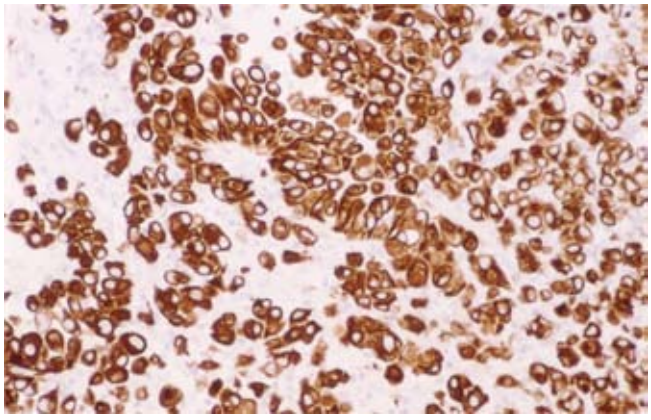

Fig 1. Immunostaining revealed strong positivity for calretinin and cytokeratin which are considered to be sensitive and relatively specific markers for MDM.

These findings were consistent with the diagnosis of MDM. Combination chemotherapy with pemetrexed and cisplatin was initiated but she required multiple hospital admissions

for therapeutic abdominal paracentesis. Our patient died 14 months after diagnosis.

MDM was first characterised in 1994[1] and accounts for approximately 4% of all mesotheliomas[2]. In contrast to "classical" pleural mesothelioma, the most common site of disease is the peritoneum although a pleural form has been described. The most common presenting feature is ascites. There is a female preponderance (F = M ratio, 1.4:1) and younger age at presentation (<40 years). Rates of asbestos exposure are generally lower than "classical" mesothelioma (c.35%)[2].

MDM is a highly malignant neoplasm with mean survival time reported as 7.33 months (range 1-29.4 months)[2]. Treatment is not curative and the main therapeutic goal is symptomatic palliation. To date, there is no standard treatment for MDM. Using established regimens for peritoneal mesothelioma, limited success has been observed using cytoreductive surgery and intraperitoneal hyperthermic chemotherapy[3].

MDM is the example *par excellence* for the difficulties that clinicians face in the differentiation between benign and malignant disease. Moreover, this case highlights the usefulness of diagnostic laparoscopy in investigating unexplained ascites. MDM is, and is likely to remain, a diagnostic challenge for clinicians, even the astute ones.

The authors have no conflict of interest

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Letters to the Editor are welcomed on new scientific advances and should be no more than 500 words and contain up to 5 references and one figure and / or table.

Correspondence on articles on this issue of the journal can be sent by email as an attached word file, or by post on CD to the editorial office, and should be less than 300 words and a maximum of three references and one table or figure.

Ulster Med J 2008; **77 (2)** 135-137

Abstracts

78th Meeting of Ulster Society of Internal Medicine, Friday 19th October 2007.

Ulster Medical Society Rooms, Belfast City Hospital, Belfast.

AGENDA

1.55pm Welcome - Chairman: Dr David Higginson

2.00pm Plenary I – presented abstracts

3.10pm Invited Lecture. "Management of Upper GI Bleeding'.
Dr Tony Tham, Ulster Hospital.

3.35pm Afternoon Tea

4.00pm Invited case from Belfast City Hospital

4.10pm Plenary II - presented abstracts.

4.35pm Presentation of prize for best abstract

4.40pm Guest lecture: "Biologic Therapies in Psoriatic Arthritis"
Prof Oliver Fitzgerald Consultant Rheumatologist, St Vincent's University Hospital Dublin.

PRESENTED ABSTRACTS

1. Prevalence of cardiac channelopathies in a tertiary referral centre in Northern Ireland

JR Bennett, J McOsker, TCL Jardine, PJ Scott, PP McKeown.

Regional Medical Cardiology Centre, Royal Victoria Hospital, Belfast Health and Social Care Trust, Belfast

Several primary cardiac arrhythmia syndromes are known to have a genetic basis and are caused by mutations in ion channel genes. These mutations cause abnormal ionic currents which can lead to ECG abnormalities and cardiac arrhythmias. These syndromes, known as cardiac channelopathies, include long QT syndrome (LQTS), short QT syndrome (SQTS), Brugada syndrome (BS) and catecholaminergic polymorphic ventricular tachycardia (CPVT), and are responsible for up to 40% of all cases of Sudden Adult Death Syndrome[1].

To date 32 families have been genetically diagnosed with LQTS. In these families 250 individuals have been genetically screened; 141 (56%) carry a mutation for LQTS and 95 (38%) are non-carriers (results pending in 14 (6%)). A further 10 families have a clinical diagnosis of LQTS with no gene mutation identified (sensitivity of 70% for picking up LQTS[2]). These families were identified following; investigation of syncope (35.4%), routine ECG (19.3%), screening following sudden death in family (16.1%), successful resuscitation of cardiac arrest (13%), investigation of palpitations (13%) and investigation following a near drowning episode (3.2%). Nine families have been referred for investigation of likely BS; 3 have mutations in SCN5A detected by genetic screening (sensitivity of 30% for picking up BS[2]). One family has been diagnosed with CPVT on genetic screening and CPVT is a possible diagnosis in 1 other family. No SQTS families have been identified.

Cardiac channelopathies are important primary cardiac arrhythmia syndromes. Genetic testing aids in the identification of individuals carrying these gene mutations so that appropriate management can be implemented.

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2. Anti-Xa activity with local treatment protocols for acute coronary syndrome.

KS Lyons, IBA Menown .

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Abstract: Enoxaparin is now the recommended anti-thrombotic treatment for patients with acute coronary syndromes (ACS). While plasma monitoring of the biological activity of enoxaparin is not usually required due to its predictable pharmacokinetics and pharmacodynamics, it may be assessed by measuring plasma anti-Xa levels (therapeutic range 0.5-1.2IU/ml). In patients with ACS, low anti-Xa activity is independently associated with increased 30-day mortality.[1] Guidelines and licensing suggest an ACS treatment dose of 1 mg/kg bd, although in Northern Ireland, many local treatment protocols dose cap enoxaparin at 60mg bd to reduce bleeding risk. We studied 20 consecutive patients admitted with ACS. All received 60mg enoxaparin bd. Peak plasma anti-Xa activity was measured as described by Montelescot et al, 4-6 hours after administration of enoxaparin.

Results: Of the 20 patients, 14 were male, mean TIMI risk score was 4.2/7 and mean weight was 81.9kg. One third (35%) of patients (5 male, 2 female) were found to have

sub-therapeutic anti-Xa levels (mean 0.35 IU/ml, range 0.2–0.49 IU/ml). The remainder had anti-Xa levels within the therapeutic range **(**mean 0.73 IU/ml, range 0.5 – 1.12 IU/ml**)**. Mean weight was higher in those with sub-therapeutic compared with therapeutic anti-Xa levels (89.9 vs 77.6kg; p value = 0.041). 5 patients in the therapeutic group and 1 patient in the non-therapeutic group had impaired renal function (eGFR 30-60 mls/min). In conclusion, dose capping of enoxaparin at 60mg bd in ACS patients may result in a significant proportion achieving sub-therapeutic anti-Xa levels, potentially correlating with poorer outcome.

1. Montalescot G, Collet JP, Tanguy ML, Ankri A, Payot L, Dumaine R, Choussat R, Beygui F, Gallois V, Thomas D. Anti-Xa activity relates to survival and efficacy in unselected acute coronary syndrome patients treated with enoxaparin. *Circulation* 2004;**110:**392-398.

3. A randomised placebo-controlled interventional trial of omega-3-polyunsaturated fatty acids on endothelial function and disease activity in systemic lupus erythematosus

SA Wright[1,2,3], FM O'Prey[1], MT McHenry[2,3], WJ Leahey, AB Devine[1,] EM Duffy[2,4], DG Johnston[1], MB Finch[2,3], GE McVeigh[1], AL Bell[2,3]

[1] Department of Therapeutics and Pharmacology, Queens University Belfast, [2]Lupus Research Group, Queens University Belfast,
[3] Department of Rheumatology, Musgrave Park Hospital, Belfast,
[4] Northern Ireland Centre for Food and Health (NICHE), Department of Biomedical Sciences, University of Ulster.

We aimed to determine the clinical effect of dietary supplementation with low dose omega-3-polyunsaturated fatty acids on disease activity and endothelial function in patients with systemic lupus erythematosus.

A 24 week randomised double-blind placebo-controlled parallel trial of the effect of 3g of omega-3-polyunsaturated fatty acids on 60 patients with SLE was performed. Serial measurements of disease activity using the revised Systemic Lupus Activity Measure (SLAM-R) and British Isles Lupus Assessment Group index of disease activity for SLE (BILAG), endothelial function using flow mediated dilation of the brachial artery (FMD), oxidative stress using platelet 8-isoprostanes and analysis of platelet membrane fatty acids were taken at baseline, 12 and 24 weeks.

In the fish oil group there was a significant improvement at 24 weeks in SLAM-R (from 9.4±3.0 to 6.3±2.5, p<0.001); in BILAG (from 13.6±6.0 to 6.7±3.8, p<0.001); in FMD (from 3.0% (-0.5-8.2) to 8.9% (1.3-16.9), p<0.001) and in platelet 8-isoprostanes (from 177pg/mg protein (23 – 387) to 90 pg/mg protein (32 – 182), $p = 0.007$).

Low dose dietary supplementation with omega-3 fish oils in SLE not only has a therapeutic effect on disease activity but also improves endothelial function and reduces oxidative stress and may therefore confer cardiovascular benefits.

4. Effect of ingestion of food on the inhibition of DPPIV activity by oral metformin in type 2 diabetes.

J Cuthbertson[1], S Patterson[2], FPM O`Harte[2], PM Bell[1]

[1] Regional Centre for Endocrinology and Diabetes, Royal Victoria Hospital, Belfast. [2]School of Biomedical Sciences,University of Ulster, Coleraine

The incretin hormones glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) constitute the enteroinsular axis which promotes postprandial insulin secretion. The therapeutic potential of these hormones in diabetes is limited by their rapid inactivation by the enzyme dipeptidylpeptidase-IV (DPP-IV). Here we investigated the acute effects of metformin in the presence and absence of food on DPP-IV activity in type 2 diabetes

Ten subjects with type 2 diabetes (6 male/4 female, age 65.8±15.8 years (mean±SEM), body mass index 30.0±7.5kg/m^2, HbA1c 6.3±1.2%) received metformin 1g orally or placebo together with a standard mixed meal (SMM) in a random crossover design. Six subjects reattended fasting and received metformin 1g without a SMM.

Following SMM (n=10), DPP IV activity was not suppressed by metformin compared with placebo (area under curve AUC $_{0\text{-}4h}$ 1574±4 and 1581±8 µmol/min respectively). No differences were observed in plasma glucose, insulin and total GLP-1. After fasting (n=6), DPP IV activity was suppressed (P<0.02) when compared to those given metformin with a SMM (AUC $_{0\text{-}4h}$ 1494±9 vs 1578±4 µmol/min). Metformin plasma levels were significantly higher (P<0.03) after fasting than SMM (AUC $_{0\text{-}4h}$ 457±55 vs 350±66 mcg/ml).

Thus metformin inhibits DPP IV activity in type 2 diabetic patients in the fasting state but not when taken with a standard mixed meal. Metformin plasma concentrations are lower if taken with food. Metformin may have potential for combination therapy with incretin hormones.

5. An interesting cause of hypopituitarism: infiltrative versus idiopathic

AS Lewis[1], ME Callender[2],E Chew[3], CH Courtney[1], N McDougal[2], AB Atkinson[1]

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[3] Cardiology Department, Belfast City Hospital, Belfast.

Hypopituitarism usually occurs as the result of a pituitary tumour or as a consequence of its treatment. If, however, pituitary imaging is negative then there are a wide variety of alternative causes but no firm consensus as to which should be actively sought. We present two cases of apparent idiopathic hypopituitarism in whom the underlying diagnosis was delayed with potentially serious side effects.

Case Report: A 32 year old male presented with symptoms of hypogonadism. Testosterone (<0.7nmol/L; N 10.5-30 nmol/L) and gonadotrophins were low (FSH <0.5 U/L; LH <0.5 U/L) and prolactin was normal (118mU/L). Thyroid function was normal (fT4 9.7pmol/L; N 7.6-19.7 pmol/L, TSH 1.33mU/L; N 0.45-4.5 mU/L). Insulin tolerance testing established a normal cortisol peak of 1002nmol/L but suboptimal growth hormone response (8.1mU/L) to hypoglycaemia. Pituitary imaging was normal. He presented 5 years later in congestive cardiac failure with an elevated ferritin (6309 ug/L; N 18-325ug/L) and transferrin saturation (100%). Homozygosity for the C282Y mutation confirmed the diagnosis of haemochromatosis.

A 51 year old female presented with non-specific symptoms. Initial testing suggested hypopituitarism with a random

cortisol of <30nmol/L and a low free T_4 (6.9 pmol/L) with normal TSH (2.3 mU/L). Prolactin was 1190mU/L and gonadotrophins were post menopausal (FSH 26.6 U/L, LH 16.8U/L). Insulin tolerance testing confirmed an inadequate cortisol response (<30nmol/L) but a normal GH response (41.3 mU/L) to hypoglycaemia. Pituitary imaging was normal. Four years later, investigation revealed a raised ferritin (389ug/L) and transferrin saturation (74%). She was heterozygous for the C282Y mutation and iron overload was confirmed at liver biopsy.

Haemochromatosis causes pituitary dysfunction by depositing iron in the anterior pituitary. Due to its rarity as a cause of hypopituitarism, it is not always considered by endocrinologists as a potential diagnosis. Imaging is usually normal and patients are often wrongly labelled as having idiopathic hypopituitarism. However, early diagnosis is important as treatment may reverse the pituitary deficit and prevent future sequelae in other organs. We recommend iron studies in all patients who present with hypopituitarism and normal pituitary imaging.

6. Implementing the European Society Of Cardiology Guidelines for evidence based therapy in Heart failure: An audit of Pharmacotherapy at discharge from an Acute Hospital.

K Morrice, J Hastings. B McClements.

Cardiology Dept, Mater Hospital, Belfast

The consistent implementation of guidelines on the use of evidence-based drug therapy in heart failure patients remains a challenge in clinical practice. The purpose of this study was to determine the extent of this problem in a single centre that seeks to adhere to European Society of Cardiology guidelines (2005), to discern its possible causes and to assess whether there is a difference depending on LV systolic function.

281 consecutive patients (150 male, mean age 77 years) admitted between April 2005 and December 2006 were identified from the Mater Hospital Heart Failure database. Of these, 245 patients who had recent echocardiographic data available formed the study population: 154 (63%) had LV systolic dysfunction (LVEF < 40%) (Group LV-S) and 91 had relatively preserved systolic function (Group LV-P).

Results: The groups were similar except for percentage with hypertension (LV-P 80% v LV-S 44%, p<0.001). Mortality was 10.4% in LV-S and 10.9% in LV-P (p NS). Mean serum creatinine was 149µmol/l in LV-S and 135µmol/l in LV-P on admission and 158 µmol/l and 141 µmol/l respectively at discharge.

Review of the clinical records of 24 patients in LV-S not on treatment with ACEi/ARB at discharge revealed that 20 had significantly impaired renal function (mean serum creatinine 264 µmol/l), 2 had profound hypotension with initiation of ACEi, one had severe aortic stenosis and one self-discharged against advice.

The proportion (%) of patients in each group on prognosis modifying medication on admission (A) and at discharge (D) were:

		LV-S	LV-P
ACEi/ARB	A	60	46
	D	83	76
Beta-Blocker	A	55	55
	D	91	94
AA	A	30	24
	D	50	49

ACEi / ARB= Angiotensin converting enzyme inhibitor or Angiotensin Receptor Blocker;

AA = aldosterone antagonist

Conclusions: In this single centre study, use of beta-blockers was very satisfactory. All LV-S patients were on treatment with ACEi/ARB or had a documented contra-indication, usually renal impairment. There appears to be scope for greater use of AA in LV-S. It was also interesting to note the frequent use of AA in heart failure with relatively preserved systolic function.

7. Trends In Lipid Levels In Patients Admitted With Myocardial Infarction To A Regional Cardiology Centre 2000-2006

P Scott, V Kodoth, R Noad, J Bennet, C Murphy, G Manoharan, AAJ Adgey.

Regional Medical Cardiology Centre (RMCC), Royal Victoria Hospital Belfast, Belfast Trust, Belfast, UK.

Introduction: Hypercholesterolemia is a major risk factor for coronary artery disease. Revised Joint British Society Guidelines 2005 (JBS-2) have recommended tighter lipid targets for both primary and secondary prevention. We reviewed trends in fasting lipid levels of patients admitted with Myocardial Infarction (MI) to our centre and assessed compliance with these guidelines.

Methods: Fasting lipid profiles were analysed on patients admitted with an MI from January 2000 to December 2006 (n=1346). For patients admitted in 2005 lipid profile values were re-evaluated at least 6 months after admission to determine if JBS-2 target lipid values had been achieved.

Results: Average Total Cholesterol decreased from 5.26 mmol/L in 2000 to 4.73 mmol/L in 2006 (p=0.026), LDL Cholesterol from 3.14 mmol/L in 2000 to 2.57 mmol/L in 2006 (p<0.001) and HDL Cholesterol rose from 1.11 mmol/L in 2000 to 1.58 mmol/L in 2002 (p=0.013) but declined to 1.33 mmol/L in 2006 (p=0.423). ST elevation Myocardial Infarction (STEMI) patients had significantly higher Total Cholesterol (5.11 Vs 4.78; p<0.001), LDL (2.97 Vs 2.69; p<0.001) and lower HDL (1.28 Vs 1.39: p=0.399) when compared with those admitted with Non ST-elevation Myocardial Infarction (NSTEMI). In 2005, 69% had achieved Total Cholesterol, 74% LDL and 71% HDL cholesterol targets 6 months after their admission.

Conclusion: Our study reveals reduction in lipid profile values on admission from 2000 to 2006. We also noted that patients admitted with STEMI had a higher Total Cholesterol, LDL and lower HDL than NSTEMI. Current guidelines for primary and secondary prevention of coronary heart disease has led to more fastidious use of anti-lipid medications and has had a significant impact on the reduction of cholesterol.

Ulster Med J 2008; **77 (2)** 138-140

Abstracts

77th Meeting of Ulster Society of Internal Medicine, Friday 18th May 2007.

Clinical Education Centre, Altnagelvin Area Hospital, Londonderry.

PROGRAMME

1.55pm Welcome - Chairman: Dr David Higginson

2.00pm Plenary I – presented abstracts

3.00pm Invited Abstract: "Fits, falls and faints" Dr Kevin Dynan Consultant Physician, COTE, Ulster Hospital.

3.25pm Afternoon Tea

3.40pm Two case presentations from Altnagelvin Area Hospital

4.00pm Plenary II - presented abstracts.

4.20pm Presentation of prize for best abstract

4.25pm Guest lecture: "Modern management of Arial fibrillation" Dr Carol Wilson, Consultant Cardiologist, Royal Victoria Hospital.

PRESENTED ABSTRACTS

1. The Experience of Lay First Responders in the Northern Ireland Public Access Defibrillation (NIPAD) Project.

AJ Hamilton[1] JE Jordan[2], MJ Moore[1], K Cairns[3], AAJ Adgey[1], F Kee[4].

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Objective: The Northern Ireland Public Access Defibrillation (NIPAD) project was established to train lay volunteers as First Responders (FRs) in the use of an automated external defibrillator (AED) at an out of hospital cardiac arrest (OHCA). We wished to establish the background and experience of the FRs.

Methods: A questionnaire was distributed to FRs with a pre-paid reply envelope and a follow up reminder letter was sent to non-respondents after six weeks.

Results: There were 178 questionnaires returned of whom 71/178 (39.9%) were male. The mean age of the FRs was 45.9 yrs (SD 10.7). The education level of the FRs was assessed: 49/178 (27.5%) had received no school education after age 16 and 60/178 (33.7%) were educated at university.

Basic medical skills prior to enrolling in the NIPAD project were assessed. 30/178 (16.9%) had no previous first aid training, 45/178 (25.3%) had participated in a basic first aid course, 81/178 (45.5%) had training in basic life support and 17/178 (9.6%) had training in advanced life support.

Following training 163/178 (91.6%) felt "totally confident" or "reasonably confident" in using an AED at the scene of an OHCA. No volunteer considered the AED difficult to use. In total 34/178 (19.1%) of FRs were willing to hold an AED permanently. No FR required the use of the confidential counselling service employed by the project.

Conclusion: First Responders can be recruited from a variety of backgrounds. The First Responders reported the AED to be easy to use following training.

2. Infective discitis in a District General Hospital

EMA McCausland [1], NW Liggett[1], RB Forbes [2]

[1] Dept of Rheumatology, Craigavon Area Hospital,

[2] Dept of Neurology, Craigavon Area Hospital, 68 Lurgan Rd, Craigavon, Northern Ireland.

Infective discitis is a serious but treatable cause of back pain in adults. We report a series of cases presenting to a district general hospital over a three year period (2004-6). We reviewed case notes of eleven patients with a discharge coding diagnosis of 'discitis', and extracted clinical information: symptoms, predisposing factors, radiological imaging, time to diagnosis, microbial organisms, antibiotic therapy and functional outcome.

All eleven patients (mean age 62 yrs, range 45-90) reported back pain at presentation. Pyrexia >37.5 was present in 10 patients with a mean CRP of 252 mg/l (range 101-560). Diabetes was the most common predisposing factor (27%), and one patient had had a recent invasive spinal procedure. Diagnosis was confirmed by MRI in the majority (63%). Median time from admission to confirmation of diagnosis was 6 days (1-15). *Staphylococcus aureus* was isolated from 5 patients. Choice of antibiotic and duration of treatment varied. At the time of this study 6 were walking independently, 4 with assistance, 1 was immobile and 1 was dead.

Discitis accounted for 0.023% of DGH medical and surgical admissions during this period. The diagnosis is often not considered prior to imaging. It is more commonly appreciated as a complication of spinal surgery or invasive spinal

procedures[1] however spontaneous discitis is associated with advanced age, diabetes and systemic infection[2]. Therefore in the setting of back pain, fever and elevated inflammatory markers infective discitis should be considered, especially in high risk groups.

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2. Honan M, White GW, Eisenberd GM. *Spontaneous infectious discitis in adults. Am J Med* 1996;**100(1):**85-9.

3. Significance of ST segment elevation on the exercise electrocardiogram in patients without prior history of myocardial infarction.

JC Murphy, PJ Scott, P McKavanagh, HJ Shannon, B Glover, J Dougan, SJ Walsh, AAJ Adgey

Regional Medical Cardiology Centre, Royal Victoria Hospital, Belfast.

Background: Exercise induced ST segment elevation (STE) in patients without a history of myocardial infarction may be due to coronary artery spasm or stenosis.

Methods: Between January 1998 and Dec 2005 14,941 exercise stress tests were performed in our department for assessment of chest pain in patients without prior history of myocardial infarction or Q-waves on the resting electrocardiogram (ECG). Patients who developed STE during exercise or in the recovery phase were identified and a review of case histories was carried out.

Results: The incidence of STE was 0.78% (116/14941). The majority were male (92) with no age difference between the genders (male 56.4 +/-10.8 vs female 59.1years +/-11.9 p=0.287). Coronary angiography was performed in 108 patients and 6 had myocardial scintigraphy. All patients undergoing angiography had at least one severe coronary artery stenosis (>70%). The site of ST elevation was subsequently confirmed by angiography to be 93.5% predictive of a tight stenosis in the corresponding coronary artery. A left anterior descending (LAD) artery stenosis was seen in 40/41 (97.6%) patients who developed anterior STE. A right coronary artery or dominant left circumflex artery (LCx) stenosis was seen in 61/66 (92.4%) of patients who had inferior STE. Lateral STE was rare (1/116). Of the 6 who had scintigraphy 3 had reversible reperfusion defects which correlated with the site of STE and 2 had inferior STE with fixed inferior defects. One patient had a normal perfusion study.

Multivariate regression analysis was performed on those who underwent angiography. The only independent predictor of multi-vessel disease was increased time to resolution of STE with OR 1.097 (95% CI 1.014-1.187 p=0.021).

Conclusion: STE on the exercise treadmill is rare but specific for ischaemic heart disease. The territory of STE is predictive of a severe stenosis in the corresponding artery.

4. Risk Factors in Patients with an Out-of-Hospital Cardiac Arrest

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[2] Department of Applied Mathematics, Queen's University, Belfast.

[3] Department of Epidemiology and Public Health, Queen's University, Belfast.

Objective: To determine the risk factors leading to death from Out-of-Hospital Cardiac Arrest (OHCA).

Methods: The Emergency Medical Service patient report forms from North and West Belfast were examined from 8/6/2005 to 28/3/2006 for any OHCA death as per Utstein criteria. The General Practitioner (GP) records and the post mortem result were obtained.

Results: There were 131 cases of OHCA; 76 were male (58%) mean age 68 years. At the time of death 51 (39%) lived alone and 112 (85%) had OHCA at home. A history of smoking occurred in 72 (55%), hypertension in 63 (48%), hypercholesterolaemia in 42 (32%), and diabetes mellitus in 24 (18%). The median time from the last GP attendance to death was 103 days (interquartile range 21-296 days). In only 6 (5%) cases was chest pain the reason for this attendance. A history of ischaemic heart disease was present in 48 (37%) and 28 (21%) had had a previous coronary angiogram. The use of Aspirin occurred in 56 (43%), B-blockers in 46 (35%), Statins in 54 (41%) and ACE inhibitors in 61 (47%) cases. At post mortem there were 27/42 (63%) with ≥moderate coronary atheroma in 3 coronary arteries and left ventricular hypertrophy in 26/42 (62%) cases.

Conclusion: OHCA remains difficult to predict with few patients presenting with prior chest pain. The high incidence of OHCA in individuals living alone at home will constrain improvements in survival.

5. Vasoactive intestinal polypeptide secreting pancreatic tumour (VIPoma) with recurrent metastases in a 46 year old male, long term survival after orthoptic liver transplantation.

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[1] Regional Centre for Endocrinology and Diabetes, Royal Victoria Hospital, Belfast, BT12 6BA.

[2] Neuroendocrine Tumour Group, Royal Victoria Hospital, Belfast, BT12 6BA.

Case Report: A 46 year old male presented in 1981 with a two year history of profuse watery diarrhoea, three stone weight loss and fatigue. On examination he appeared gaunt with diffuse muscle weakness. Investigations revealed hypokalaemia - 2.5mmol/L (3.5-4.5), achlorydria and a raised vasoactive intestinal polypeptide (VIP) -500ng/L (0-100). Abdominal CT revealed a 5 cm pancreatic mass but with no focal liver pathology. A distal pancreatectomy was performed the histology of which confirmed an islet cell carcinoma (VIPoma).

His symptoms recurred one year post surgery, at which time liver metastases were demonstrated radiologically. He responded initially to three courses of Streptozotocin but ultimately developed resistance. For fifteen years his symptoms were controlled by octreotide injections, initially Sandostatin (subcut) and later Sandostatin LAR. The patient also underwent hepatic chemoembolisation.

By 1997 sixteen years after his initial surgery, treatment

failure occurred with a profound deterioration clinically and debilitating diarrhoea. No evidence of extra hepatic disease was found. After extensive discussion he underwent orthoptic liver transplantation which resulted in resolution of his symptoms[1,2].

Recurrence was noted two years post transplant in the para aortic lymph nodes but not in the liver. He remained mildly symptomatic with gradual deterioration of his general health and died 9 years after liver transplantation.

This case is the longest reported (25 years) survival of a VIPoma after initial diagnosis. The case also has several notable features including the absence of liver metastases at diagnosis, the variety of modalities of treatment used for symptom control including successful orthoptic liver transplantation.

1. Le Treut YP, Delpero JR, Dousset B, Cherqui D, Segol P, Mantion G, Hannoun L, Benhamou G, Launois B, Boillot O, Domergue J, Bismuth H. Results of liver transplantation in the treatment of metastatic neuroendocrine tumours. A 31 case French multicentric report. *Ann Surg* 1997;**225(4):** 355-64.

2. Lang H, Schlitt HJ, Schmidt H, Fleming P, Nashan B, Scheumann GF, Oldhafer KJ, Manns MP, Raab R. Total hepatectomy and liver transplantation for metastatic neuroendocrine tumours of the pancreas- a single centre experience with ten patients. Langenbecks *Arch Surg* 1999; **384 (4):**370-7.

6. Intravascular lymphoma – a clinical conundrum

N Chapman, HK Boyd, R Convery

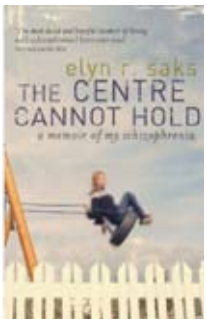
Craigavon Area Hospital, United Kingdom.

Case Report: A 75-year-old lady presented with a 5-week history of severe progressive fatigue; loss of appetite and thrombocytopenia. Scanning revealed an adrenal mass and hepatic abnormality suspicious of malignancy. Over the next 6 weeks the patient developed symptoms suggestive of Transient ischemic attacks. She suffered a myocardial infarction and developed pyrexia. Severe pain occured in the left hypochondrium. She developed deranged liver function and pancytopenia. Bone marrow biopsy revealed an intravascular large B Cell non-Hodgkin's lymphoma.

There was a good response to initial palliative treatment and subsequently the patient tolerated 6 cycles of intensive chemotherapy (PMitCEBO) plus Rituximab and intrathecal Methotrexate. Ten months after presentation remission was shown by follow-up CT Scan and Bone marrow biopsy.

Discussion: This patient demonstrates the varied symptoms of this rare form of lymphoma, a diagnosis typically made post mortem. So far the response to chemo and immunotherapy has been good indicating that early diagnosis and modern management may dramatically improve the outlook for patients with this aggressive lymphoma.

Book Reviews



The Centre Cannot Hold (My Journey Through Madness). Elyn R Saks. Hyperion, New York, August 2007. 352pp. £12.58. ISBN 978-1-40130-138-5

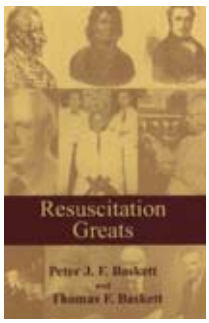
If you walk into any branch of Waterstones, near the biography section there is a section called "Lost Lives". This is the result of the increasing numbers of memoirs dealing with various types of abuse in childhood and various degrees of subsequent transcendence. The genre has also less charitably been dubbed "Misery Lit", and described as "the book world's biggest boom sector." I am happy to report however that this book doesn't belong in that section.

It is in fact a very clear and unsentimental account of one person's struggle with schizophrenia. This starts with an uneventful American childhood, with only minor obsessional symptoms, before evolving into a full blown psychosis at College. There is a remarkably touching description of her relationship with a Klienian analyst in Oxford, where she had a scholarship, and the continuing story of her successful academic career in the US.

One of the key negative aspects of her experience is the use of physical restraint in her early American hospital admissions. This leaves her with a feeling of dehumanisation and she uses this experience in her subsequent career as a human rights lawyer to help change this practice.

This is a remarkable book, bold and clearly written. I would recommend it to anyone interested in a first hand account of psychosis. It is particularly thought provoking for those of us at the "other side" of the experience. It is not always an easy read but never strays into the more unctuous excesses of the "Misery Lit" genre.

Francis Anthony O'Neill



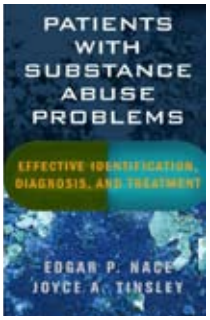
Resuscitation Greats. Peter JF Baskett, Thomas F Baskett. Clinical Press Ltd, Bristol, October 2007. £25.00. pp380. ISBN 1-854-57049-8

This miscellany of historical articles on famous medical pioneers of resuscitation is an excellent read. The authors – two brothers – a Professor of Anaesthetics, and a Professor of Obstetrics and Gynaecology, and both originating from Belfast, do a whistle-stop tour through the earliest records of resuscitation efforts from Biblical times, right through to cardiac resuscitation and modern technological advances. There were clearly some great characters in the last two millennia – read about keen physicians from diverse and varied parts of the world including Moritz Schiff and the history of open heart massage, famous resuscitations such as that of Abraham Lincoln, early pioneers including William Harvey, and Andréas Vesalius, and a host of other 'greats'.

The individual chapters are taken from a series of published papers in the journal *Resuscitation* and have been arranged in chronological order. The summaries and pictures are excellent, and the only criticism I could find is that the font layouts are not entirely all the same – presumably there were journal typesetting changes over the period of publishing the articles in the journal – a small quibble in a truly excellent book.

There are of course some 'greats' from Northern Ireland including accounts of Professor Frank Pantridge, and Sir Ivan Magill. Readers from every aspect of medical life will enjoy this book and appreciate how far we have advanced. Particular thanks should go to the Belfast born 'greats' for their contribution, and the authors for putting the anthology together in such a readable way.

Patrick J Morrison



Patients with Substance Abuse Problems: Effective Identification, Diagnosis, and Treatment. Edgar P Nace & Joyce A Tinsley. WW Norton & Company, New York, April 2007. 224pp. £14.99. ISBN 978-0-39370-511-9

The global problem of substance abuse has been well documented, yet training and resource allocation in this area is often unsatisfactory. The WHO's Global Burden of Disease Study (1996) found that alcohol use was the fourth leading cause of disease burden, preceded only by cardiovascular disease, major depression and ischaemic heart disease – all of which can be exacerbated by substance abuse. Research quoted here shows that 14% of Americans are alcohol dependent, and substance abuse is estimated to cost the American economy more than $200 billion per year. There is a high prevalence of substance dependence in patients with psychiatric disorders and this is typically associated with a poorer prognosis.

This book by two leading psychiatrists in the USA is aimed primarily at non-specialists in primary care and psychiatric practice. It appears to be particularly aimed at those clinicians who have become disheartened and pessimistic about the ability of their patients to recover in the longer-term. The authors are clearly passionate about their work and have produced a very readable and understandable overview of the biopsychosocial model of addiction and how to effectively recognise and treat addiction problems.

A feeling of optimism permeates every section of the book. It begins by highlighting the rapid progress made over the past 20 years in scientific understanding of addiction. This is based very much on the theory of addiction as a disease of the brain, focusing on the dopamine-rich reward pathway. The authors effectively summarise the available scientific evidence

for those not well-acquainted with complex neuroanatomy and neurochemistry. The book also neatly describes pathological psychological defence mechanisms employed by addicts such as denial. An understanding of these defences can help explain why these patients continue to engage in activities that are clearly harmful to themselves and others and can be used by the clinician to advance treatment.

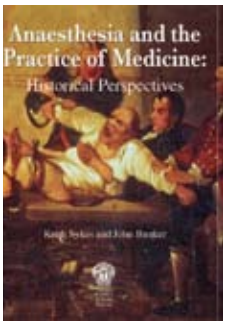
There follows a comprehensive section on identification and diagnosis of the different substance abuse problems. Useful screening questions and tools are provided and clinical vignettes are used to illustrate and further explain concepts. This earlier part of the book neatly summarises a large body of work in a readable fashion. This style is carried into the section on treatment, but I was left disappointed that there was not more detail in this area. The authors describe how to decide the intensity of care required and the appropriate treatment setting and how to effectively use motivational interviewing. Unfortunately there is considerably less information on cognitive-behavioural approaches and facilitation of twelve-step programmes. Brief interventions are described but again, not in a lot of detail, somewhat surprisingly given their increasing use in primary care.

The chapter on pharmacological treatment effectively summarizes the evidence for Acamprosate, Disulfiram and Naltrexone in alcoholism, including details on these medications' modes of action and side effects. The use of substitute prescribing in opiate dependence is outlined, and a useful section in the appendix describes medication regimens that could be used in the management of alcohol and drug withdrawal, although some specific drugs and doses would appear to differ from local practice. The book concludes with chapters on nicotine dependence and specific challenges in treating substance abuse problems in the elderly and adolescents.

This enjoyable and readable book will be of particular use to general practitioners, general medical physicians and general adult psychiatrists. It provides a useful introduction for those wishing to specialise in the field of addictions, but its brevity ensures that these individuals will also need to invest in other more detailed texts.

Rowan McClean

Anaesthesia and the Practice of Medicine: Historical Perspectives. Keith Sykes, John P. Bunker. Royal Society of Medicine Press, London, January 2007. 303pp. £15.95. ISBN 978-1-85315-674-8



This is a delightful volume written by two retired anaesthetists, one a Cambridge graduate and the other a graduate from Harvard. Both worked together at the Massachusetts General Hospital in 1954-55. The book is divided into five parts.

Part 1 deals with the origins of anaesthetic drugs. The first use of anaesthetics is open to considerable doubt but excluding alcohol, hemlock, hemp and laudanum, the earliest recorded soporific effects of ether were described as far back as 1540. Nitrous oxide, discovered by a clergyman, Joseph Priestley, started off as a recreational drug and as a cure for tuberculosis and other respiratory illnesses. Beddoes and Humphrey Davy identified its pain relieving properties and in 1800 proposed its use in surgery. It was not until 44 years later that nitrous oxide was used to relieve pain during surgical procedures. Volatile anaesthetics ether and chloroform also started off as recreational drugs and cocaine, the first effective local anaesthetic, continues in that role. Cocaine was initially used to anaesthetise the cornea in eye surgery but as far back as 1889 it was used by the German surgeon August Bier to produce spinal anaesthesia. The last chapter in this section deals with the mechanical aspects of anaesthetics and their development – ventilators, heart-lung machine, and various types of anaesthetic apparatus.

Part 2 identifies the impact of a number of historical events, notably the Second World War, and the individuals who helped to establish anaesthetics as an important scientific and clinical discipline. The section concludes with three chapters on curare and neuromuscular blockade reflecting the enormous contribution of these drugs to modern day anaesthesia and the strong research interest of the authors.

Part 3 deals with the extension of anaesthesia into other areas of medical practice – maintenance of respiration in poliomyelitis and other diseases requiring respiratory intensive care, cardiac bypass for open heart surgery, cardio-pulmonary resuscitation and the development of short-acting anaesthetic agents for day surgery. Halothane hepatitis and the safety of anaesthetic agents are also discussed.

Part 4 discusses the role of the anaesthetist in childbirth and in the care of the newborn. Opposition to pain relief during Victorian times was largely silenced by Queen Victoria'a pronouncement, "We are going to have this baby and we are going to have chloroform". The important contribution of Virginia Apgar to neonatal intensive care is also discussed. She introduced her Apgar score in 1953, which is probably the most famous eponymous acronym in medicine – Appearance, Pulse, Grimace, Activity, Respiration.

The final section concludes on a less optimistic note. This chapter concludes that anaesthetics, like a number of other medical academic disciplines, faces two major problems: the impact of the European Working Time Directive on clinical services and training, and the erosion of the academic base that is essential for the future development of the discipline.

Together Keith Sykes and John Bunker have built up a wonderful and engaging story of anaesthesia over the last two centuries from laughing gas parties and ether frolics to the targeted use of local and general anaesthetics used today. The volume clearly details how the skills that were developed in the operating room have been increasingly applied to many other diseases and disciplines within medicine. Anaesthetists, surgeons, those involved in pain management and intensive care and those interested in medical history will be enthralled and captivated by this book.

Dennis Johnston

Trearment Collaboration - Improving the Therapist, Prescriber, Client Relationship. Ronald J Diamond & Patricia L Scheifler. Norton Professional Books, New York, May 2007. 208pp. £17.99. ISBN 978-0393704730

What an unusual book – I have just finished reading it, and find myself somewhat unable to describe what I have just read! If I were to liken the book to a piece of household equipment, it would be a large toolbox that contains some sort of tool for almost any job. Written primarily for the mental health setting, it contains helpful insights into the life of a mental health patient and enjoyable descriptions of issues in multi-disciplinary working. Its wide scope also includes recovery in mental illness, psychiatric presentation of medical illnesses, appropriate blood levels of mood stabilising drugs and, surprisingly, an appendix about diabetes.

Almost anyone who sits down to read this book – psychiatrist, physician, psychologist, patient, interested family member – will derive some benefit from it. It helpfully describes treatment collaboration and the possession of power and responsibility in a treatment team. By way of reviewer's paraphrase, prescribers carry a legal obligation toward the health of their patients and as such have power in the doctor-patient relationship. The patient, on heading home, usually has the liberty and power to throw the prescription in the bin, showing decisive power. The therapist may know the patient better than any other team member, and thus has a heavy responsibility for the patient's well being, with the influence that carries.

Perhaps reflecting a lack of mental flexibility on my part, I found the presentation of the book a little annoying. Moving from one chapter to the next, I was at times distracted by wondering which of the authors had written which chapter, so different were they in style. Was the repetitive and slow-paced Chapter Four written by the Social Worker or the Professor of Psychiatry? Who authored the fast-flowing Chapter Five? The sudden appearance of summary boxes in the second-half of the book required further mental adjustment and the abrupt ending of the book was a disappointment. The reason for including an explanation of raised fasting triglyceride level in diagnosing diabetes caused me further head-scratching (is this an important diagnostic tool in mental illness that I am not aware of?). The turn-about style of the book, with one section written to professionals, the next written to patients, will demand further mental manoeuvring from the interested reader.

While perhaps deserving the description "Jack of all trades, Master of none", this book would be worthy of a place on most psychiatrically-oriented book shelves.

James Nelson

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Cover Legend – left – X-Ray showing wrist watch in right iliac fossa – later retrieved (right figure) and still functioning. See paper on Foreign Body Ingestion in Prisoners, by M Bisharat (page 110).