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Editorial

Quis Custodiet Ipsos Custodes

The Roman poet Juvenal, in his *Satires*, asked the question, " Who watches the watchmen?" It would appear that it isn't completely clear to many of my medical colleagues what metrics are currently applied to admit students into the arts and inner mysteries of our medical schools. The admissions process, viewed across the United Kingdom, does exhibit significant variation. There is a long list of entry criteria: academic achievement, interviews, the personal statement, UKCAT examination, competitive interviews and OSCE's are all used by some. The UKCAT examination, for example, is an evaluation process that is billed as not requiring advance preparation. There is however a plethora of preparation material available, and many sixth-form students approach it with the fervour of the convert. What this does for the subsequent result analysis is for expert interpretation, and not for me.

Queen's University has not used the competitive interview for some years (for undergraduate entry into medicine), although this is all set to change in 2012. There are also compelling arguments for encouraging medicine to exist as a graduate subject, as it does in the United States, for example. Graduates are more focused, have been through the 'rite of passage' that attends the end of school life and the beginning of independence, and, it has been argued, their relatively impecunious state helps concentrate their minds wonderfully. The question that naturally follows is: where is the mesh between undergraduate and graduate application? What happens if some UK schools of medicine are undergraduate and others are exclusively graduate? Should they all jump together, or not at all? You may, reader, have a view on this.

I am indebted to Keith Steele, the Dean of Admissions, for setting out the selection criteria with such lucidity. For, although not all of us understand the process, everyone has an opinion on the quality of our medical students and junior doctors. It would be less than candid to assert that it was universally positive. It was all so different once. However, nostalgia isn't what it used to be and there is, of course, attendant danger in applying the retrospectoscope. The certainty of Gordon's Sir Lancelot Spratt, the bucolic idyll that was Cronin's Tannochbrae, and the sterilised saccharine of Dr Chamberlain, can be beguiling, but might mask an uncomfortable truth. Medicine was, maybe, never actually like that. Not all students looked like Dirk Bogarde - contemporary students might more closely ape Captain Benjamin Franklin 'Hawkeye' Pierce of the 4077th. They won't know who he was, of course, but luckily have Google. Connoisseurs of 'MASH' will, I suspect, recall that everyone wanted to be Hawkeye, despite the unkempt look, the iconoclasm, the excess, the dalliances, and let's not forget, the illegal 'still' he kept by his bed. Still, you say, there was a war on. Isn't there always? So, having gained admittance, what's it like to be a medical student? Gail McLachlan reminisces in our section, ' So you want to be a medical student?'

Sadly, not all runners finish the race. Loss, of course, is a component of our professional life. Any loss is painful to those left behind, but a young life ended seems additionally unjust. When that person is a medical student, an extra poignancy is palpable in our wider medical family. One cannot help considering the lost potential, and recalling what one was doing oneself as a callow twenty something. The 16th century French classics scholar Henri Estienne had it when he wrote, " Si jeunesse savait, si viellesse pouvait - If youth but knew, and age but could". One hopes that, at least, there was no suffering. But what if there was? I am privileged to publish the James Logan Essay Prize within these pages. James was such a student. The James Logan Trust was set up to encourage doctors and others to recognise and treat cancer pain. Victoria Campbell is it's first and very worthy prizewinner. Also in this edition, I am delighted to publish the Ulster Medical Society's Presidential lecture, delivered with considerable élan by Margaret Cupples. Continuing our 'Grand Rounds' series, Harpreet Ranu has produced an exemplary article on pulmonary function tests, comprehensible even to this middle-aged radiologist.

Finally, I am delighted that after a period of nomadic existence, the Ulster Medical Society and Journal have returned to our home in the Whitla Medical Building. We are delighted to be back in our elegant new office. Please, as ever, continue to send me your good papers.

Barry Kelly
Honorary Editor.

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Review

Selecting Tomorrow's Doctors

Keith Steele

Accepted 3 April 2011

Application to medical school is a competitive process. In 2009 there were 27,429 applications for approximately 8000 places in the UK, up 13.7 per cent on the previous year[1] . The cost of training a medical student is circa £200,000 but the cost of selecting the wrong applicant can be even greater[2].

Traditionally medical schools have relied on performance in knowledge-based examinations for selection and although these distinguish academically able applicants, it is often the failure to develop non-cognitive competencies such as motivation and/or empathy and ability to communicate that lead to problems for doctors in their professional lives. If we accept that we want our doctors to have the non-cognitive skills to relay information to us as patients and also to have the cognitive skills to consider management/prognosis with us then it follows that we should accept our applicants to medical schools on both their cognitive and non-cognitive abilities. There is now worldwide support for this approach both in the UK from the Medical Schools Council and the GMC and in the US from the Accreditation Council for Graduate Medical Education[3].

Widening participation so that medical students are representative of the population they serve has assumed importance politically. In 2008 the four lower socioeconomic classes accounted for only 15 per cent of medical students in the UK[4] . Some schools seek to actively redress this by selecting on aptitude rather than achievement, the latter being related to socioeconomic factors and type of school attended.

Given the highly competitive nature of selection which can be secretive and varies between Universities, the Schwartz report into fair admission to Higher Education has recommended the following five principles and two guidelines: 1) the selection process should be both transparent and should be published and available online; 2) selection should consider both achievement and potential; 3) selection methods should be reliable, valid and informed by best practice; 4) the predictive validity of selection methods should be monitored; 5) staff should receive training in selection processes; 6) there should be feedback to unsuccessful candidates; 7) barriers to selection should be minimised e.g. disability considered post selection[5].

Given that attrition rates in medical school are low it can be argued the selection exercise is of even higher importance. Instruments used for selection include personal statements, academic references, tests of previous academic performance, aptitude tests, personality tests, random selection and interviews. Not surprisingly given the variety of instruments there is considerable controversy surrounding their most effective use.

METHODS USED TO SELECT MEDICAL STUDENTS

Personal Statements and Academic References

Ferguson et al followed up the 1995 cohort at Nottingham Medical School over a five year period. They used manifest coding to categorise applicant's personal statements and academic references[6]. They found that information on the academic reference did not predict academic performance whereas there was a correlation between content matter in the personal statement and aspects of clinical performance. On the other hand in a recent paper which defined selector practice from Bart's. and the London where personal statements are used to screen for interview, the authors commented that the study confirmed the subjective nature and low reliability of this process[7]. Personal statements are subject to plagiarism and UCAS has claimed that up to five per-cent of personal statements amongst eight hundred applicants to Medicine contained material borrowed from three online example statements. They have recently introduced copycat software to address this[8].

In my experience of examining academic references over the last three years I have yet to find an unfavourable one.

Tests of previous academic performance

A-level results have been found to be a consistent predictor of academic performance in medical school in the UK[6]. At McMaster, grade point average has been found to be a predictor of academic performance and clinical performance in their graduate entry programme. Unfortunately A-levels/ GCSEs have become less useful because of grade inflation, as the vast majority of applicants achieve 3A grades. Over the past 20 years the proportion of A-grades has risen from 9-27 per-cent[9]. For this reason the A star grade which is based on performance at A2 and is awarded to approximately the top ten per-cent across all A-level subjects has been introduced (70 per-cent of the 2010 cohort accepted on the basis of A-level performance to QUB Medical school had at least one A star and one student had five). Females perform better in both GCSEs and A-Levels than males[10]. It has also been argued that A-levels are biased and that grades can be affected by type of school attended. Widening participation was a priority of the Department of Health under its proposal in

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2004 to increase the number of training places in the UK for medicine[11] . For graduate entry the use of grade point average is fraught with difficulty because some degrees are seen to be easier than others and there is variability of grades awarded between different universities[12] . Our own findings relating to the 2008 entry cohort to Medicine at Queens University Belfast (QUB) show that the best predictor in both first and second year examinations is GCSE performance (Cronbachs alpha 0.8).

McManus et al in a longitudinal study of students entering Westminster Medical school have shown that A-level grades have long term predictive value for undergraduate and postgraduate careers including time taken to obtain membership. The authors argue that A-level assesses achievement and that past achievement affects future achievement[13] .James has shown that for 1986-90 entrants to the undergraduate course at Nottingham medical school achieving a high grade in A-level Chemistry predicted success at BMedSci and a high grade in A-level Biology predicted success in BMBS[14] .

Aptitude Tests

These tests are designed to assess the applicant's aptitude for medicine. They include the Graduate Medical Schools Admission test (GAMSAT) used both in Australia and for graduate entry in the Republic of Ireland, the Medical Colleges Admission test used in the US (MCAT), the Biomedical Admissions test (BMAT) and UK Clinical Aptitude test (UKCAT) used in the UK. The rationale behind these tests is that they should be free from bias, assess ability rather than achievement and would help distinguish between candidates scoring at the GCSE/A level ceiling. BMAT, GAMSAT and MSAT are in various formats but essentially consider written communication, critical reasoning and problem solving. They have a scientific component. The UKCAT consists of four cognitive subtests namely verbal reasoning, quantitative ability, abstract reasoning and decision analysis (all attributes felt to be important in medicine). It was first administered as an online test in 2006 by the UKCAT Consortium comprising 26/31 of the UK Medical schools by its agent Pearson Vue in testing centres throughout the world. Each cognitive test has a scale score ranging from 300-900 with a mean set to 600 using the 2006 reference cohort. Universities and candidates receive both subtest scores and the total test score which ranges from 1200-3600. A fifth test, currently administered for research purposes only, is a behavioural test intended to measure a number of non-cognitive competencies to include empathy, robustness and integrity: features associated with good doctors. Reliability scores of the cognitive subtests range from moderate to high. Scores showed a negative correlation with age; males performed better than females and the ethnic grouping black/British were the lowest performing group. The UKCAT Consortium claims it is a fair and reliable test [15].

There have been several small studies on the predictive validity of UKCAT. One from Dundee/Aberdeen and one from Nottingham show no predictive validity whereas one from Newcastle does[16-18]. Our own findings at QUB for our 2008 entry cohort show no relationship between UKCAT score (both total score and subtest scores) and performance in years 1 and 2 of the course. This may change in the later part of the course where there is more emphasis on clinical reasoning and problem solving. All these studies suffer from small numbers and problems with generalizability. The potential for the UKCAT project is that it now has 4 cohorts of applicants who have taken the test accompanied by progression data from member Medical schools. This is an enormous achievement with considerable potential and it is hoped that as a result the predictive validity of the test will be determined.

There is mixed evidence internationally for the predictive validity of aptitude tests. McManus followed a Westminster cohort of medical students for 20 years. Whilst A-levels were predictive of outcome a standard IQ test was not[13]. Tests such as MCAT in the US have shown predictive validity. Emery has shown predictive validity for preclinical examinations with BMAT but only includes one medical school and numbers are small[19]. Concerns have been raised about UKCAT. A recent study from Scotland of 1st year medical students has raised concerns about the cost and fairness of the test , the use of the data in selection processes by medical schools and the influence of test preparation[20]. UKCAT state that 6.5 per-cent of their applicants receive bursaries and that their website offers two timed practice tests which address issues around candidates needing to pay commercial organisations for test preparation[15]. A recent study of A- level and UKCAT performance in applicants applying to UK Medical and Dental schools in 2006 found that UKCAT moderately correlated with A-level and that the total score did provide a useful proxy for A-levels in the selection process. It did show a bias toward males and social class 1 applicants[21]. The definitive verdict on how much UKCAT gives added value to the selection process should be available in the next few years and is keenly anticipated.

Personality testing

Ideally doctors should be safe practitioners who manifest considerable job satisfaction. We know that introverted, neurotic doctors can burn out although conversely the same traits can be associated with safe practitioners[22]. There is no consensus of opinion on the personality best suited for the practising physician. Doherty and Nugent have reviewed seven longitudinal studies which examined student's scores on valid personality tests and compared these with outcome measures around performance and stress. The studies come from UK, Belgium, US and Norway. Four of the studies looked at personality factors and academic success, one considered personality and clinical competence and two looked at relationship between personality and stress. The authors concluded that not only does conscientiousness predict long term success in medical training but also vulnerability to stress if it is accompanied by high levels of neuroticism and low levels of extraversion[23]. These findings are in keeping with job performance findings in other professions[24] .

Powis claims that the inclusion of personality tests in selection to Australian Medical schools significantly adds to the ability to predict candidates who will perform well in the course[25]. UKCAT includes psychological tests within its battery of non-cognitive tests which are currently being administered for research purposes only and are not currently being used in the selection process.

Random Selection

Dutch Medical schools select sixty per-cent of their intake using predetermined criteria and the remainder by national ballot. Applicants can apply three times. Dutch students are in favour of this as they argue that it redresses the power of the Medical schools[26]. In 2003 Queen Mary's London, previously referred to as Bart's. and the London introduced a ballot for entry into its graduate entry programme. The negative publicity created by the ballot led to its withdrawal.

Interviews

Traditional interviews are used as part of the selection process in most medical schools in UK, US and Australia. The process usually comprises two or three interviewers using either unstructured or semi-structured questions. Medical students, NHS staff, the public and academics have all been used as interviewers. Traditional interviews are subject to bias in terms of gender, age, race, halo effects, hawk/dove interviewer effects, tendency to place weighting on unfavourable information, effect of similarity/dissimilarity of interviewer to interviewee etc[27]. In addition the interview process can be affected by the impact of the previous candidate and the effects of pre-interview information about the applicant. While the face validity of interviews is strong Kreiter has shown that they have a low to moderate reliability and has called into question the fairness of the interview in the selection process[28] . Harasym et al in their paper on reliability and validity of interviewers judgments using simulated candidates have shown that interviewer accuracy was only moderate (56 per-cent) and questioned the validity and reliability of two person interviews[29]. The context of the interview can also affect outcome i.e. the individual's ability to problem solve can be affected given differing scenarios. Even though examiner reliability can be improved by training and the use of semi-structured questions a single interview in a specific context may not provide a true assessment of the applicant's ability. Similar arguments led to the development of the Objective Structured Clinical Examination which tests clinical skills using a multiple sample approach. Eva and his colleagues from McMaster coined the term Admissions OSCE or Multiple Mini Interview(MMI) in response to concerns about the reliability of interviews[30]. This consists of multiple stations each with a different assessor, set in different contexts (non-clinical) designed to test predetermined non-cognitive competencies held to be important for a medical career. The fresh start with each station dilutes hawk/dove assessors and allows independent assessment in multiple situations. His original paper tested for the domains of critical thinking, ethical decision making, communication skills and knowledge of the healthcare system. A reliability coefficient (Cronbach's Alpha) of 0.65 was reported which is much higher than that associated with traditional interviews. Axelson and Kreiter have shown that increasing the number of interview stations added more to reliability than increasing the number of interviewers per station[31]. Reiter et al have looked at violations of test security. They describe several studies where MMI station stems were randomly allocated to some groups of applicants. This did not influence applicants' performance ranking[32]. Rosenfield in another study from McMaster concluded that although MMIs require greater preparatory effort and the need for an assessment centre they require fewer person hours and have cost advantages over traditional interviews[33]. Humphrey et al used MMIs to recruit paediatric SHOs in Warwickshire. Both candidates and interviewers agreed that the process was a fair and acceptable tool for selection in UK specialist training[34]. Eva has shown that for Canadian students the correlation between admissions MMI and the number of stations passed in the OSCE component of the Canadian Qualifying Examination required for licensure was $r=0.43 (p<0.05)$. It was also a better predictor when compared with other selection instruments used in McMaster[35].

GRADUATE –V-UNDERGRADUATE ENTRY TO MEDICAL SCHOOL

In North America medical school programmes are almost exclusively 4 year graduate entry programmes (GEP) whereas in Australia and the UK there is a mixture of GEPs and undergraduate programmes to which graduates can be admitted. James in his retrospective study of predictors of success in the undergraduate course in Nottingham Medical school 1970-95 showed that mature or graduate entrants were more successful in obtaining a first class BMed.Sci. degree but were less successful in passing BMBS[14]. A study comparing the academic performance of graduate and undergraduate entry medical students completing the same preclinical curriculum at the University of Melbourne showed that graduate students performed better in all four bioscience assessments and also on early clinical skill assessments[36]. This study reflects our own findings at QUB for the 2008 entry cohort in that although our numbers of graduates are small over the first 2 years of the course, the graduates performed

Table 1

Graduate v Undergraduate performance in Examinations for Y1 and2 of the Medical Course QUB (2008 entry)

Group Statistics						
	Graduate	N	Mean	Std. deviation	Std. Error Mean	P value
Bioscience exams Y1	no	220	68.51	7.12	0.48	0.03
	yes	15	72.58	5.33	1.38	
Bioscience exams Y2	no	219	70.89	8.16	0.55	0.18
	yes	15	73.79	7.24	1.87	
Three Clinical Exams(OSCE) Y1 and 2	no	219	74.5	7.42	0.50	0.03
	yes	15	78.82	6.95	1.80	

better in all tests and significantly so in yr1 Bioscience exams and across all yr 1 and 2 Objective Structured Clinical Exams. (Table1)

Arguments for graduate entry include higher motivation, widening diversity, faster production of doctors and proven ability in an academic tertiary environment. School leavers on the other hand are close to the academic ceiling and have good study skills. Although there is evidence that graduate entry widens diversity there is no evidence that graduates make better doctors[37].

In March 2007 the QUB/DHSSPS Strategic group met to discuss graduate entry to Medicine at QUB[38] . A separate graduate programme was rejected because of cost and the sustainability of two courses competing with each other side by side for placements/resources. It was felt that instead there should be multiple entry points into the Medical course and a strategy was developed to double the percentage of graduates from 6 per-cent in 2007 to 12 per-cent. It was felt that this mix of students some of whom had already completed a degree programme would bring diversity to the student experience given the mature approach of graduates and their different life experiences when compared to school leavers

SELECTION FOR MEDICINE (2012 ENTRY) AT QUB

There is considerable variation in the selection tools used by Medical schools in the UK. Most schools_interview but criteria for shortlisting for interview vary from evidence of previous academic ability, performance in aptitude tests, predicted performance at A-level, scoring of personal statements or a combination of the above[39].

Relaying bad news to a cancer patient requires both communication skills and empathy along with cognitive knowledge of the management options and prognosis. The desired endpoint is not a bookworm or a butterfly but a well rounded doctor who exhibits both cognitive and non-cognitive competencies[35]. This concept along with best evidence on selection from the literature and our own research findings at QUB on the predictive validity of our selection tools has fashioned a change in our processes for 2012 entry.

Alongside this has been our strategy to internationalise the school and to encourage graduate entry to medicine. Our 2010 entry cohort includes 17.6 per-cent graduate entry, 16 per-cent from GB and ROI and 5 per-cent are international students. Fifty four per-cent of the 2010 intake were female. 20.8 per-cent of our 2009 entry cohort were from socio-economic groups 4 and 5; higher than most other schools[4]. The Department of Health (N.I.) has recently increased our international numbers from 12 to 26 for 2011 entry in keeping with the proportion of international students in other UK medical schools. We are currently actively recruiting both students and staff from South East Asia and North America.

For 2011 entry we had 850 plus applicants competing for 236 EU and 26 international places. There are a number of entry pathways into the Medical school and these include Y14, post A- level and graduate entry.

It has been agreed by both the School and University that for 2012 entry there will be a two stage Admissions process. In keeping with the best practice this process is transparent, has been published , is available on line[40] and the predictive validity and reliability of our selection instruments is monitored in keeping with Schwartz guidance[5]. The first stage will recognise past academic achievement in keeping with evidence from the literature along with recognition of the importance of aptitude tests (UKCAT). We do not exclude applicants on the basis of aptitude tests alone. In stage one which is cognitive, applicants will be scored and ranked as follows

For Y14 applicants the best 9 GCSEs will be considered with 4 marks for an A star and 3 for an A. Maximum 36 points

For graduates holding a 2:1 Honours degree or better (or predicted to achieve same) and who hold 3Bs at first attempt(ABB from 2013 entry) in the specific subject requirements at A level-36 points will be allocated.

For post A -level applicants who already have 3As at A-Level and an A at AS Level 36 points will be allocated.

For ROI applicants the best 9 junior cert intermediate are considered with 4marks for an A and 2 marks for a B. The maximum mark is 36 points

TABLE 2:

UKCAT banding scores of EU applicants applying for medicine at QUB in 2011

Band Score	Scoring Range	Medicine Banding Total 2011 APPLICATION	%
0	1200 - 1299	6	1
	1300 - 1399		
	1400 - 1499		
	1500 - 1599		
	1600 - 1699		
	1700 - 1799		
	1800 - 1899		
1	1900 - 1999	22	3
	2000 - 2099		
2	2100 - 2199	87	11
	2200 - 2299		
3	2300 - 2399	198	24
	2400 - 2499		
4	2500 - 2599	259	33
	2600 - 2699		
5	2700 - 2799	160	20
	2800 - 2899		
6	2900 - 2999	63	8
	3000 - 3099		
	3100 - 3199		
	3200 - 3299		
	3300 - 3399		
	3400 - 3499		
	3500 - 3600		
	Total	**795**	**100**

All applicants will take UKCAT in the year of entry and their overall score will attract up to six points The distribution of total UKCAT scores for our 2011 entry cohort is shown in Table 2.This score will be added to their knowledge based score and all applicants ranked. The top circa 500 applicants will then be considered under stage 2 of the selection process which will consist of a nine station multiple mini interview to determine non-cognitive performance. Multiple Mini Interviews are used to test non-cognitive competence in keeping with best evidence available from the literature. The applicant's personal statement is considered within this process. The non-cognitive competencies which are tested have been determined using a Delphi technique by both the public and Faculty and have been published[40]

Final decisions about whether or not to make an offer will be made on the basis of interview ranking alone (i.e. Stage 2 results) and not in combination with other factors. During the 2011 entry process, approximately 200 applicants took our MMI. Each station lasted for 5 minutes and the examination was blueprinted to test for motivation, communication, empathy, problem solving, integrity and ethical reasoning. One third of our stations involved role-players and the others were semi-structured interviews. Prior to the interviews all assessors were trained and all participated in a standardisation process on the day of the assessment. For our 2011 MMIs the Cronbach's alpha was 0.56. and there was a Gaussian distribution of marks from 30-85 per-cent for candidates. The MMIs were standard set using the borderline regression method and offers were made to applicants who reached the cut score as determined by the panel of assessors. The school is currently actively recruiting assessors and these positions are open to both clinical academic, non-clinical academic and NHS staff. The MMI process is a considerable challenge for us and will require 120 days of assessor time per annum.

While some of our Admission instruments will favour certain groups we try to achieve an overall balance and are currently monitoring all of our selection tools to ensure equality.

Further details regarding the admissions process for Medicine at QUB along with video clips of MMIs are available on www.qub.ac.uk/schools/mdbs/medical/Prospectivestudents.

We feel we now have a selection process which meets GMC recommendations in that it is transparent, objective, uses a variety of selection tools which are constantly monitored in keeping with best practice and also considers both cognitive and non cognitive factors. We hope this approach will widen participation compared to the previous approach which was largely cognitive and relied on selection using very narrow parameters. Our approach to selection also has an advantage in that NHS colleagues, the wider public and academic staff will all have an input into selecting tomorrow's doctors.

CONFLICT OF INTEREST

The author is a Director on the UKCAT Board and a member of the UKCAT Development and Research groups

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Paper

Referral patterns, clinical examination and the two-week-rule for breast cancer: a cohort study

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ABSTRACT

Introduction: Current NHS guidelines require patients with suspected breast cancer to be seen urgently at a specialist breast clinic. The aim of this study was to assess referral patterns and clinical findings of patients referred to a specialist breast clinic.

Materials and Methods: A prospective database was maintained for consecutive patients referred. Symptoms and clinical findings in primary and secondary care were recorded. Correlation with final diagnoses was made. Tertiary referral patients were excluded.

Results: 1098 patients attended a specialist breast clinic over six months. 588 (54%) were referred as urgent, 285 (26%) routinely and 225 (20%) were unspecified. 492 (45%) patients were referred with the incorrect referral priority. 42 patients were unexamined in primary care. Examination findings in primary and secondary care correlated in only 487 (46%) patients. Examination in primary care when compared with secondary care was highly sensitive for detecting breast lumps, but specificity was low. 86 patients (8%) were diagnosed with breast cancer, 72 (84%) were referred urgently, 6 (7%) routinely and 8 (9%) as unspecified priority. Regardless of the clinical expertise of the referrer, sensitivity and specificity of the two-week guidelines for cancer are low.

Conclusions: Examination findings in primary and secondary care correlate in only 46% of referrals. Additionally, 55% of referrals were of the correct priority. The two-week rule guidelines have poor sensitivity and specificity for cancer. The safest and fairest policy would be to abandon the concept of urgent referral criteria and see all patients in a timely fashion. Alternatively, simplifying the referral criteria would improve sensitivity and specificity for cancer without leading to increased waiting times.

Key words: Breast neoplasms, referral and consultation, guidelines

INTRODUCTION

Breast cancer is the most common malignancy among women with a lifetime risk of 11%.[1] Over 45,000 women are diagnosed with breast cancer each year in the UK.[2-5] Towards the end of the 20th century, UK survival rates for breast cancer were among the lowest in Europe, with long waiting lists for both diagnosis and treatment thought to be at least partly to blame.[6-8] In 1998 the Department of Health attempted to address this problem in their circular, "*Breast Cancer waiting times- achieving the two week target"* with the aim to facilitate access to specialist services and ultimately improve survival.[9] Despite the lack of strong scientific evidence this circular stated that, by April 1999, all patients with suspected breast cancer should be referred urgently to secondary care and seen by a specialist within two weeks of referral.[10, 11]

The effectiveness of two-week-wait guidelines for cancer in general and breast cancer in particular continues to be questioned. Of particular concern is the poor predictive value of symptoms and symptom clusters for cancer.[12-14] Additionally, there has been reluctance about switching responsibility for decision making regarding referral priority to the non-specialist.[15, 16] General Practitioners (GPs) express concern about missing a cancer diagnosis and thus have a propensity to refer patients urgently, while specialists complain of the rule compromising their professional autonomy, report poor adherence to guidelines by primary care and patients with cancer referred outside the two-week-rule experience much anxiety. [13,16]

An increasing proportion of patients are referred urgently and while two-week targets are currently being met, a corresponding increase in waiting time for the routine group has been reported.[12, 17] Most worryingly, the proportion of cancers detected in patients referred routinely also appears to be on the rise.[12]

The Ulster Hospital Dundonald serves a population of over 260,000 in Belfast and North County Down. It provides services for both secondary and tertiary referral and plays an important role in breast screening. Each year approximately 300 new cases of cancer are diagnosed. At the time of data collection the breast care service included two consultant surgeons, one staff grade breast physician, two specialist registrars and three breast care nurses. The aim of this study

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was to compare clinical findings at the specialist breast clinic with those documented in primary care, examine adherence to referral criteria by primary care and analyse the two-week-rule with regard to appropriate patient selection for cancer.

MATERIALS AND METHODS

Data were prospectively collected over a six-month period between 1st October 2006 and 31st March 2007. All consecutive referrals from primary care were included for analysis. Tertiary referrals, in-hospital referrals and screen-detected cancers were excluded. Data collection sheets were completed for each patient attending the breast clinic. Assessment included information on patient demographics, referral priority, clinical findings and diagnosis. All patients referred urgently were seen within two weeks, and those referred routinely were seen within four weeks.

Referral priority and its accuracy in relation to two-week-wait guidelines were examined while clinical findings in primary and secondary care were compared and correlated with final diagnoses. The predictive value of the two-week-rule was evaluated. Age was expressed as mean and standard deviation. Data were collected on Microsoft Excel (Microsoft Corp, Redmond, WA, USA) and then analysed using SPSS (Version 12, SPSS Inc, Chicago, Il, USA). Differences in age group were analysed using Kruskal-Wallis and the difference in proportions using Chi-squared test, with a p value of less than 0.05 considered significant.

RESULTS

During the study period the Ulster Hospital Specialist Breast Service received 1098 referrals from primary care. The mean age at referral was 46.9 years (± 15.5) and at cancer diagnosis 65 years (± 15.6). No patients were diagnosed with cancer under the age of 30 years. The risk of cancer, as expected, increased with age (p<0.0001) (Figure 1).

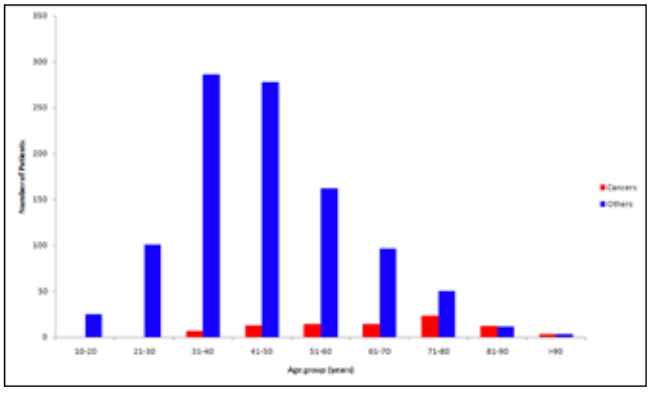

Fig 1. The proportion of patients diagnosed with cancer for age group within the whole cohort.

There were disparities in clinical findings between the breast clinic and primary care. Examination findings in primary and secondary care were significantly different and correlated in only 487 (46%) patients (p<0.0001) (Table 1, Figure 2). Examination in primary care when compared with secondary care was highly sensitive for detecting breast lumps, but specificity was low. Forty-two patients were not examined in primary care with one cancer diagnosed in this group. 48 (87%) of 55 patients with nipple discharge were referred as urgent, with no cancers in this group. It was not recorded if discharge was blood stained. No significant difference in accuracy of examination findings was found between different healthcare professionals in primary care, compared to the breast clinic.

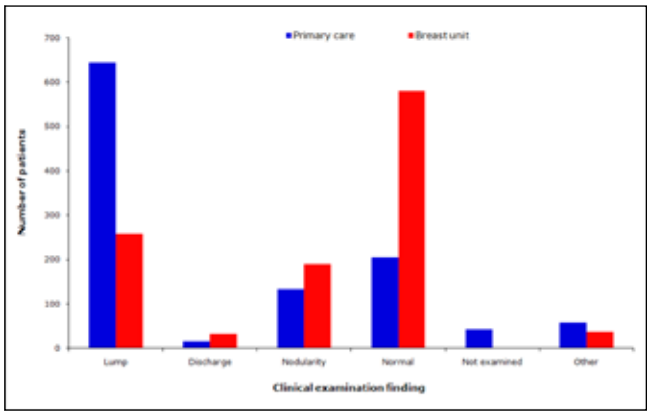

Fig 2. Clinical examination findings in primary and secondary care (p<0.0001).

TABLE 1:

Sensitivity and specificity of clinical examination in primary care compared with secondary care (To calculate GP sensitivity and specificity Breast Clinic findings were assumed to be both 100% specific and sensitive.)

	Sensitivity (%)	Specificity (%)
Lump	97	40
Discharge	36	48
Nodularity	24	70
Normal	31	35
Other	46	64
To calculate GP sensitivity and specificity Breast Clinic findings were assumed to be both 100% specific and sensitive.		

588 (54%) patients were referred urgently, 285 (26%) routinely and 225 (20%) had an unspecified priority. According to documented symptoms and examination findings in primary care, 492 (45%) patients were referred with an incorrect referral priority; 141 (24%) urgent referrals did not fulfil the necessary criteria; 127 (56%) unspecified priority referrals and 126 (44%) routine referrals should have been referred urgently. All those referred as urgent or routine were seen as such, with the unspecified priority referrals triaged on a daily basis by a Consultant Surgeon. The 127 unspecified priority referrals which should have been referred urgently were seen within 2 weeks, meaning 715 patients were seen within 2 weeks of referral.

Seven hundred and eight (64%) patients referred had no identifiable breast pathology when seen in secondary care; 330 had been referred urgently. 271 (25%) had benign breast problems, such as fibroadenomata and duct ectasia; 168 were referred urgently. Eighty-six (8%) had cancer; 72 had been referred urgently, 6 routinely and 8 were of unspecified priority. Eighteen had other non-breast problems, ranging from eczema to sebaceous cysts.

Table 2:

Number of urgent referrals, cancers referred urgently and sensitivity and specificity of current and proposed urgent referral guidelines for breast cancer.

	Number of urgent referrals	Number of cancers referred urgently	Sensitivity	Specificity
Current Guidelines				
Actual GP Priority	588	72	84%	49%
GP priority + triaged referrals	715	79	91%	37%
According to two-week-rule by GP findings[1]	700	78	91%	39%
According to two-week-rule by BC findings[2]	307	74	86%	76%
Proposed Guidelines				
By GP findings i.e. Current clinical expertise[3]	691	82	95%	32%
By BC findings i.e. Ideal clinical expertise[4]	395	85	99%	65%
Statistical significance 1 vs 2- p<0.0001; 3 vs 4- p=0.0004; 1 vs 3- p=0.77; 2 vs 4- p=0.58				

Strict application of current guidelines, based on the primary care clinical findings, would have increased the number of urgent referrals from 588 (54%) to 700 (64%), but decreased the number actually seen on an urgent basis from 715 to 700 (p=0.77). Sensitivity for cancer would have improved from 84% to 91%, while specificity would have decreased. If the breast clinic clinical findings had been used to refer patients according to current guidelines, the priority would have been markedly different, with only 307 (28%) referrals being classified as urgent (p<0.0001). Although specificity of the guidelines for cancer would improve when compared with primary care, sensitivity would only reach 86%, missing 14% of cancers (Table 2).

Proposed Guidelines

Urgent Referrals

1. Female >30years with
   a. A breast lump
   b. Asymmetric nodularity
2. Male aged >50 years with a palpable unilateral swelling

Fig 3. Proposed alternative two-week referral guidelines

Data were analysed further to assess for any link between particular examination findings and cancer. Alteration of the guidelines (Figure 3) shows a trend towards improved sensitivity and specificity for cancer in primary care (Table 2) (p=0.77). If breast clinic findings are used according to these proposed guidelines, sensitivity and specificity for cancer would improve significantly compared with primary care (p<0.0001).

DISCUSSION

Since breast cancer is the commonest cancer among women in Europe, the UK government was justifiably concerned about the low survival rates in comparison to other western countries. The two-week-rule aimed to improve patient access to specialist services and allow rapid diagnosis and earlier treatment. Since its introduction the quality of both guidelines and referrals has been questioned.

In this study, a large number of sub-optimal referrals were received, evidenced not only by the 225 referrals whose priority was unspecified, but also by the incorrect grading of referrals (45%). More than twice the number of patients who would have been referred urgently based on breast clinic findings were seen on an urgent basis, suggesting a tendency to refer urgently in primary care. This may, as other studies have suggested, be due to a decrease in diagnostic accuracy among general practitioners, concern about missing a cancer diagnosis or a lack of assurance in the referral guidelines.[16, 18] Moreover, patient anxiety may pressurise general practitioners into referring urgently.[16]

Clinical findings in primary and secondary care were often contradictory (54%). This can be explained by an expected lower level of clinical experience in primary care and perhaps uncertainty in declaring an examination to be normal.[16] While there will remain to be room for improvement with regard to sensitivity and specificity of examination in primary care, specialist clinical examination applied to the two-week-wait criteria would also yield poor sensitivity and specificity for cancer. Non-urgent referrals would have included 12 (14%) cancers if breast clinic findings had been used to refer. Thus the main areas of concern with the current system lie with either the concept of urgent referrals or the referral guidelines themselves, rather than the clinical expertise of the referrer. As clinics have struggled to meet demands set by the two-week-rule, patients referred routinely are being forced to wait longer for diagnosis and treatment, creating a two-tier referral system. Although our unit is committed to seeing routine referrals within 28 days, other institutions may have significantly longer waiting times.[15]

While rapid access to specialist services is to be welcomed,

the current system would appear to be disadvantaging a significant proportion of patients with cancer.[12,19,20] All patients with suspected breast malignancy experience high levels of anxiety and distress during the period leading up to their assessment and deserve to be seen promptly from both a psychological and oncological perspective.[21]

The safest and fairest policy would be to abandon the concept of urgent referral criteria and see all patients in a timely fashion. Several institutions have suggested seeing all patients within two-weeks of referral.[12] This would require a dramatic increase in capacity and therefore funding to bring the backlog in the system up to date. While this may be an ideal scenario, ongoing budget cuts requiring efficiency savings make this option unlikely. Evidence has shown that significant differences in survival rates may only begin to become apparent after delays of over 3 months[8] Therefore, we would suggest a maximum period of 4 weeks is reasonable from an oncological and psychological point of view, without compromise of patient safety or outcome.

It is clear that government is committed to the principle of an urgent referral system and it is unlikely that the concept will be abandoned. An alternative would be to simplify the referral criteria (Figure 3), improving sensitivity and specificity for cancer without leading to a corresponding increase in urgent referral numbers, thus preventing diagnostic and treatment delay (Table 2). An improvement in clinical expertise in primary care would allow greater diagnostic confidence and reduce the referral of patients who do not need to be seen by a specialist. This would help reduce diagnostic and treatment delays for those who do need referred.

The authors have no conflict of interest.

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Paper

Prevalence of patent foramen ovale in a consecutive cohort of 261 patients undergoing routine "coronary" 64-multi-detector cardiac computed tomography.

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ABSTRACT

Background: A patent foramen ovale (PFO) is strongly associated with cryptogenic stroke (CS), neurological and other phenomena. The reported prevalence of PFO varies according to the imaging technique used and population studied.

Purpose: To measure prospectively, the prevalence of PFO in a cohort of consecutive patients attending for routine "coronary" CT angiography using standard, everyday coronary protocols including low-dose prospective ECG gated studies.

Methods: Standard coronary imaging protocols were used. PFOs were graded according to the classification of Williamson *et al*.[1]

Results: 261 patients were studied. A PFO was identified in 22.6% (11.5% grade 1 (closed flap), 6.5% grade 2 (open flap) and 4.6% grade 3 (open flap with jet)). A further 6.1% had an atrial septal aneurysm.

Conclusions: The prevalence of all grades of PFO (22.6%) and open flap PFO (11.1% = grade 2 and 3) with this technique compares with 24.3% by trans-oesophageal echocardiography (TOE) and 14.9% by saline contrast echocardiography (SCE)[2, 3] Further comparative studies are required but we believe an open flap PFO or ASA should be identified and recorded during cardiac CT. This approach may identify those at risk of cryptogenic stroke as well as avoid unnecessary tests in stroke patients.

Keywords: Patent foramen ovale; atrial septum; cardiac anatomy; computed tomographic angiography; non-invasive angiography.

Although the primary clinical role of 64 Multi-detector coronary CT (64-MDCT) is assessment of the coronary arteries, the excellent spatial resolution of the technique allows detailed imaging of other cardiac structures during a routine "coronary" examination.[4] The inter-atrial septum (IAS) is one area that lends itself to such investigation, but it has been neglected in some otherwise comprehensive assessments of non-coronary cardiac CT pathology.[5, 6]

One study has however, looked at the prevalence of patent foramen ovale (PFO) in a mixed cohort of research volunteers and suspect ischaemic heart disease (IHD) patients using retrospective ECG gating –a relatively high dose technique by 2010 standards[7]. We set out to measure prospectively, the prevalence of PFO in a cohort of consecutive suspect IHD patients attending for routine coronary CT angiography using standard, everyday coronary protocols (including use of low-dose prospective ECG gated protocols as frequently as possible).

The IAS is formed from the union of two separate layers that form a flap valve in utero to facilitate the fetal circulation. Failure of the flap valve to close after birth can result in a PFO. This communication between right (RA) and left (LA) atria provides an anatomic substrate for paradoxical embolisation of thrombus and is strongly associated with cryptogenic stroke (CS).[8] An atrial septal aneurysm (ASA) can also occur and is associated with both PFO and CS.[8]

METHODS

The study was approved by the Western HSC Trust Research and Development (Ethics) Chair. Data was collected prospectively on patients attending for 64-MDCT between the 18th June 2009 and 27th February 2010.

COMPUTED TOMOGRAPHY

64-MDCT was performed using a Philips Brilliance 64 system (Philips Medical Systems, Eindhoven, Netherlands). Patients were monitored on electrocardiogram (ECG) and a 20FG intravenous cannula placed in an ante-cubital fossa vein. All patients were in sinus rhythm. After heart rate optimisation and sub-lingual administration of 400 micrograms of glyceryl tri-nitrate, non-ionic contrast material (Iohexol, Omnipaque

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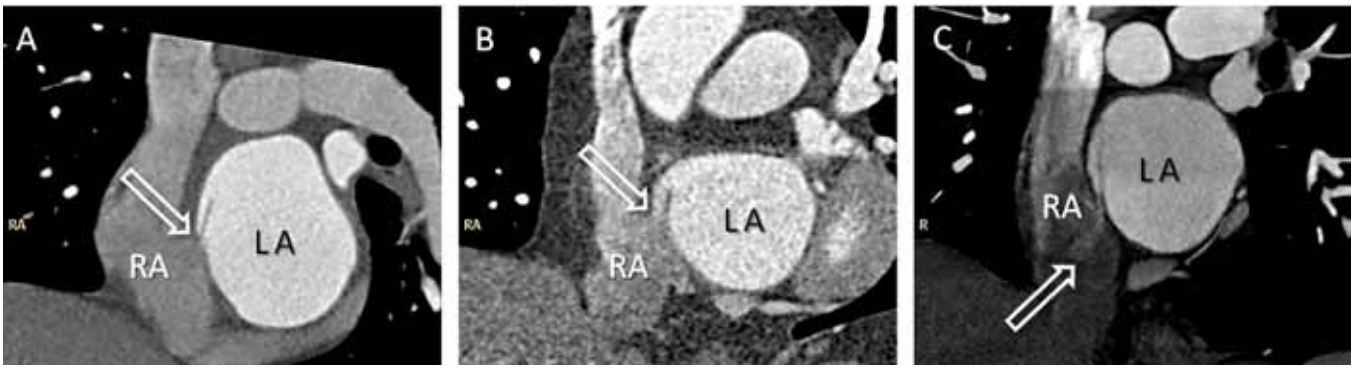

Fig 1. Panel A. Oblique coronal view: hollow arrow demonstrates closed flap (Grade 1 PFO), left atrium =LA, right atrium =RA. **Panel B.** Oblique coronal view: hollow arrow demonstrates open flap (Grade 2 PFO . **Panel C.** Oblique coronal view: hollow arrow demonstrates jet from open flap (Grade 3 PFO).

350, GE Healthcare AS, Norway) was injected into the vein (90 ml at a flow rate of 5.5 ml/sec followed by a saline chaser of 50mls at 5.5 ml/sec). A bolus tracking technique was used to determine when contrast density was optimal for coronary imaging. Scanning was performed during a single breath hold. In patients with a low and stable heart rate (<64 beats per minute), prospective ECG triggering was used for data acquisition; otherwise retrospective ECG gating was used. In all cases, data was obtained at a single time point (75% of the R-R wave interval on ECG). Detector collimation was 64 x 0.625mm with images reconstructed to a slice thickness of 0.6mm. Tube voltage was 120kV with a rotation time of 400 msec. Standard axial images and 2D multiplanar reformations were used for image interpretation. Coronal oblique projections through the IAS were specifically evaluated for the presence of each of the CT criteria for PFO outlined below.

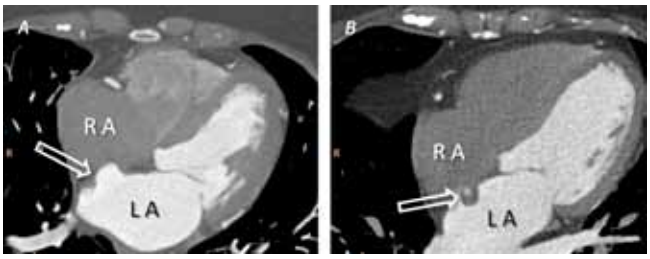

Fig 2. Panel A. Axial view with atrial septal aneurysm highlighted by hollow arrow, left atrium =LA, right atrium =RA. **Panel B.** A small rounded mass is identified over the fossa ovalis with a vascular supply (hollow arrow). This proved to be a left atrial myxoma.

CLASSIFICATION OF PFO AND ASA

Williamson *et al.* devised a classification system based in part on chart review of 20 patients with PFO who underwent both CT and Trans-oesophageal echocardiography (TOE).[1] PFO anatomy on 64-MDCT was classified by 3 criteria:

1. A distinct flap at the expected location in the LA (closed flap, Figure 1, panel A).
2. A continuous column of contrast material between the septum primum and septum secundum, connecting the LA and RA (open flap, Figure 1 panel B).
3. An open flap plus a jet of contrast material from the column into the RA (open flap with jet, Figure 1, panel C).

When compared with TOE diagnosis, the positive predictive value of criterion 1 alone was 75%, criteria 1 +2 together was 80% and 1+2+3 together was 100%.[1]

ASA was defined as a redundant and hyper-mobile portion of the IAS that demonstrated more than 10-mm excursion from the centre line (Figure 2, panel A).[9]

We also categorised any potential IAS source of cardio-embolism into medium and high risk according to the TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification.[10]

RESULTS

The study population consisted of 261 consecutive patients of whom 54% were male (mean age 56 years, range 21 to 81 years) and 46% were female (mean age 57 years, range 36 to 81 years). Study quality was sufficient for PFO classification in all cases. Study quality for coronary imaging was graded as excellent in 50%, good in 28%, fair in 16% and poor in 6%. A low dose prospective ECG triggered protocol was used in 38%. Results are displayed in Table 1. Amongst the 261 patients, 59 (22.6%) demonstrated a PFO. This could be subdivided into 30 (11.5%) with a grade 1 PFO, 17 (6.5%) with grade 2 and 12 (4.6%) with grade 3. In total, 29 (11.1%) of patients had an open channel between the atria during the CT scan (grade 2 or 3 PFO).

An atrial septal aneurysm was identified in 16 (6.1%) patients but no jet of contrast from left to right atrium was seen in association with this.

One patient was seen to have an early (1.1cm diameter) left atrial myxoma with prominent central vasculature (Figure 2, panel B).

Table 2 lists patients with conditions classified by the TOAST criteria for medium or high risk of cardiac embolism.[10] Of note, 17.2% of patients had medium cardio-embolic risk.

DISCUSSION

PFO is strongly linked with conditions such as CS, pulmonary embolus and more controversially, migraine with aura.[8, 11, 12] Major studies to determine the role of PFO closure devices are underway.[13] The reported prevalence of PFO depends

however, on the imaging modality used and the population studied. Prevalence based on normal heart autopsy is 27%, whilst SCE and TOE yield figures of 14.9% and 24.3% respectively in normal adults.[2, 3, 14]

Table 1.

Numbers and percentages of patients displaying conditions of the inter-atrial septum.

Condition	Number of Patients	Percentage of Total
Normal	185	70.9%
Myxoma	1	0.38%
Grade 1 PFO	30	11.5%
Grade 2 PFO	17	6.5%
Grade 3 PFO	12	4.6%
Atrial septal aneurysm	16	6.1%
All PFOs (Grades 1,2 +3)	59	22.6%
"Open" PFOs (Grades 2 +3)	29	11.1%

Table 1 Legend: PFO = patent foramen ovale. Graded by Williamson classification[1].

Prevalence is higher in vulnerable groups; amongst migraineurs in the MIST 1 study, a moderate or large PFO was detected in 37.7% by SCE, whilst 43.9% of young CS patients were demonstrated to have a PFO by TOE.[15, 16] TOE is regarded as the gold standard imaging technique for PFO assessment.[17, 18] Recently, real time 3D TOE has proved useful in guiding PFO closure device procedures.[19]

Moving away from echocardiography, only a handful of studies of PFO anatomy have been performed on 64-MDCT.[1, 7, 20, 21]

Table 2.

Conditions classified under the TOAST criteria for cardioembolic risk. [11]

Condition/Risk Status	Number of Patients	Percentage of Total
High-risk source		
Myxoma	1	0.38%
Medium-risk source		
Grade 2 or 3 PFO	29	11.1%
Atrial septal aneurysm	16	6.1%
TOTAL	**46**	**17.6%**

Table 2 Legend: PFO = patent foramen ovale. Graded by Williamson classification[1].

Two studies have concentrated on comparing 64-MDCT with TOE. Williamson *et al*. reviewed 214 charts of patients attending for 64-MDCT and found 20 who had also undergone TOE. Of the six with PFO on TOE, *all* had grade 1 or higher PFO by the criteria defined in that study.[1] Kim *et al.* retrospectively analysed images from 152 stroke patients who had undergone both TOE and CT. Twenty-six PFOs were identified by TOE with 19 of these patients having a grade 3 (open flap with jet) PFO appearance on CT.[20] The authors also noted a "channel-like appearance" of the IAS which corresponded to grade 1 (closed flap) and grade 2 (open flap) in the Williamson *et al.* paper. Compared with TOE, the two papers combined yield a sensitivity of 67-73%, specificity of 98-100%, positive predictive value of 91-100% and negative predictive value of 85-95% for a grade 3 CT appearance. In a more generalised study, CT was compared with TOE for detection of cardiac sources of embolism in 137 stroke patients.[21] Just under a quarter of the patients had PFO, ASA or an atrial septal defect identified by TOE. Overall sensitivity of CT was 89% with a positive predictive value of 100% for all embolic causes. The overall prevalence of all 3 grades of PFO in our study was 22.6%. We agree with previous authors that an open flap with direct communication between atria (grades 2 and 3) is more likely to represent clinically significant PFO, in which case, the prevalence falls to 11.1%.

STUDY LIMITATIONS

One major problem with assessing PFO by 64-MDCT is that the information is purely anatomical and obtained during a breath hold rather than Valsalva manoeuvre. The functional and flow information obtained with TOE cannot be emulated.

It is interesting to note that the prevalence of all 3 grades of PFO at 22.6% is very similar to TOE and autopsy reference data, perhaps some of the closed flaps (11.5%) would open if right atrial pressure was elevated. Unfortunately, the rise in central venous pressure associated with Valsalva manoeuvre or coughing also impedes the passage of intravenous contrast to the heart. Unacceptable respiratory motion artefacts would also be introduced.

Potentially, cine CT angiography[22] could give information about directional flow in a PFO and mobility of ASA, but the Valsalva manoeuvre problem would remain.

The point we wish to stress in this paper is that much useful information can be obtained during a routine coronary study without additional measures or high dose protocols.

The prevalence of ASA in our study (6.1%) falls within the range seen in TOE studies on non-stroke patients (4-8%) - this figure can rise up to 15 - 28% in stroke populations.[23, 24] We did not observe left to right contrast flow through an aneurysm but it is accepted that approximately 33% of adults with ASA also have PFO and ASA is considered a medium risk source of embolus by TOAST criteria.[8,9]

CURRENT GUIDELINES

The Society of Cardiovascular Computed Tomography (SCCT) guidelines on reporting studies state that any [non-coronary] abnormalities should be described and that cardiac chamber shunts are a required element of a comprehensive report[25] but given that 17.2% of our patients attending for routine coronary CT had a medium cardio-embolic risk (open flap PFO or ASA) perhaps more emphasis should be placed on this requirement.

CONCLUSIONS

64-MDCT allows accurate assessment of the IAS during routine "coronary" examination. We found the prevalence of open flap PFO and ASA to be 11.1% and 6.1% respectively

in a population of 261 patients undergoing routine 64-MDCT coronary study. Further comparative studies against SCE and TOE are required but we believe open flap PFO and ASA should be clearly identified and recorded during routine coronary CT angiography. This approach may identify those at risk of cryptogenic stroke as well as avoid unnecessary tests in stroke patients.

The authors have no conflict of interest.

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Case Report

Enterocutaneous fistulae presenting as a late complication of a non-functioning Ventriculo- Peritoneal shunt catheter.

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Accepted 22 February 2011

Abstract: A patient with spina bifida and hydrocephalus who had undergone multiple shunt revisions, presented with a 9 month history of chronic discharging sinuses related to a retained shunt catheter not visible on x-ray. This case report demonstrates the importance of clinical history and investigation in patients with retained catheters presenting with cutaneous sinuses.

Key Words: Ventriculoperitoneal shunt, retained ventricular catheter, shunt complications, congenital hydrocephalus, CSF shunt complication.

INTRODUCTION

Since the 19th century the peritoneal cavity has been used as a site for the secondary absorption of CSF (cerebrospinal fluid) via ventriculo-peritoneal shunts.[1] This practice has given rise to multiple complications including abdominal wall perforation, ascites, CSF fluid fistula, hernia, hydrocele, scrotal extrusion, ileus, intramuscular cysts, intussusception, migration of the peritoneal catheter, torsion, peritonitis, pseudocyst/tumour, vaginal and viscus perforation and volvulus. [1] Abdominal complications of ventriculo-peritoneal shunts are reported from 10-30% [2], and bowel perforation in 0.1-1.0% of cases. [3,4] This case discusses a rare complication of enterocutaneous fistulae via a non-functioning peritoneal shunt catheter.

CLINICAL DETAILS

We report a 39 year-old wheelchair bound man with a background history of spina bifida and myelomeningocele. He suffers from poikilothermia, restrictive lung disease and chronic renal failure. His initial treatment was undertaken elsewhere with closure of the spinal defect at birth and a ventriculo-peritoneal shunt inserted shortly after. He subsequently underwent 13 shunt revisions in the first 2 years of life. His family subsequently moved to the United Kingdom where he underwent a further 5 shunt revisions for shunt blockage and infection. His last shunt revision was performed at the age of 19 years. History from the patient's family revealed that he had 3 shunt catheters in situ; one on the right side which had been tunnelled over the scapular region and then down around his flank into the peritoneum, the second was a ventriculo-atrial (VA) shunt and the third which was a ventriculo-peritoneal (VP) shunt was inserted anteriorly down the right side. The reason for the unusual catheter course over his scapula is unknown. Most of his early neurosurgical records were unavailable at this presentation.

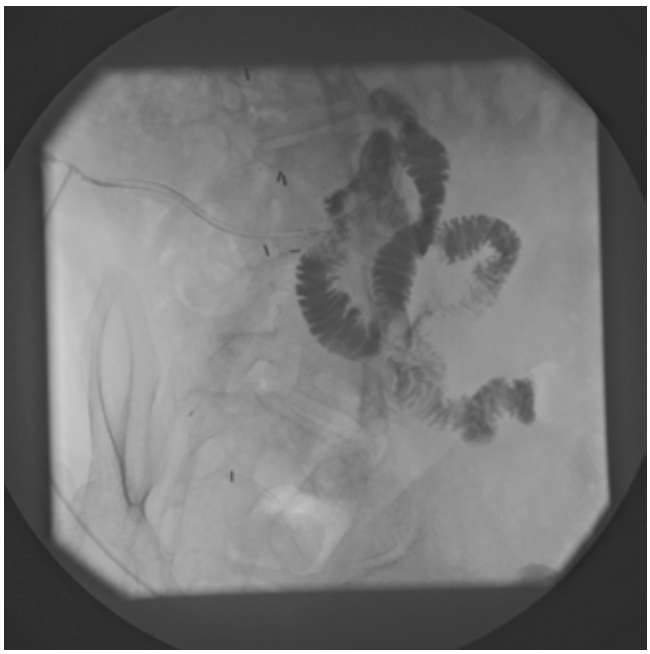

Fig 1. Right abdominal sinus fistulogram with arrows showing the outline of the shunt tubing entering the small bowel and contrast within the small bowel.

He presented to our unit with 2 discharging sinuses. The first sinus had been present for 9 months and was found on the anterior abdominal wall in the right hypochondrium. The second sinus began discharging 3 months prior to admission and was located suprascapularly on the right side. These were initially dressed on a daily basis; with later attempts of laying open the sinuses by general surgeons. Due to their persistent nature and the fact that he posed a poor anaesthetic risk he was referred to neurosurgery for further advice.

He had no new neurological deficit on admission, there was nothing to suggest that the working shunt had malfunctioned in any way, and he had no systemic evidence of infection. He was apyrexial, he had no meningism, there was no evidence of inflammation along any of the shunt tubing tracts and his abdomen was soft and bowel function normal. The peripheral white cell count and inflammatory markers were in the normal range.

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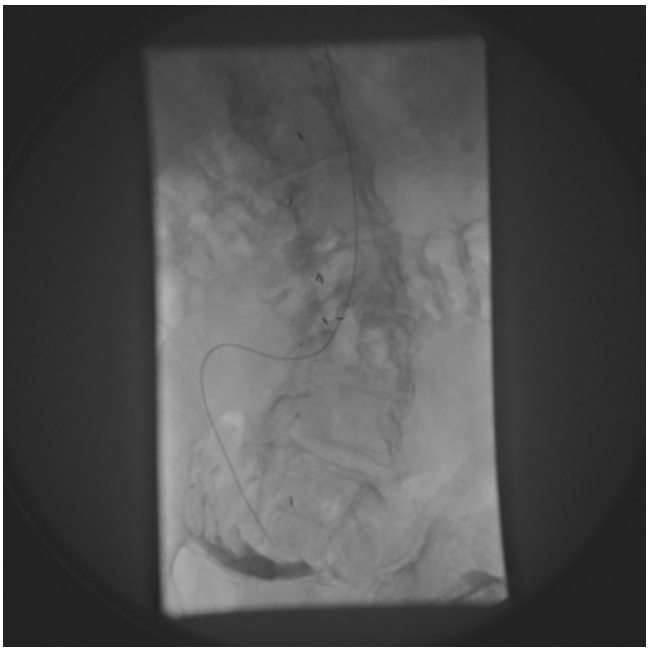

Fig 2. Shuntogram via the functioning shunt shows normal peritoneal drainage of contrast. Arrows show the catheter and drainage of contrast into peritoneum.

A shunt series of x-rays did not show any shunt tubing, although these were palpable in parts. A computer tomography scan of the brain showed evidence of a Chiari type 2 malformation, marked ventricular enlargement and a thickened skull vault. Swabs taken from both sinuses cultured pseudomonas, with MRSA (Methicillin-resistant Staphylococcus aureus) isolated from the abdominal wound only. We performed a fistulogram study using water-soluble contrast media for the abdominal sinus, which showed a well-defined lumen in keeping with the abdominal portion of the shunt tube, and a connection between the skin surface and a loop of small bowel distally with opacification of small bowel loops in the midline (FIG-1). Furthermore, it was noted that there was retrograde flow of contrast up the peritoneal shunt catheter. The supra-scapular sinus was not amenable to catheterisation.

To facilitate further investigation a shuntogram was performed via the valve on the functioning shunt, which showed no contrast extravasation into the skin or bowel with normal drainage into the peritoneal cavity (FIG-2). A small bowel series did not show the previously noted fistula.

As the patient had a sensory level at T6 he underwent exploration of the abdominal fistula without anaesthesia. The tract was explored and the tubing identified. The offending catheter was removed completely with surprising ease, following which the tract was curetted and wound packed with kaltostat. After this procedure the dorsal scapula fistula appeared dry and both fistulae began to close spontaneously.

DISCUSSION

Although the pathogenesis of intra-abdominal complications of VP shunt is uncertain, various possible mechanisms have been proposed. These include chronic low-grade inflammatory reaction and fibrous encapsulation secondary to irritation from catheter, infected CSF or sterile xanthochromic CSF.[2] Encasing fibrosis which has an anchoring effect on the tubing with resultant decubitus ulceration of the bowel wall and eventual bowel perforation has been described as one of the possible mechanisms of bowel perforation. [4] It has also been suggested that children with myelomeningocele and congenital hydrocephalus may have poorly innervated bowel leading to weakness and therefore a susceptibility to perforation. [4] Bowel perforation associated clinical peritonitis was documented in less than 15-25% of cases, as reported by Sells CJ, et al, and Yousfi MM, et al, making clinical diagnosis of this pathology difficult. [4,5,6]

The reports relating to bowel perforation secondary to ventriculo-peritoneal shunts have implicated the spring-coiled Raimondi peritoneal catheter as a cause and incidence has been reduced secondary to softer, more flexible Silastic® catheter usage.[4] The use of these catheters have perhaps contributed to the rarity of fistulae formation with relation to retained shunt hardware.

We are reporting a rare and unusual delayed complication of ventriculo-peritoneal shunting. The fact that the functioning shunt was intact and the retained old non-functioning peritoneal catheter was perforating the small bowel makes our case extremely rare. A literature review identified two previous cases of small bowel perforation in patients with functioning shunts. In both instances the shunt continued to function with no abdominal signs or symptoms. One patient presented with recurrent gram negative ventriculitis and the second patient was asymptomatic. [7] In the majority of cases removing the redundant catheter is difficult because of degradation of the tubing, calcification and fibrous tissue anchorage. In our case chronic low-grade infection had a role in releasing the catheter from surrounding fibrous tissue and facilitated its removal. In order to prevent long-term bowel complications removal of redundant catheters may be considered. In the majority of cases, abdominal shunt complications concerning patients with functioning shunts present with shunt blockage or infection at early stages. Our case which had translucent shunt tubing, an unusual catheter course and no previous documentation available highlights the importance of clinical history and examination accompanied with appropriate radiological investigations for patients with retained non-functioning peritoneal catheters presenting with a cutaneous sinus.

The authors have no conflict of interest.

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Case Report

Primary carcinoid tumour of the testis

David Neely, Samuel Gray

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INTRODUCTION

Testicular carcinoid tumours are very rare and account for less than 1% of all testicular neoplasms.[1] These tumours may be classified into three distinct groups, most commonly (1) primary testicular carcinoid, (2) carcinoid differentiation within a mature teratoma, and (3) metastases from an extra-testicular source. Testicular carcinoid tumours do not follow the age category of men affected most commonly by germ cell tumours (20-40 years), cases have been reported ranging in age from ten to eighty-three years.[2] Presentation of carcinoid tumours may be with self-detected testicular mass or testicular ache as with common testicular tumours, or uncommonly with carcinoid syndrome.

We report a case of primary carcinoid tumour of the testis without features of carcinoid syndrome.

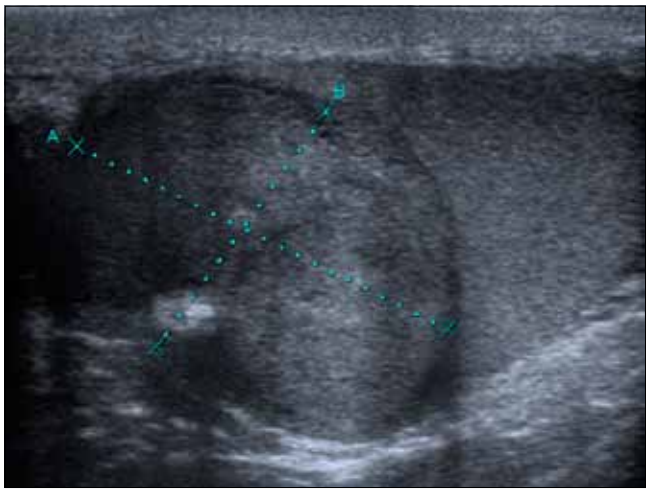

Fig 1. Ultrasound image of the right testis showing mixed echogenic mass in upper pole in keeping with testicular tumour

CASE REPORT

A 29-year-old male presented to the outpatient clinic with a several week history of a painless right sided testicular swelling found on self-examination. He had no recent history of trauma, urinary tract or sexually transmitted infections. On examination he had a hard mass in the upper aspect of his right testis which felt strongly suggestive of testicular tumour. An ultrasound scan showed normal appearance of the left testis and a mixed echogenic mass occupying the majority of the superior aspect of the right testis. The mass measured 3.5 x 2.3 cm and had increased vascularity (Figure 1). Tumour markers (beta human chorionic gonadotrophin, alfa-fetoprotein and lactate dehydrogenase) were normal and a pre-operative chest radiograph did not reveal any metastases. The patient underwent radical orchidectomy and insertion of testicular prosthesis soon after diagnosis.

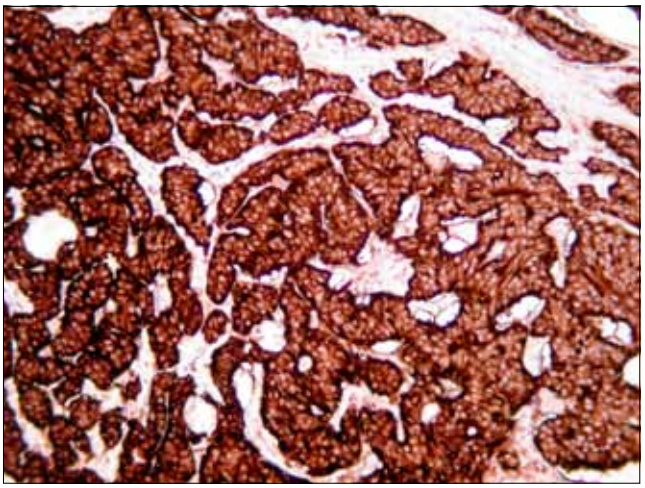

Fig 2. Monomorphic cells in nested trabecular pattern. Staining strongly positive with chromogranin

Histological analysis showed a well circumscribed tumour composed of monomorphic cells arranged in a nested trabecular pattern. The tumour cells had granular chromatin and scarce mitotic figures. Immunohistochemistry showed strong positive staining with chromogranin (Figure 2), synaptophysin (Figure 3), CD56 and PGP9.5. These features were in keeping with a well differentiated carcinoid tumour with no teratomatous components or other germ cell elements. There was no lymphovascular invasion, the tumour was confined to the testis and had a low proliferation index.

The patient subsequently had a staging computed tomogram (CT) of chest, abdomen and pelvis, which showed no significant para-aortic or iliac lymphadenopathy and no pulmonary abnormality. Multiple mesenteric nodes were noted which were not said to be typical of spread of testicular tumour.

The patient was referred to a specialist gastroenterologist for further investigation to rule out the possibility of testicular

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metastasis from an extra-testicular primary carcinoid. NM octreotide scan with SPECT showed two to three subtle foci of activity towards the dome of the right lobe of the liver in segment four and eight. These were not definite for liver metastases, however, these could not be excluded. No lesions were found to be over expressing somatostatin receptors. Further evaluation with MRI confirmed that the areas of abnormality within the liver were consistent with simple cysts.

DISCUSSION

Testicular carcinoid tumours are a rare entity and are almost never suspected preoperatively. The majority are only diagnosed on histopathology as they do not become clinically apparent until there is metastatic spread or the presence of carcinoid syndrome.[2] Carcinoid tumours arise from neuroendocrine cells, however, the presence of neuroendocrine cells has not been described in the testis, leaving the origin of primary testicular carcinoid debatable.[3] Several cellular origins of these tumours have been proposed. Mai et al found that the origin of testicular carcinoid tumours was located in the same progenitor cell from which Leydig cells derive.[4] Merino et al support the possibility of a germ cell origin, finding intra-tubular germ cell neoplasia in the testicular tissue surrounding a pure carcinoid.[3] Thus primary testicular carcinoid may be the remaining component of a burnt out teratoma or due to a one-sided development of teratoma.[3,5]

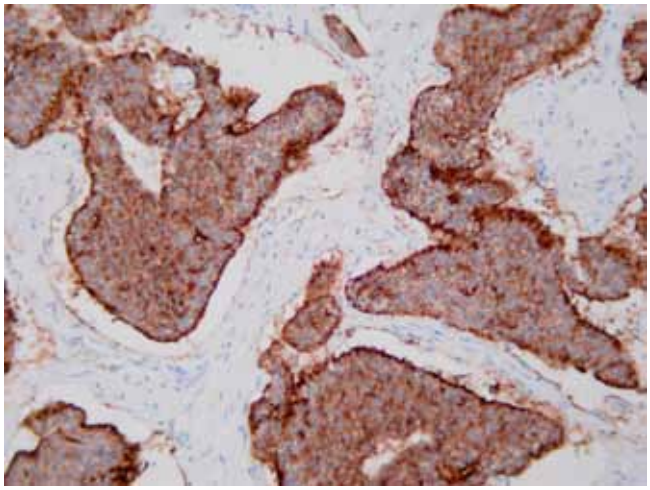

Fig 3. Cells staining strongly positive with synaptophysin

Carcinoid syndrome is manifestation of carcinoid tumours and occurs as a result of the action of vasoactive tumour products. The syndrome is rare, occurring in approximately 10% of patients[5] typically only once the tumour has metastasised to the liver or lungs. Serotonin is the most common tumour product and when released into the systemic circulation it causes the symptoms of carcinoid syndrome.[6] These include increased gastro-intestinal motility, bronchoconstriction, vascular constriction and dilatation.[6] Serotonin is metabolised to 5-hydroxyindoleacetic acid (5-HIAA) which can be measured in the urine. Any patient with vasoactive symptoms and a testicular lump should have 24 hour urinary 5-HIAA performed prior to surgery.

Given that almost 10% of testicular carcinoids are metastases from another location,[2] it is essential to thoroughly investigate these patients to find or exclude an extra-testicular primary source. A multimodal approach has been recommended. Barium contrast studies and CT may detect mucosal thickening or luminal narrowing to suggest bowel involvement. CT is also good for detecting mesenteric extension of the tumour and presence of liver metastases.[7] Somatostatin receptor scintigraphy using indium-111 labelled octreotide is now superior to CT in localisation of primary tumour site and has a sensitivity for detecting metastases of up to 96%.[7] It has superseded meta-iodobenzylguanidine scanning which has a sensitivity of 50% for detecting metastases.[7] These investigations also serve to detect synchronous tumours, as it is known that carcinoids have a high rate of second primary malignancy.[6]

Radical orchidectomy is curative for testicular confined carcinoid.[5] The long-term prognosis of carcinoid tumours is dependent on size, association with teratoma and presence of metastases. Zavala-Pompa et al showed that larger tumours (7.3 vs 2.9cm) and the presence of carcinoid syndrome predicted increased metastatic potential and hence poorer prognosis.[8] The prognosis of carcinoid tumours arising within teratoma is better than pure testicular carcinoid.[8] There have been several reports of carcinoid tumours causing delayed metastases, in one case 17 years after initial diagnosis, highlighting the need for long-term follow-up.[9] Patients should undergo biochemical and radiological follow-up, however, the frequency and duration of follow-up remains open to debate. Sutherland et al suggest that patients should undergo three monthly 5-HIAA measurements for the first year after diagnosis and annually thereafter.[10] More recent guidelines suggest that urinary 5-HIAA levels do not accurately correlate with disease progression and metastases may occur in the absence of an elevated urinary 5-HIAA. Serum chromogranin A (a glycoprotein secreted by carcinoid tumours) has been reported to be a sensitive and specific marker which may correlate with relapse in gastrointestinal carcinoids.[7] It may also be of use in the follow-up of testicular carcinoids, a fast rising level being associated with a poor prognosis.

In conclusion, testicular carcinoid tumours are very rare. It is imperative that once a testicular carcinoid tumour has been diagnosed; the patient undergoes thorough investigation to rule out an extra-testicular primary and metastases. Long-term biochemical and radiological follow-up is essential given potential for delayed metastases.

The authors have no conflict of interests

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Case Report

Sesamoid Bone Blocking Fracture Reduction in Traumatic Injury of First Metatarsal

David J. Spence, Owen J. Diamond, Brian J. Mockford

Accepted 16 December 2010

ABSTRACT:

We describe a patient who sustained an extra-articular, oblique and angulated first metatarsal fracture. The medial hallucal sesamoid bone was subsequently found to have entered the fracture gap preventing reduction. We describe treatment of this rare injury with a successful outcome.

Keywords: Sesamoid, fracture, metatarsal, reduction

INTRODUCTION:

Metatarsal neck and shaft fractures are common injuries while fractures of the head are relatively uncommon. These injuries usually occur as a result of direct trauma and the majority heal with conservative management.[6] Indications for surgical intervention include those fractures angulated greater than 10 degrees in any plane, displacement greater than 3-4mm, or a significant intra-articular component to the fracture.[5] We describe a fracture of the shaft to the first metatarsal which required removal of the medial hallucal sesamoid bone from the fracture gap to allow reduction. We believe this has not been previously reported.

CASE REPORT:

A 26 year old male fitter presented to our department having dropped a heavy weight onto his left foot. He complained of pain over the antero-medial aspect of the foot. He was unable to weight-bear and on examination was tender in the region of the head of the first metatarsal. He was unable to fully flex the first interphalangeal and metatarsophalangeal joint. X-rays of his foot showed an oblique fracture of the distal first metatarsal in the sagittal plane with 20 degrees of dorsal angulation (Figure 1A to 1C). There was an associated undisplaced fracture of the second metatarsal. A manipulation under anaesthetic +/- open reduction and internal fixation was planned.

Under general anaesthetic and image intensifier control a closed reduction of the first metatarsal was attempted but the fracture could not be reduced.

The fracture was then opened and explored. This revealed that the medial hallucal sesamoid bone had entered into the fracture gap preventing reduction. On removal from the fracture gap, immediate and accurate reduction was achieved and held with a single interfragmentary screw (Figure 2A and 2B). The foot was immobilised in a cast and he had restricted weight-bearing for six weeks.

Fig 1A. Lateral x-ray of the left foot on presentation.

Fig 1B. AP x-ray of the left foot on presentation.

Fig 1C. Oblique x-ray of the left foot on presentation.

DISCUSSION:

This unusual problem caused by the sesamoid bone blocking the reduction of the fracture has not been reported in the literature. Medial and lateral hallucal sesamoids form part

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Fig 2A. Lateral x-ray of the left foot post-operative showing the fracture reduced and held with an interfragmentary screw.

Fig 2B. AP view of the left foot post-operative.

of the sesamoid capsuloligamentous complex. This complex includes attachments from the flexor hallucis longus (FHL), flexor hallucis brevis (FHB), and metatarsosesamoid and intersesamoid ligaments.[8] They provide two of six contact points for the forefoot.[2] There are a number of injuries reported affecting the sesamoids including fracture,[7] dislocation, inflammation,[1] chondromalacia[4] and osteochonditis.[3] No mention of the problem caused by the sesamoids blocking fracture reduction of a metatarsal fracture has been reported to our knowledge. We believe left untreated this would potentially have led to non-union, chronic pain and loss of flexor function of the first ray.

The authors have no conflict of interest

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Grand Rounds

Pulmonary Function Tests

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ABSTRACT

Pulmonary function tests are valuable investigations in the management of patients with suspected or previously diagnosed respiratory disease. They aid diagnosis, help monitor response to treatment and can guide decisions regarding further treatment and intervention. The interpretation of pulmonary functions tests requires knowledge of respiratory physiology. In this review we describe investigations routinely used and discuss their clinical implications.

INTRODUCTION

Pulmonary function tests (PFTS) are an important tool in the investigation and monitoring of patients with respiratory pathology. They provide important information relating to the large and small airways, the pulmonary parenchyma and the size and integrity of the pulmonary capillary bed. Although they do not provide a diagnosis per se, different patterns of abnormalities are seen in various respiratory diseases which helps to establish a diagnosis. We describe the indications for performing PFTS, describe abnormal results and correlate these with underlying pathology.

TABLE 1

Indications for Pulmonary Function Tests

1. Investigation of patients with symptoms/signs/ investigations that suggest pulmonary disease e.g. • Cough • Wheeze • Breathlessness • Crackles • Abnormal chest x-ray
2. Monitoring patients with known pulmonary disease for progression and response to treatment e.g. • Interstitial fibrosis • COPD • Asthma • Pulmonary vascular disease
3. Investigation of patients with disease that may have a respiratory complications e.g. • Connective tissue disorders • Neuromuscular diseases
4. Preoperative evaluation prior to e.g. • Lung resection • Abdominal surgery • Cardiothoracic surgery
5. Evaluation patients a risk of lung diseases e.g. • Exposure to pulmonary toxins such a radiation, medication, or environmental or occupational exposure
6. Surveillance following lung transplantation to assess for • Acute rejection • Infection • Obliterative bronchiolitis

GENERAL CONSIDERATIONS AND NORMAL VALUES

Guidelines for performing and interpreting PFTS have been published both by the European Respiratory and American Thoracic Societies[1-6]. Indications for performing PFTS are listed in table 1[7]. Performing PFTS is generally safe but specific contraindications exist. These are listed in table 2[7]. PFTS are effort dependent and therefore patient cooperation and understanding in performing the tests is essential in obtaining optimal results. Suboptimal results may be obtained in patients who have chest or abdominal pain or from patients who do not fully understand directions given to perform the tests.

TABLE 2

Contraindications to performing PFTS[7]

Myocardial infarction within the last month
Unstable angina
Recent thoraco-abdominal surgery
Recent ophthalmic surgery
Thoracic or abdominal aneurysm
Current pneumothorax

Patients with active respiratory infections such as tuberculosis are not precluded from having PFTS however the tests should ideally be deferred until the risk of cross contamination is negligible. If patients with infectious disease must undergo testing then extra precautions in addition to the standard decontamination of equipment may be necessary. This may include performing PFTS at the end of the day to allow

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disassembly and disinfection of equipment, undertaking tests in the patients' room rather than the lung function laboratory and reserving equipment for sole use in patients with infections[1].

A sitting position is typically used at the time of testing to prevent the risk of falling and injury in the event of a syncopal episode, although PFTS can be performed in the standing position. Patients are advised not to smoke for at least one hour before testing, not to eat a large meal two hours before testing and not to wear tight fitting clothing as under these circumstances results may be adversely effected[1]. False teeth are left in place unless they prevent the patient from forming an effective seal around the mouth piece.

Normal or predicted ranges of values are obtained from large population studies of healthy subjects. Values are taken for people matched for age, height, sex and where appropriate ethnicity. PFTS should be performed three times to ensure that the results are reproducible (less than 200ml variation) and accurate. Dynamic studies are performed first (spirometry, flow volume curves, peak expiratory flow rates), followed by lung volumes, bronchodilator testing and finally diffusion capacity. Each of these aspects of PFTS will now be reviewed in more detail.

SPIROMETRY

Spirometry is the most frequently used measure of lung function and is a measure of volume against time. It is a simple and quick procedure to perform: patients are asked to take a maximal inspiration and then to forcefully expel air for as long and as quickly as possible (a forced vital capacity manoeuvre- figure 1). Measurements that are made include

- Forced expiratory volume in one second (FEV1)
- Forced vital capacity (FVC)
- The ratio of the two volumes (FEV1/FVC)

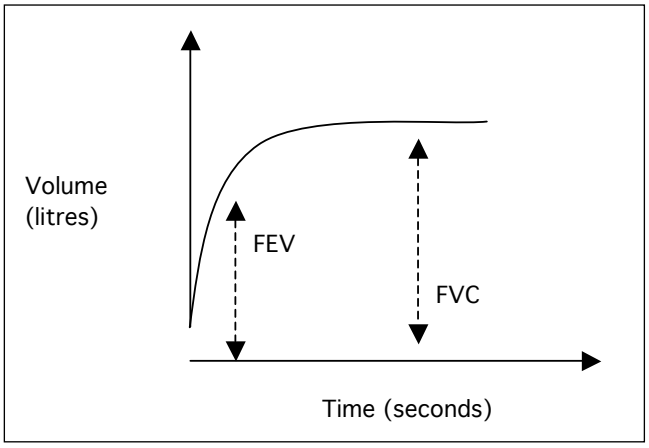

Fig 1. Normal Spirometry

Spirometry and the calculation of FEV1/FVC allows the identification of obstructive or restrictive ventilatory defects. A FEV1/FVC < 70 % where FEV1 is reduced more than FVC signifies an obstructive defect (figure 2). Common examples of obstructive defects include chronic obstructive pulmonary disease (COPD) and asthma. The FEV1 can be expressed as a percentage of the predictive value which allows classification of the severity of the impairment (table 3)[8]. An FEV1/FVC > 70% where FVC is reduced more so than FEV1 is seen in restrictive defects such as interstitial lung diseases (e.g. idiopathic pulmonary fibrosis) and chest wall deformities (figure 3).

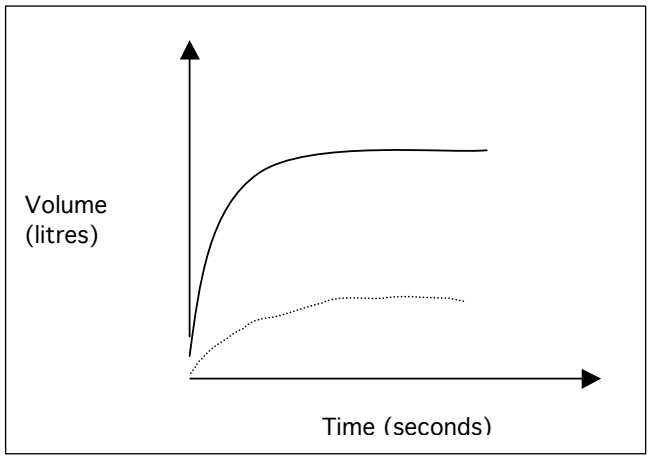

Fig 2. Spirometry in obstructive lung disease.

TABLE 3

Severity of airflow obstruction based on percentage (%) predicted forced expiratory volume in 1 second (FEV1).

FEV1 % predicted	Stage
>80%	Mild
50-79%	Moderate
30-49%	Severe
<30%	Very severe

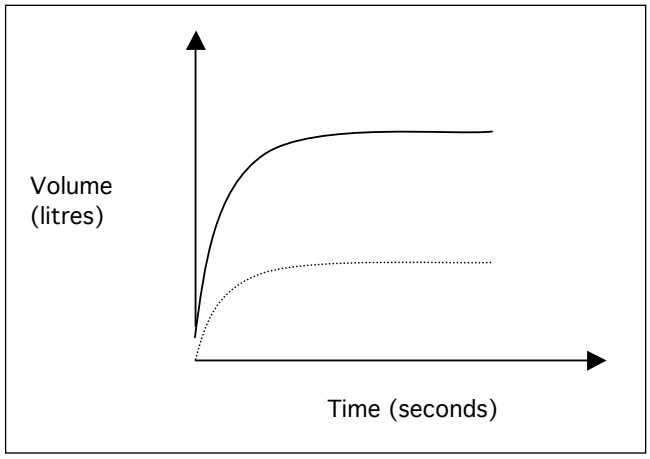

Fig 3. Spirometry in restrictive lung disease.

FLOW VOLUME CURVES

Flow volume curves are produced when a patient performs a maximal inspiratory manoeuvre which is then followed by a maximal expiratory effort. A graph is produced with a positive expiratory limb and a negative inspiratory limb (figure 4). The maximal flow rate during expiration can also be measured (peak expiratory flow rate PEFR). Furthermore the maximal flow rates between 25%-75% of the vital capacity (FEF25-

75%) can also be measured and these provide important information regarding small airway function.

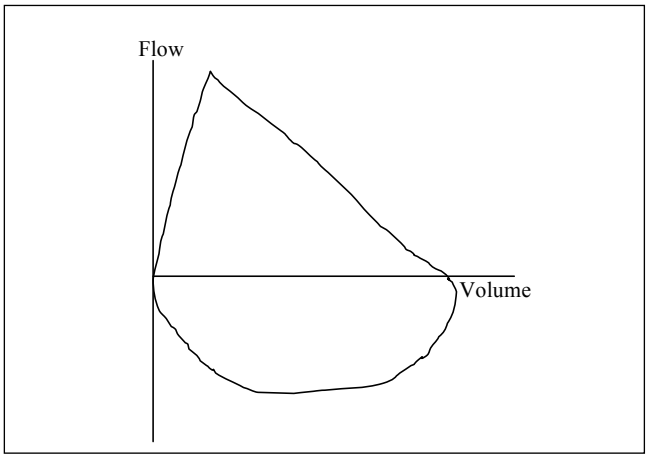

Fig 4. Normal Flow volume curve

With knowledge of the expected appearance of the flow volume loop in a normal patient, important information can be obtained from the morphology of the curve in patients with suspected respiratory disease. Patients with obstructive lung diseases with reduced expiratory flow in the peripheral airways typically have a concave appearance to the descending portion of the expiratory limb (figure 5) rather than a straight line. In patients with emphysema the loss of elastic recoil and radial support results in pressure dependent collapse of the distal airways with more pronounced "scalloping" of the expiratory limb. Even if the flow volume loop morphology is normal, a reduction in PEFR may be an indication of asthma with early airways obstruction. Similarly a reduction in FEF25-75% indicates small airways obstruction. This can also occur in patients with asthma with a normal PEFR, and is useful in providing a better overall picture of asthma control. It is also helpful in monitoring response to treatment and this may be particularly important for patients being considered for general anaesthetic and surgical intervention.In restrictive defects the expiratory limb has a convex or linear appearance because flow rates are preserved but the problem relates to a parenchymal disorder e.g. lung fibrosis which reduces lung volumes.

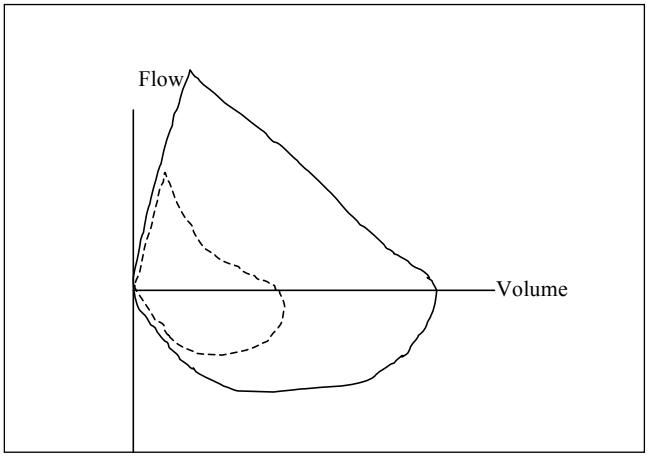

Fig 5. Flow volume curve in obstructive lung disease e.g. COPD

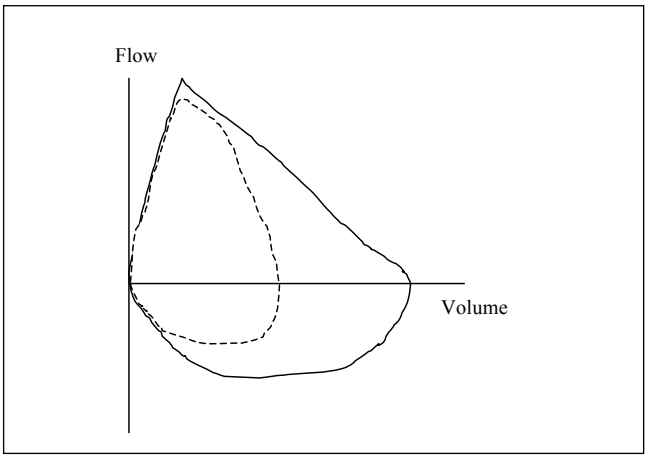

Fig 6. Flow volume curve in restrictive lung disease e.g. interstitial lung disease.

Flow volumes curves are helpful in the detection of large airway abnormalities. Typically intra-thoracic large airway obstruction (e.g. from a lower tracheal or bronchial tumour figure 7) results in flattening of the expiratory limb alone with preservation of the inspiratory limb (figure 8). Normally in expiration there is a rise in intrathoracic pressure, which is transmitted to the intrathoracic airway causing some narrowing of the airway. The presence of an obstructing lesion coupled with a rise in intrathoracic pressure during expiration results in a more pronounced and pathological reduction in airflow through the obstructed or partially occluded intrathoracic airway.

In fixed extra-thoracic large airway obstruction (e.g. vocal cord paralysis or tracheal stenosis figure 9) there is symmetrical flattening of both the inspiratory and expiratory limb as airflow is limited in both directions and is not affected significantly by intrathoracic pressure changes (figure 10)[9].

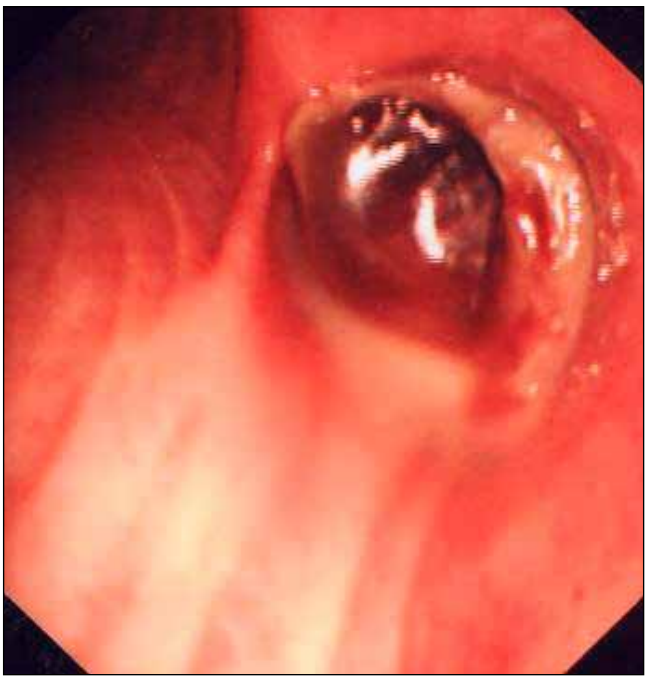

Fig 7. A bronchial carcinoma obstructing the right main bronchus.

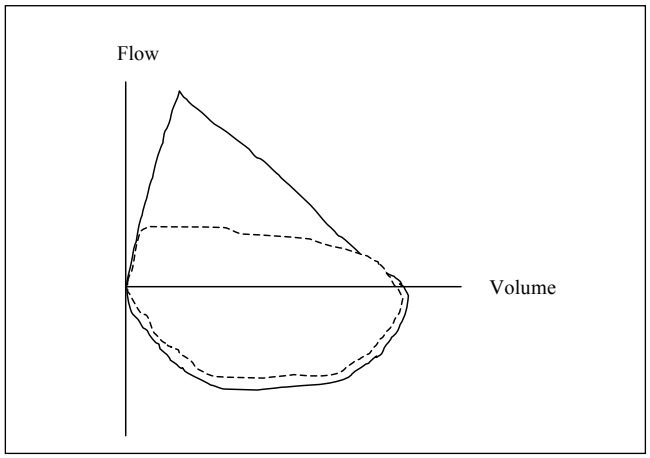

Fig 8. Flow volume curve seen with intra-thoracic airway obstruction.

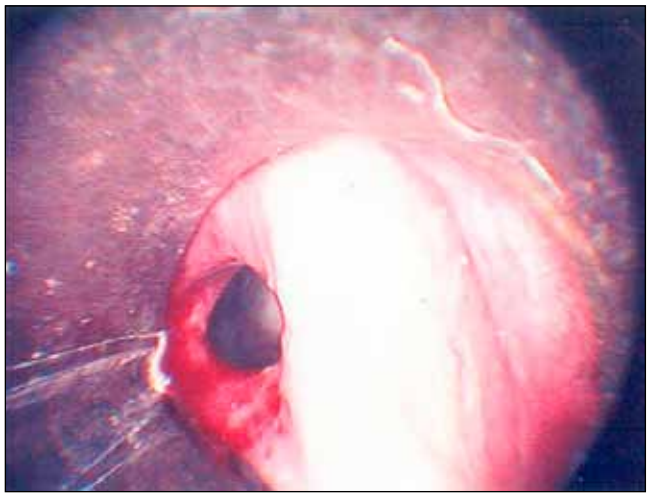

Fig 9. Tracheal stenosis seen at rigid bronchoscopy.

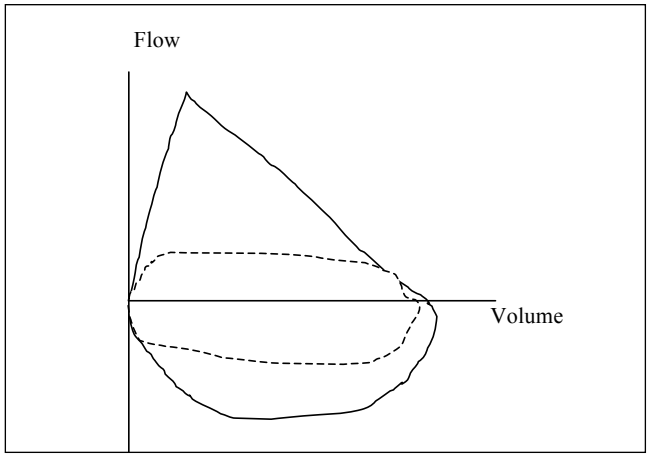

Fig 10. Flow volume curve seen with fixed extra-thoracic airway obstruction

BRONCHODILATOR TESTING

The diagnostic hallmark of asthma is the presence of reversible airways obstruction. Patients with controlled or stable asthma may have apparently normal spirometry and flow volume curves. It is therefore useful to see if there is any change in the airway indices following the administration of a bronchodilator such as 2.5mg of nebulised salbutamol. A positive response in adults is defined as a 12% increase in baseline (pre bronchodilator) FEV1 with an increase of 200mls or more following the administration of a bronchodilator. A negative test does not mean a patient will not derive any benefit from a trial of bronchodilator therapy such as inhaled salbutamol or corticosteroids. It is therefore important to use the patient's history and examination in addition to the above in formulating a diagnosis and treatment plan. In this regard home peak flow charts are helpful. Bronchial challenge testing may also be considered where a 20% fall in FEV1 in response to small doses of inhaled bronchoconstrictors such as methacholine is indicative of asthma.

LUNG VOLUMES

Static lung volumes are measured with the use of whole body plethysmography in an airtight body box. Other techniques that can be used to measure static lung volumes included nitrogen washout or helium dilution[4]. They cannot be measured by spirometry.

In body plethysmography, the patient sits inside an airtight box, inhales or exhales to a particular volume (usually FRC), and then a shutter drops across their breathing tube. The subject makes respiratory efforts against the closed shutter. Measurements are based on Boyle's law which states that at constant temperature the volume of a given mass of gas varies inversely with pressure. Therefore the increase in their chest volume slightly reduces the box volume (the non-person volume of the box) and thus slightly increases the pressure in the box. Static lung volumes can be obtained either by measuring the changes in pressure in a constant volume box or volume in a constant pressure box[4].

RESIDUAL VOLUME

Residual volume (RV) is the amount of air remaining in the lungs after a maximal expiration (normally 500mls). In patients with obstructive lung diseases where there is incomplete emptying of the lungs and air trapping, RV may be significantly increased. Patients with high RV who require surgery and mechanical ventilation require high peri-operative inflation pressures. This increases the risk of barotrauma, pneumothorax, infection and reduced venous return due to high intra thoracic pressures. The RV can also be expressed as a percentage of total lung capacity and values in excess of 140% significantly increase the risks of these complications.[7] Patients referred for lung volume reduction surgery typically have RV in excess of 180% predicted.

TOTAL LUNG CAPACITY

Total lung capacity (TLC) is the total volume of air in the lungs after a maximal inspiration. It is the sum of RV and vital capacity (the difference in volume between maximal inspiration and maximal expiration). TLC may be increased in patients with obstructive defects such as emphysema and decreased in patients with restrictive abnormalities including chest wall abnormalities and kyphoscoliosis.

FUNCTIONAL RESIDUAL CAPACITY

Functional residual capacity (FRC) is the volume of air in the lungs following normal expiration. Patterns of abnormal FRC are similar to abnormalities given above for TLC and RV.

DIFFUSION CAPACITY

The measurement of diffusion capacity (DLCO also known as transfer factor) gives important information regarding the integrity and size of the alveolar blood membrane. It measures the diffusion of gas across the alveolar membrane which is determined by the surface area and integrity of the alveolar membrane and the pulmonary vascular bed. Normally the value is corrected for the patient's haemoglobin (DLCOc). DLCOc is measured using carbon monoxide gas, which is soluble and binds to haemoglobin with its uptake limited by diffusion only. It is measured by a single breath technique where 10% helium and 0.3% carbon monoxide are rapidly inspired, held for 10 seconds and then expired with the measurement of the remaining carbon monoxide. Comparison of the inspired and expired CO fractions allows calculation of DLCO[3].

DLCOc is determined by the surface area of the alveolar membrane and as such, is impaired in conditions where the surface area is reduced e.g. pulmonary fibrosis, emphysema or pulmonary emboli. The transfer coefficient (KCO) is DLCOc corrected for alveolar volume. In patients with a pneumonectomy DLCOc will be reduced due to the loss of approximately half of the surface area of alveolar membrane but KCO will be normal as the remaining lung is normal with normal function of the alveolar blood membrane. Similarly variation can be seen in diseases that effect the lungs in a heterogeneous manner e.g. COPD or alpha 1 antitrypsin emphysema. In COPD the upper lobes tend to be preferentially damaged whereas in alpha 1 antitrypsin deficiency the lower lobes are predominantly involved. Therefore DLCOc will be lower than KCO. Pulmonary emboli should be considered in patients with an isolated reduction in DLCOc without any other obvious respiratory cause.

RESPIRATORY MUSCLE FUNCTION

A number of diseases such as motor neurone disease can result in respiratory muscle weakness, which can ultimately lead to respiratory failure. These diseases can effect not only chest wall muscles but also the diaphragm which is the major inspiratory muscle. Serial measurements of vital capacity may be necessary to detect deterioration in lung function in patients with neuromuscular disease such as Guillan Barre Syndrome. Once the vital capacity falls below 1 litre in such patients mechanical ventilatory support may be indicated. Other measures of respiratory muscle function include [7]:

Inspiratory mouth pressures – a measure of inspiratory muscle function in which subjects generate as much inspiratory pressure as possible against a blocked mouth piece[10]. The pressure generated (maximum inspiratory pressure MIP) is therefore largely a function of the inspiratory respiratory muscles rather than lung volumes which do not change significantly during the test[10]. A normal value is approximately 100 cm of water. Values of 80 cm of water or more exclude any significant inspiratory muscle weakness [11].

Expiratory mouth pressures- a measure of expiratory respiratory muscle function where patients generate a maximal expiratory pressure (MEP) against a blocked mouthpiece (a valsalva manoeuver) at TLC. The range of normal values is wide and results should be compared with published data [11].

Erect and supine vital capacity- in normal subjects there is a 5% decrease in vital capacity in the supine position. A fall of 25% or more may indicate diaphragmatic paralysis and further confirmatory tests e.g. ultrasound screening of diaphragm may be necessary.

ARTERIAL BLOOD GASES

Arterial blood gas sampling provides important information on gas exchange and oxygen delivery to the tissues. Type 1 respiratory failure is defined as a partial pressure of oxygen (PaO_2) < 8 kPa with normal partial pressure of carbon dioxide ($PaCO_2$). Causes of type 1 respiratory failure include pneumonia and pulmonary embolism. Type 2 respiratory failure occurs when hypoxia is accompanied by hypercapnia ($PaCO_2$ > 6.5 kPa). This is seen in ventilatory failure and examples of causes include respiratory muscle weakness and COPD. Type 2 respiratory failure may also occur in patients with advanced type 1 respiratory failure as they tire and develop ventilatory failure. Such patients may require ventilatory support in the form of non-invasive or invasive ventilation.

OVERNIGHT OXIMETRY

Patients who complain of excessive daytime sleepiness (as measured by the Epworth Sleepiness Scale) and snoring with or without witnessed apnoeas should be investigated for obstructive sleep apnoea (OSA). Overnight oximetry can be used initially in the assessment of OSA. Typically 10 oxygen desaturations per hour of more than 4% would be considered to be indicative of OSA. Normal overnight oximetry does not exclude OSA and more detailed sleep studies including polysomnography should be performed in patients where there is a high clinical suspicion of OSA.

CARDIOPULMONARY EXERCISE TESTING

Cardiopulmonary exercise testing (CPET) involves patients exercising on a treadmill or cycle ergometer with measurements of variables such ventilation, heart rate, oxygen uptake ($V'O_2$) and cardiac output. This allows causes for a reduced exercise tolerance to be identified, which may be due to ventilatory abnormalities in those with chronic lung disease or impaired cardiac output in patients with cardiac disease. It may be useful in patients who complain of excessive breathlessness and in whom investigations such as echocardiogram and pulmonary functions tests are normal. A $V'O_2$ peak standardized by body mass below 80% predicted is considered to be abnormal[12].

USING PULMONARY FUNCTION TESTS IN PRE-OPERATIVE EVALUATION OF PATIENTS

It is important to address a number of concerns in evaluating a patient prior to surgery. These include determining if a patient is [7]:

- Fit for a general anesthetic
- Appropriate for the planned surgical procedure
- Requires further treatment for any underlying respiratory problems (which may or may not have been identified prior to the evaluation).

These decisions are typically made by anaesthetists, with input

from respiratory physicians and intensive care physicians[7]. In a patient with chronic respiratory disease it is important to identify how much of their breathlessness is caused by their lung disease particularly if the patient is being considered for cardiac surgery. If their breathlessness is predominantly due to respiratory disease, this will not necessarily be improved by any corrective cardiac surgery. Surgery may also not be justified if their respiratory disease carries a poor prognosis in itself. It is important to try and identify any contributing causes for breathlessness particularly in patients with multiple co morbidities so that these can be addressed, investigated and treated as appropriate. This short history illustrates the point. A 71-year-old male smoker with COPD was referred for consideration regarding aortic valve replacement for aortic stenosis (AS). Physical examination revealed features compatible with COPD and AS but in addition he had a disproportionately loud pulmonary component to the second heart sound and a right ventricular heave. A ventilation/perfusion scan was ordered which confirmed multiple pulmonary emboli and abdominal imaging diagnosed a renal tumour involving the inferior vena cava. Cardiac surgery was postponed.

It is important to identify patients with respiratory problems that are at increased risk of peri-operative complications such as respiratory infection including ventilator acquired pneumonia, atelectasis, acute lung injury and prolonged respiratory failure with may all result in difficulty weaning from mechanical ventilation post operation. Risk factors for peri-operative pulmonary complications include increased age, COPD and smoking[13, 14]. The risk of complications is also related to the surgical site and its proximity to the diaphragm with increased complications seen following aortic aneurysm repair, and thoracic and upper abdominal surgery[13]. Procedures longer than 3 hours in duration are also associated with increased risk. Although there are no clear guidelines regarding the routine use of pre-operative PFTS, they are generally used in the assessment of symptomatic patients undergoing major thoraco-abdominal surgery. It should be remembered that pulmonary complications may occur in patients without risk factors and that strategies to reduce the risk of these complications such as smoking cessation and lung expansion techniques (e.g. deep breathing exercises) should be used in all patients with particular attention given to those at increased risk.

Patients with chronic respiratory disease or with impairment of PFTS at pre operative evaluation are challenging to assess. We recommend that where there is doubt regarding suitability for a general anaesthetic appropriate advice from anaesthetists, intensive care and respiratory physicians is sought and efforts to optimise the patient as much as possible are made.

PULMONARY FUNCTION TESTS IN PATIENTS UNDERGOING LUNG RESECTION

Resection of primary lung cancers in the form of lobectomy or pneumonectomy remains the treatment of choice in patients with early stage disease[15]. Many patients with lung cancer will also have COPD and it is important to try and determine the effect of lung resection on these patients both in terms of postoperative complications and long term disability[16, 17].

The British Thoracic Society guidelines advise that pneumonectomy can be considered in patients with FEV1 > 2.0 L and lobectomy if FEV1> 1.5 L in the absence of any interstitial lung disease or unexpected disability due to shortness of breath[15]. As absolute values may be lower in older patients and women, patients are generally considered suitable for resection if FEV1> 80% predicted and DLCO > 80% predicted[18]. In patients with borderline lung function the post operative predicted FEV1 and DLCO can be calculated either with knowledge of the number of lung segments to be resected or through quantitative lung perfusion scanning. Patients with a post operative predicted FEV1 or DLCO < 40% are deemed at high risk of peri-operative death and complications[17]. Further investigations including CPET may be necessary for further risk stratification.

PFTS are used in the assessment of patients for lung transplantation. Patients with PFTS below 30% predicted may potentially be considered for lung transplantation assuming no other contraindications are present[19, 20].

RIGHT HEART CATHETERISATION

Chronic respiratory diseases may result in pulmonary hypertension and eventually right-sided cardiac failure and death. Pulmonary hypertension should be considered in patients with symptoms or signs of right-sided cardiac failure or perhaps with more dyspnoea than expected on the basis of their PFTS and clinical presentation.

A Doppler trans thoracic echocardiogram is a useful non-invasive tool in screening for pulmonary hypertension. Right heart catheterisation is considered the gold standard tool and can diagnose pulmonary hypertension with the measurement of a mean pulmonary artery pressure > 25mmHg[21]. In experienced centres it can be performed safely and provide information on pulmonary haemodynamics including cardiac output, pulmonary vascular resistance and an approximation of mean left atrial pressure by measuring the mean pulmonary capillary wedge pressure[22]. Patients with pulmonary hypertension are at increased risk of peri-operative complications including pulmonary hypertensive crises where an acute rise in pulmonary pressures results in right ventricular failure and a subsequent fall in cardiac output. Knowledge of pulmonary haemodynamics allows careful pre-emptive management of these problems. Furthermore some patients with co existing pulmonary hypertension and cardiac or pulmonary disease may benefit from specific targeted therapy for their pulmonary hypertension e.g. using sildenafil[23-28].

CONCLUSION

Pulmonary function tests are an important tool in the assessment of patients with suspected or known respiratory disease. They are also important in the evaluation of patients prior to major surgery. Interpretation of the tests, which requires knowledge of normal values and appearance of flow volume curves, must be combined with the patient's clinical history and presentation.

The authors have no conflict of interest.

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Ulster Medical Society Presidential Address

Threads of life and health - a heritage of quality in practice

Margaret Cupples

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The Ulster Medial Society is a unique organisation in which medics of all ages, backgrounds, and disciplines can meet, share experiences and learn together. This network of varied individuals can be considered to form a rich virtual tapestry of talent. The opportunities the Society offers for developing good links between individuals and disciplines helps to promote an aim of improving effectiveness in the work of healthcare provision and planning.

Recognition that there is value in learning from others is the base from which this address has evolved. It will reflect on a wealth of different life experiences and weave these loosely together to illustrate the quality of practice, both in medicine and in textiles, that is our Ulster heritage. Key points include the flax flower, various textiles, the cardiac defibrillator, renal dialysis and the Strangford stone, a granite legacy of high quality teamwork.

THE 'THREAD' OF LIFE

According to Greek mythology, the metaphorical thread of life of every mortal from birth to death is controlled by three mythological figures, the 'Moirae' ("apportioners"). A 16th century tapestry depicts three ladies - the "spinner" who spun the thread, the "allotter" who measured the length allotted to each person and the "cutter" who chose the manner of death; and when the time was come, cut the life-thread with her shears. The concept of life resembling a thread which may be broken easily and outwith one's control remains within lay language today, such that when someone is critically ill it is said 'he's hanging on by a thread'. Within medicine the 'thready' pulse is defined as 'a small fine pulse that feels like a small cord or thread under the finger': its presence suggests life-threatening conditions and a need for decisive and urgent action.

TAKING A MEDICAL HISTORY

To formulate a diagnosis and management plan in any clinical encounter medical students are taught that a medical history should be obtained by asking first about the presenting problem, reviewing specific body systems and then asking about past medical and family history. In preparation for this talk, I came across the mnemonic *'JAM THREADS'* - an aide memoire to asking about specific conditions: ***J****aundice,* ***A****naemia,* ***M****yocardial infarction,* ***T****uberculosis,* ***H****ypertension,* ***R****heumatic fever,* ***E****pilepsy,* ***A****sthma,* ***D****iabetes and* ***S****troke.* It may have been more useful to students in times past than today but for any doctor consulting with a new patient most of these conditions continue to have relevance.

In general practice we teach medical students about the 'threads' which we consider are always relevant to health – physical, psychological and social issues. Exploring these allows diagnoses to be based on a biopsychosocial model of disease as opposed to the simpler biomedical model. Omitting to ask a 45 year old lady presenting with difficulty swallowing about her current social circumstances, which include imminent bankruptcy and marriage breakdown, and her father having died recently with oseophageal carcinoma, may not allow the physician or surgeon to make best decisions for her optimal management. In palliative care the importance of a fourth thread is recognised increasingly– that of a person's spiritual needs. Every good GP trainee knows that competence in clinical practice requires that each of these threads should be duly considered when making a diagnosis and constructing an appropriate management plan for any patient.

FLAX AND FAMILIES

Flax, in Northern Ireland, has truly been a 'thread of life'. It was the means by which products were made that could be sold to obtain money to buy things which could not be grown or made on the farm and was the catalyst which held families and, indeed, communities together, ensuring care from 'cradle to grave' – before the days of the National Health Service.

The process of flax-growing began with finding the best seed, traditionally from the 'low countries' and Holland. Seeds sown in April, flowered in summer and plants were harvested in August. The flax plant grew with a single slender stem approx 1m high. In harvesting, stems were pulled from the ground, not cut, in order to preserve the full length of fibres. Small bundles were laid out in fields to dry and the seeds removed, for the next crop of flax or for cattle food. The plants were then 'retted' – traditionally soaked in stagnant water for about two weeks. The retting process depended on bacteria working between the fibres, loosening them. More recently developed chemical agents have allowed better control of this process. Retted plants were dried in fields again before scutching - beating them to further loosen individual fibres and remove debris. Scutching was a dusty job, done often by hand in confined spaces. Scutch mills, powered by an adjacent river, provided a mechanical process of beating which was faster, but dangerous – clothing or limbs could be caught by the blades and the mills often caught fire, ferociously, fed by abundant dry fibres.

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Flax seeds were usually sown by men, with women weeding the growing plants. Everyone, including children, was involved in the harvesting. Young children wound scutched fibres loosely into bundles, older children spun more refined fibres and women spun finished fine quality threads. Fathers and older boys worked looms and took products to the market. Extended families and local communities worked together, sharing resources. At times good seeds could be hard to find and especially so in Northern Ireland during the first World War. The inscription on a clock presented to my grandfather who lived near Markethill, Co Armagh, reads: 'To Jackson Pillow from his neighbouring farmers, in appreciation for his obtaining flax seed for them from Riva, Russia, 1916'. Involvement in the linen industry engendered a sense of loyalty and mutual support within families and communities.

FACTORIES AND COMMUNITIES

If the flax was not fully processed at home, it was taken, after scutching, to factories for further combing ('hackling' and 'carding'). These were dusty processes but nothing was wasted. Woody stems were used for chipboard, short fibres were spun into a heavy yarn, for ropes and furnishings, longer coarser fibres were spun into threads for shoes, leather goods, canvas or carpeting. Fine quality threads were reserved for handkerchiefs, tablecloths and bedding. Bleaching the fine linen once relied on washing and laying on grass in sunshine but the development of chemicals made the process less dependent on weather, and more efficient. Textile workers with responsibility for preparing these chemical mixes required competence in numeracy. Just as medical students and doctors must calculate doses of drugs correctly, so factory staff were required to calculate correct quantities of chemicals for various processes - or hours of hard labour could be destroyed irreversibly with huge financial loss.

Factory work was not easy – the hours were long, often from 5.30am to 6pm weekdays and 3pm on Saturdays. Longer hours were required in summer and shorter in winter. Decisions regarding time were not those of the workers. Nevertheless, the work was appreciated, as expressed poetically:

'I'll ne'er despise the weaving trade
The shuttle's lighter than the spade
By it I had a living made
Monie a day'

John Dickey [1818]

Linen thread production based in Lisburn and the braided and woven products of the factories established there by the Barbour family earned a world-wide reputation for NI's high quality of textiles (Fig 1). NI was recognised as a world-leader in this area of work, even exporting knowledge and skill to America. Belfast, at one time, was the city with the largest spinning mill, largest rope works and largest shipyard in the world.

As the linen industry flourished, it supported the development of communities. Perhaps the best well known of these is **Bessbrook** - founded by Richardson in 1845 as a 'model village', based on principles of "Three P's": no public houses, pawn shops or police, believing that with no public house, no pawn brokers or police stations would be needed. The houses constructed for the mill workers were of good quality; many are still inhabited today. Each house had an allotment garden for growing vegetables. Sadly, in more recent years houses have been built on these, reducing such opportunities for today's local population. The village of **Milford** in County Armagh, was also established around the local linen mill. Rich and poor lived amicably in close proximity. Today the factory is idle but the neat terraces of red bricked houses, built by the mill owner, William McCrum, for the workers, remain comfortable homes.

Fig 1. Linen factories, Lisburn

The immense water-power of the River Mourne was the reason for choosing the site for **Sion Mills** in 1835. The mill and village built there provided better living standards for the community - by 1842 piped gas from the mill provided light for the village street and for every house. The owners, Herdmans, recognized people's social welfare and health needs: a canteen catered for bachelors and visitors (though not for most of the workers, who lived only a 2-3 minute walk from their work) and there was a resident doctor and nurse, paid for by workers' contributions. There was no public house (until a court case was lost in 1896) but there was a village band, with singing classes for the girls. For the first 30 years everyone attended Church together; work, housing and schooling was provided for all, without discrimination. Interestingly, the new state primary school in the 1970s was the first integrated state school in NI. This community found it hard to believe when the mill, the central pivot of village life for six or more generations, closed in 2004. Lower wages in other countries made the textile industry in NI uncompetitive. Local popular demand for cheap clothing did not recognize the paradox of also wanting higher wages for local workers and the wider implications for a community's well-being.

TEXTILES AND LEISURE

The value of leisure time activity to people's health was recognized by the early linen communities. The sporting tradition of Sion Mills began in 1864, with a cricket team, which included both workers and gentry. Cricket is still an important feature of that community which readily recalls the celebrated moment in July 1969 when an Irish team defeated a West Indian touring team in the village.

In NI the textile industry may be considered to have led the way in promoting health by encouraging people's participation in sports. However, textile products themselves have relevance within many sports. Not only is team clothing important, but also the quality of materials used, for example, in sails, parachutes, skipping ropes and fishing lines. Fine precision

Figure 2a. Engineering care

Figure 2b: Precision in design (Herzog braiding machine)

in weaving allows textiles to provide strength and resilience in all sorts of conditions. Textile manufacturers are often asked to adapt their products to meet different specifications. Ropes of high quality are essential for climbing but as Dr Nigel Hart and others in their recent 'Extreme' Mount Everest expedition illustrated, successful climbs depend also on retaining clothing and equipment. A dropped glove would not be retrieved easily at high altitudes and would certainly be a threat to well-being. Attaching items to people's bodies using lightweight, durable, flexible cordage, mostly made in NI, in Tandragee, was an important yet simple part of the successful expedition.

Linen has been used in covering aircraft wings, for years. Its durability and strength is demonstrated in a small aerobatic aeroplane, built in 1966, which has given countless hours of pleasure to various pilots in NI with the original fabric remaining intact and blemish free. The positive impact of flying on mental health is recounted by many pilots. Since this is National Poetry Day, one such poetic reflection may be given –

"Sunward I've climbed and joined the tumbling mirth
Of sun-split clouds - and done a hundred things
You have not dreamed of - wheeled and soared and swung
High in the sunlit silence……"

John Gillespie Magee Jr.

MEDICAL TEXTILES

The earliest medical textile was linen: poultices, drawing infection from wounds, used linen cloth for application. One such poultice, used in Belfast in 1942,[1] involved mixing boric acid with starch 'to a consistency of cream' and then adding boiling water 'to form a translucent jelly', to be spread on cloth, applied to the lesion and re-applied every four hours. Life today seems so much easier! Many preparations are available in tubs or tubes and some are already integrated with the cloth.

Attention to detail in engineering, keeping machines running smoothly, underpins the quality of textile products. Precision is required in each component thread of every product to create the desired design (Fig 2). Some local products that are used in medical practice and have been distributed worldwide include sutures, bandages, tapes and dressings. Research in biotextiles is creating new interactive fabrics with sensors, actuators and logic circuits. The applications will include wound management, tissue repair, rehabilitation, pressure garments, patches for drug delivery systems, and implantable devices. Scientists are developing new fibrous scaffolds that are biocompatible and support the growth of new tissues, encouraging cell attachment, proliferation and migration through pores. For example, research continues to examine how a polymer scaffold can be used to bridge bone defects and compare effects of different stem cells on bone growth. An effective scaffold must have structural and mechanical properties that are suitable for the type of tissue being grown. Using knowledge based in the textile industry scientists can customize structures for each cell type.

BYSSINOSIS AND PEMBERTON

However, not all health outcomes linked to textiles are good. Byssinosis, caused by inhalation of textile dust may cause inflammation, airway constriction and respiratory difficulty. The symptoms commence a few hours after returning to work on a Monday morning, ease later in the day but become more severe and prolonged each week. Initially in the UK, byssinosis was defined as occurring in cotton workers and entitled workers to compensation. It was unclear if it also occurred in flax workers. Elwood[2] reports how John Pemberton was asked to address this question. His survey of mill workers in NI and in England found that, of over 2500 workers, 17% reported respiratory symptoms, 48% in the early stages of flax preparation but fewer in later, less dusty stages and none where dust was absent. This finding allowed flax workers to receive industrial compensation but Pemberton also noted that symptoms were rare in those who did not smoke cigarettes and worse in those who did. A 20-year follow-up study concluded that there was no excess permanent respiratory disability among former textile workers: lung damage was closely linked to cigarette smoking. This work was re-assuring for the industry, helping to stem a rising tide of compensation costs.

PRINCIPLES AND PRACTICE

Pemberton was concerned about the impact of people's living conditions on their health. A fascinating overview of his life is given in a BMJ obituary earlier this year.[3] As a medical student in 1934, he published a paper which showed that unemployment benefits in England were insufficient to sustain healthy families. In October 1936, he applied theory to practice, taking an interest in the 200 men from Jarrow,

North-East England, who marched 300 miles to London with a petition highlighting their poverty following closure of their local shipyard. Pemberton and his fellow students set up a first aid station to feed them and tend their feet. His next major contribution to public health was a national survey, on which successful nutritional policy for the war years was based – that was considered the major reason for the UK's improved health after 1939 and worthy of advocacy today.

He was a leader in the international dissemination of research, including issues relevant to general practice. In his holidays he worked as a locum to Will Pickles of Wensleydale, an eminent GP and founder-president of the Royal College of General Practitioners. Pemberton came from Sheffield to Belfast in 1958 and linked with George Irwin who subsequently established the Department of General Practice in Queen's University, Belfast, (QUB) the fifth in the UK. Professor Irwin's vision and dedication has fuelled GPs' pioneering work in medical education. He always taught by example, even in late Friday afternoon surgeries, inspiring a desire to provide best quality care for all patients.

Following retirement in 1976 Pemberton continued to be active – in painting, hiking, postgraduate public health training and research. He died aged 97; his last academic letter was published a week before his death.[4] Before he retired his interests expanded to include coronary artery disease – and the establishment in Belfast of a World Health Organisation centre for the multinational monitoring of cardiovascular disease, subsequently led by Professor Alun Evans, and now by Professor Frank Kee.

CORONARY CARE AND PANTRIDGE

Linked to Professor Pemberton through community studies of cardiac disease was Professor Frank Pantridge, also of worldwide renown. He has been claimed as the Father of Emergency Medicine in North America; his pragmatic example and impeccable recording of clinical data[5] led to them establishing pre-hospital care. Following his development of the portable cardiac defibrillator, he established Mobile Coronary Care (MCC) in Belfast in 1966, reported in the Lancet.[6] His careful research report comparing heart attack survival in two areas, with and without MCC, provided evidence of differences in cardiac outcomes.[7] He inspired the team he led and has been described as an extraordinary medical graduate, teacher and investigator. He is reputed to have worked on the principle: *"I never felt I had done my job properly unless the patient felt better for having seen me"*. His own life was far from uneventful[8] and perhaps because of this he had a desire to ensure that his patients received the best possible quality of care.

RENAL DIALYSIS AND MCGEOWN

Professor Pantridge graduated from QUB with his MD in December 1946, as did my mother and Professor Mary (Mollie) McGeown, whose careful epidemiological research is the basis on which today's effective network of NI renal services was planned. She pioneered renal dialysis and transplantation in NI. From the first NI transplant in 1968, NI results topped the UK figures for survival. The team kept careful records and 'The Belfast recipe for renal transplantation' became known, used and respected worldwide.

Despite several absences due to childhood illness Professor McGeown's primary school (one room, two teachers and 35 pupils) gave her the foundation for admission to medicine at QUB but she was four days too young at her first application. With the outbreak of war, she returned to help her widowed mother on their farm, mucking out pigs, milking cows and 'loved it' - but her younger brother wanted to be the farmer. So she became a medical student, taking blood, performing minor operations and becoming adept at talking to patients which she regarded as a great skill. She undertook a MD with Distinction, in Pathology. Then, because she planned to get married, she was denied appointments to medical posts in favour of young men who returned from the War. So, she worked for a PhD in biochemistry, researching phosphate esters in milk but wished to return to clinical work. The Professor of Medicine offered her a post, if she could devise a research project and obtain a MRC fellowship – which she did, on the subject of kidney disease. Over time, she developed expertise in managing electrolyte problems and overcame many obstacles in setting up transplantation in Belfast.[9]

She had zeal, intelligence, and dedication. Her supporters were surgeons, nurses and technicians. Her search for perfection characterized her work, as did her committed clinical care, accurate data collection and scientific approach to management. She was one of Ulster's most distinguished physicians and clinical scientists,[10] but was also a caring loyal friend, efficient housewife and charming hostess, who took time to write 'thank you' letters after reciprocal visits with friends.

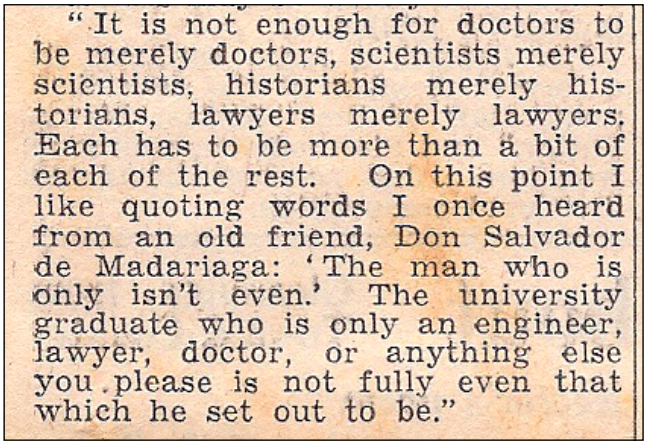
"It is not enough for doctors to be merely doctors, scientists merely scientists, historians merely historians, lawyers merely lawyers. Each has to be more than a bit of each of the rest. On this point I like quoting words I once heard from an old friend, Don Salvador de Madariaga: 'The man who is only isn't even.' The university graduate who is only an engineer, lawyer, doctor, or anything else you please is not fully even that which he set out to be."

Fig 3. Sir David Keir, Belfast Newsletter, Friday, December 20th 1946

PROFESSIONALISM

An excerpt from Sir David Keir's address as Vice Chancellor at the QUB medical graduation in December 1946 indicates what he expected from a professional graduate (Fig 3).[11] Their contribution to society should not be limited to their specialist area of knowledge. Pemberton, Pantridge and McGeown all exerted influences beyond their fields of medical expertise. Another excellent example of professionalism was that of Mr John Megaw, a skilful, scrupulous surgeon and clinical lecturer at QUB who supported Mollie whilst others discouraged her from bringing dialysis and transplantation

services to NI. He is also remembered for writing letters for wounded soldiers, transfusing, operating on and feeding them during the war. He was known as a quiet, wise man, an excellent golfer, gardener and host who practised his Christian faith.[12]

The breadth of service delivered by many rural general practitioners in NI in the same era was reflected in letters written to my mother on her retirement. Excerpts from one such letter include 'thanks for all the medical care you have shown us over the years'….'I recall the cold and frosty morning you came, took me into hospital, looked after me until my baby was born and then went to tell my husband the news' [cars and telephones were scarce]…..'the night when she was so ill'…..; 'and then there was the night we were so worried about…..'. Isolated incidents are woven into lifetime threads that make an impact which is hard to measure.

THREADS OF TIME, ANGINA AND TEAMWORK

The first president of the Ulster Medial Society, John Creery Ferguson, was born in Tandragee in 1802. He entered Trinity in 1818, studied Arts, took first place and obtained a gold medal before studying medicine in Edinburgh. Later he worked in Paris, with Laennec, inventor of the stethoscope, and Kergaradec, pioneer of foetal auscultation. He returned to Dublin and, in 1850, became the first Professor of Medicine in Queen's College in Belfast. The layout of the main street in Tandragee, where I now live, remains essentially unchanged over the past century but the horses and carts in earlier pictures have been replaced by cars, the road surface is no longer rough and lampposts and Chinese 'takeaways' have appeared.

Time, however, has not changed the importance of observation in determining the history of health or disease and the powers of remedies. Dr Samuel Black**,** born in 1764 in Co Down, studied medicine in Edinburgh, became a physician in Newry and was a careful observer. He described the sensation of angina, recorded pathological observation of ossified coronary arteries and developed the ischaemic hypothesis of angina pectoris.[13] He deduced that persons liable to angina were those of 'full and plethoric habit' and alluded to a genetic component - stating 'those who indulged to a greater extent than was suitable to the tendency of their constitution' were most susceptible. Others susceptible to angina were the psychologcially stressed, whilst those who were exempt included females, those who took strong exercise and the French. Today we recognise the same risk factors for coronary heart disease, and research is still ongoing in NI to determine the best ways of encouraging people to be moderate in their diet and take more exercise.[14] Some of my younger colleagues set excellent examples of engagement in sports and have published research relating to physical activity and health.[15,16,17]

On 25th July 1934, near Newtownhamilton, a cross-border garden fete encouraged the community to participate in physical activity. The organisers included the local GP and my father, a young minister in two small local churches. The advertising posters invited 'thousands' to come and participate in running and cycling races; all ages were catered for with a variety of other attractions.

Figure 4. The Strangford Stone & Commemorative Stamp

A thousand young people from NI did come together one day in the year 2000 and pulled ropes, to erect the Strangford stone, a 10 metre high granite block, weighing 47 ton (Fig 4). The ropes were specially designed and manufactured, by my husband Tommy Reid in Tandragee, - soft enough outside not to hurt children's hands, but with a core which was strong enough to withstand the immense weight without breaking. This achievement, a legacy of high quality teamwork, was recognised by a commemorative stamp (Fig 4) and in a poem by Michael Longley (Fig 5). The stone indicates how our past, present and future all are interwoven, to quote TS Eliot:

'Time present and time past
Are both perhaps present in time future
And time future contained in time past.'

TS Eliot

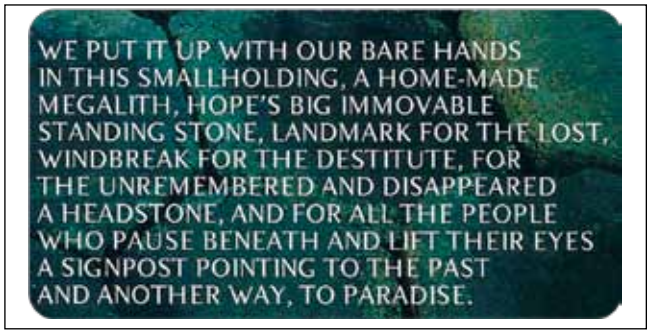

Fig 5. Strangford Stone (Stanza III) Michael Longley

CONCLUSION

Linen is a cloth of the highest quality. As a reminder of its importance in NI, the flax flower was chosen as a logo for the NI Assembly. In Biblical times when Pharaoh honoured Joseph he 'arrayed him in vestures of fine linen' (Genesis Ch 41, v 42). When Joseph of Arimathaea wished to honour Christ's body, he wrapped it in 'clean linen cloth' (Matt Ch 27, v 59). I wish to thank all my family, friends and colleagues who have supported me in preparing this address, with special thanks to Alun Evans. I hope it has shown something of the high quality which the medical professionals mentioned have demonstrated within their lives. I hope that you will concur with my conclusion that the virtual tapestry woven

from thoughts of flax, families, communities, and medical practice shows that none of us lives in isolation from others and many threads are intertwined in everyone's life – and health. Recognition of this should help us to provide the best quality of healthcare for our patients.

The author has no conflict of interest.

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Medical History

Tuberculous Scrofula: Belfast Experience

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SUMMARY

The Belfast blitzes of 1941 are blamed in our family for the scrofula of my younger brother and sister and myself. Guinea pigs and rabbits at Musgrave Park proved that each of us had bovine derived TB infection caused by failure to pasteurize milk when tuberculin-tested milk was not available. The clinical head of Harvard Medical School's anti-tuberculosis effort contacted his boss, Professor Maxwell Finland, who ascertained from Selman A. Waksman that his antibiotic streptothricin was bacteriostatic against TB but too toxic for humans. Finland, born 1902, knew Waksman (born 1888) well, each having emigrated from the Czarist-ruled Ukraine. Waksman , in 1942, had hopes for an analog to streptothricin he intended to name streptomycin: an antibiotic from *Actinomyces griseus* which had been culture-isolated in 1916 for his M.Sc. thesis. Streptomycin was still 6-9 months away from animal testing. The same Actinomyces species was also able to produce actinomycin C and D that was later supplied to Professor Sidney Farber of Harvard to start successful human cancer chemotherapy.

INTRODUCTION

In the spring of 1942 at Windy Edge, Dunmurray Lane, Ryki and I* were reading *Gray's Anatomy*. We came to Arnold's nerve, the auricular branch of the vagus. Ryki was my brother's god-father, Major Benjamin Rycroft[1,2]. He began to stare at my right ankle. He must tell the Yank Badger of his suspicions. Badger had arrived as the Chief of Medicine of Harvard's U.S. 5th General Hospital[3]. He had landed at Larne in March 1942, a year after the Luftwaffe blitzes of Belfast[2,4].

Ted Badger, came to my father, his commanding officer[3] at Musgrave Park, to say that the CO's three children had scrofula. My father brought Badger from Musgrave Park to Windy Edge, and our neck glands were palpated and our chests auscultated. My sister, Sarah, was 4 ½ years old and my brother Michael 20 months. I was 8 ½ years of age. Badger said that the skin lesion over my right Achilles tendon might be scrofulous. My mother was told the preliminary diagnosis. She said we had always been given milk from tuberculin-tested cows, or milk that had been pasteurized. During the blitzes this had not been possible, so our milk had been boiled by our cook, Kitty Lee.

CONFIRMATION OF DIAGNOSIS

Badger, as Harvard's chief tuberculosis clinician under Professor Max Finland[1], knew the importance of finding the "index case"[5]. He also knew that scrofula might be caused by exposure to human TB, but in our cases was more likely to be bovine. In humans the incubation period during childhood could be a year or more. The fact that we three children were diagnosed simultaneously suggested to Badger a strong infecting dose.

Badger asked me if anyone had coughed over me. He then asked if a cow had coughed over me. I laughed and said "No". He next asked if any of the three of us had kissed a local cow. "No." Did we like milk? "Yes." Had we been given boiled milk? "Only at the time of the blitzes." Our cook, Kitty Lee, and our nurse were then examined. They were, and had been, in perfect health. Badger then asked them if the milk had always been brought to a boil before being given to us. An awkward silence ensued. Kitty Lee said that once during the blitzes, when the regular tuberculin-tested milk, or guaranteed pasteurized milk could not be delivered, the milk for the nursery had been taken before her wood-fire had really warmed the local substitute. At very least, our milk should have been heated to 62º C for 30 minutes or 72ºC for 15 minutes. These were the rules of the Belfast Cooperative Society promulgated in 1913, said my father[6].

MANAGEMENT

What to do? Badger suggested that he preferred to use American equipment, methods and personnel. My father was in a delicate situation. The British were threatening him with court martial for purchasing illegal Éire and border-produced food for his command, the now- Allied Military Hospital at Musgrave Park[3,7]. The Whiteabbey TB Hospital scandal was being exploited by the left-wing politician Harry Midgley[4].

In 1908 TB was made a notifiable disease in Northern Ireland[6,8]. The United States authorities were convinced, not without reason, that United Kingdom TB incidence was a disgrace. In 1932, a Cattle Disease Committee was established, which reported in 1934 that approximately thirty percent of U.K. cows were tuberculous[9,10]. In Ulster, control of bovine TB was, during the period 1935-40 better than in Scotland, but not as successful as in England and Wales[10,11]. The Registrar-General's Annual Report for 1941 cites death rates from tuberculosis as 1.04 per 1,000 in Northern Ireland, 0.73 for England and Wales, 0.85 for Scotland and 1.24 for Éire[12]. According to Lionel Whitby[13], in the U.K. 5 years

* This, and all other first-person references are to the first author.

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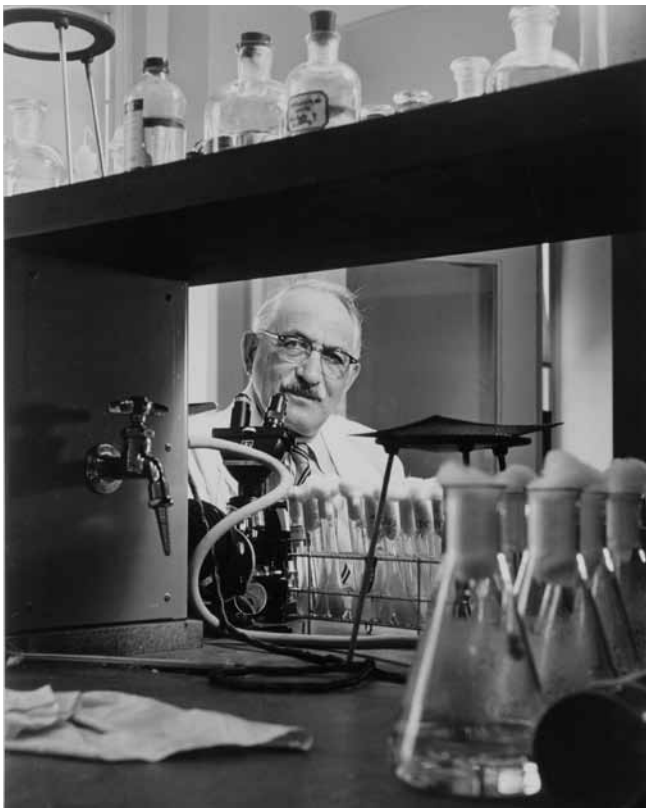


Fig 1. Selman Waksman by Philippe Halsman, gelatin silver print on paper, 1954. Image/Sheet: 34.7 x 27.4 cm (13 11/16 x 10 13/16"), mat: 71.1 x 55.9 cm (28 x 22"). National Portrait Gallery, Smithsonian Institution; gift of Steve Bello in memory of Jane Halsman Bello, © Philippe Halsman Archive, NPG.2004.45. Born in Prikula, near Kiev, on July 22, 1888, Selman Abraham Waksman matriculated in 1910 as an extern from the 5th Gymnasium in Odessa. Next year, having won a New Jersey State Scholarship, he entered Rutgers University[16,17]. In 1916, his seminal paper on Streptomycin[18,19] won him his M.Sc. degree from Rutgers. He became a U.S. citizen and was appointed a Research Fellow at the University of California, Berkeley. The University of California granted his Ph.D. in Biochemistry in 1918. The remainder of Selman Waksman's career was spent at Rutgers. He was elected to the U.S. National Academy of Sciences in 1942. Selman Waksman visited Ireland once, in 1946. He was confined with his wife Deborah to "a boarding house in Adare" in County Limerick's Golden Vale for three full days. "We were herded like cattle and told to wait. The facilities, especially the food, were very poor"[17]. After release, the Waksmans met their physician son, Byron, in Frankfurt-am-Main, where he was stationed in the U.S. Service after his having received his M.D. degree in 1943 from the University of Pennsylvania[17]. In 1952, Selman Waksman received the Nobel Prize in Physiology or Medicine. The Nobel Committee cited his work on "the microbiological population of the soil, sulphur oxidation by bacteria, microorganisms and soil fertility; decomposition of plant and animal residues, nature and formation of humus; occurrence of bacteria in the sea and their role in marine processes; production and nature of antibiotic substances; and taxonomy, physiology and biochemistry of the actinomycetes"[20]. After Stockholm he was decorated by the Japanese Government with the Second Order of Merit with the Grand Gordon of the Rising Sun and received in audience by the Emperor. He and his wife were invited to dinner at the home of H.I.H. Prince Takahito Mikasa, where plans for establishment of the Japan Waksman Foundation were formulated[21]. Selman Waksman died on August 16, 1973. Deborah, his devoted wife of 57 years, and a most talented musician, died a year later. They are buried at Wood's Hole, Cape Cod, Massachusetts. Byron, their son, an only child, joined the staff of the Massachusetts General Hospital before accepting chairs at Yale and in New York. He has returned to Harvard as a Visiting Scientist at the Center for Neurologic Diseases, where he is now the Doyen of Neuroimmunology and Mentor Extraordinaire[16,17].

before World War II, 70 percent of scrofula was caused by bovine TB. With bovine TB bacteria, rabbit intravenous inoculation leads to death within two months. Inoculation with human TB almost always leaves the rabbit unharmed[13]. When inoculated with bovine TB, guinea-pigs die in about six weeks. With human TB inoculation, the guinea pigs usually survive six months[13].

Badger said that it would take a week or so to assemble the necessary diagnostic equipment and the U.S. tuberculin for the Mantoux tests. Badger continued by saying that the British needles were blunt[14]. As to the tuberculin purity, did my father not know of the Lübeck "massacre of the innocents"—72 babies killed by contaminated tuberculin?[15]

Benjamin Rycroft[1] knew of our presumed scrofula. He asked Badger to ask his Boston boss Max Finland[1] to enquire whether the large Waksman group (Figure 1) at Rutgers University had any of their soil-derived antibiotics (Tables 1 and 2) ready to treat his godson. Rycroft and Badger knew that in 1932 the U.S. Federal Government and TB Foundations had given Professor Selman A. Waksman substantial support to find an antibiotic cure for tuberculosis[53]. This funding was continuing as were the Rutgers'[19,22-49] and Johns Hopkins'[54-56] publications.

Max Finland replied to Badger that it was a waste of time to do Mantouxs and that he "should put me on M and B 693 (Table 3) but not my brother and sister--she could take halibut-liver oil pills". My TB had spread, but theirs appeared localized. With fresh air and cod or halibut-liver oil my younger brother and sister would cure themselves: in our adulthood there would be a 5 percent chance of recrudescence[5].

Max Finland also told Ted Badger that Waksman had hopes for his newest antibiotic, streptothricin[37,42] and that Waksman was now concentrating on *Actinomyces griseus* which he had culture-isolated 26 years before for his Rutgers M.Sc.[19]. This, Waksman proposed to rename streptomycin and have tested, hopefully, on patients by two Mayo Clinic doctors[17,59-61].

Professor Waksman's son Byron, a medical student at the University of Pennsylvania, was now telling his father, relayed Max Finland, to quit treating tuberculous guinea pigs and rabbits and start on humans.

We awaited the U.S. equipment to needle biopsy our cervical glands and my right Achilles tendon[62-64] and appropriate swabs for our tonsils. The Musgrave Park guinea pigs and rabbits were thereafter inoculated and later autopsied. Bovine TB it was.

TABLE 1:

Publications of S.A. Waksman related to Development of Antibiotics, 1916-1943

YEAR	JOURNAL	REF
1916	Soil Sci	19
1918	J Infect Dis	22
1919	Soil Sci	23
1937	Soil Sci	24,25,26
1939	Soil Sci	27
1940	J Bacteriol	28
	Proc Soc Exptl Biol Med	29
	Soil Sci	30
	Chronica Botanica	31
1941	Proc Soc Exptl Biol Med	32
	J Bacteriol	33
	Bacteriol Revs	34
1942	J Pharmacol Exptl Ther	35
	J Biol Chem	36
	Proc Soc Exptl Biol Med	37,42
	Soil Sci	38,39
	J Bacteriol	40
	Science	41
1943	J Bacteriol	43,45,47
	Proc Soc Exptl Biol Med	44
	Mycologia	46
	Proc Natl Acad Sci (US)	48,49

Rycroft, on a visit to Windy Edge, told us we had the King's Evil, which could be cured by a Royal laying-on of hands. My father said he had asked Arnold Stott (Figure 2), physician to the Royal Household, to take over our management. "Second best to His Majesty," rejoined Rycroft.

After inoculation with the aspirate from my neck, the guinea pig and rabbit were unharmed, but became symptomatic when inoculated with aspirate from the lupus over my right Achilles tendon. My supratendinous aspirate was of bovine tuberculous origin. I was asked by Badger if I had ever been bitten on the right ankle by my brother or sister. " They had neck pathology, not facial," said Rycroft. My ankle healed after a fortnight of the sulphonamide treatment, which was then terminated.

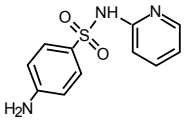
Remembering my reading lessons of the spring, I asked General Arnold Stott in September 1942 whether he had discovered Arnold's nerves in the hiding place of earwigs. "No, it was a German, Friedrich Arnold (1803-90)[70]. He died when I was your age," my Doctor Arnold retorted.

Arnold Stott took over our surveillance until 1952. Stott was a Governor of Wycombe Abbey, my sister's boarding school[67].

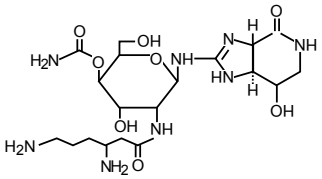
TABLE 2:

1. *SULPHAPYRIDINE (M and B 693)*[1,50] $C_{11}H_{11}N_3O_2S$
2. *STREPTOTHRICIN*[50] $C_{19}H_{34}N_8O_8$
3. *STREPTOMYCIN*[50] $C_{21}H_{39}N_7O_{12}$
4. *PAS (PARA-AMINO SALICYLATE SODIUM)*[51,52] $C_7H_6NNaO_3.2H_2O$
5. *ISONIAZID*[50] $C_6H_7N_3O$

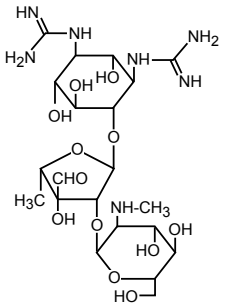
1. SULPHAPYRIDINE (M and B 693)



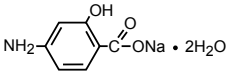
2. STREPTOTHRICIN



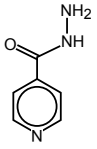
3. STREPTOMYCIN



4. PAS (PARA- AMINO SALICYLATE SODIUM)



5. ISONIAZID



Our upbringing was in no way constrained. Our schools were told by Sir Arnold Stott, from 1946 KBE, that we were in no way infectious. My sister's scrofulous neck glands were excised by a Newcastle-upon-Tyne surgeon, Ronald Watts, FRCS, Edin.—inelegantly but successfully, said my father. Stott agreed and my sister refused plastic surgery. My brother Michael's tonsils were removed. He awoke from the chloroform shouting "John's done this to me!" Not true, but

Fig 2. Sir Arnold Walmsley Stott, KBE, FRCP (1885-1958), by Walter Stoneman © National Portrait Gallery, London, and reproduced with their permission (No. x166999). Arnold Walmsley Stott was born at Oldham, Lancashire on July 12, 1885, and educated at Rugby School, Trinity College Cambridge, and St. Bartholomew's Hospital[65,66,67]. He was trained in Cardiology by Sir Thomas Lewis. Stott was recalled to Barts as Chief Assistant in Pediatrics, and then successively appointed to the Honorary Staffs of the Royal Chest Hospital and the Westminster Hospital. Stott served in both World Wars: in the First as a Major and in the Second as a Major-General. During World War II he was Consultant Physician to his second BEF and after evacuation from Dunkirk Adviser in Medicine to the U.K. Emergency Medical Service[66]. Stationed in Escrick Park near York with my father, they together inspected numerous war-time hospitals. From 1942 to late 1944 there were constant complaints from the RAF and the American Army Airforce that wounded bomber crew were not under the control of Airforce doctors. Air Vice-Marshall Geoffrey Keynes[14] moved stored blood to bomber stations and constantly visited them[68]. Stott and my father were often responsible for vetting those about to be placed in occupied Europe. Together with Elliott Cutler, Moseley Professor of Surgery at Harvard[3], and General Paul R. Hawley[69], Stott and my father planned the medical and surgical staffing for the consequences of the D-Day landings[69]. The initial medical D-Day landing meeting, according to my father's diary, was on Friday, March 5, 1943, at Thirlstaine Hall, Cheltenham, Gloucestershire. Stott used to regale me, my brother, and sister with apparently spontaneous topical rhymes seemingly based on the extraordinary activities of my brother's god-father, Benjamin Rycroft and his friend Dicky Hunter[1,2]. One of Hairy Ryki's rhythmical heroes was Ulsterman Harold Alexander, later Earl.

Stott joined the Council of Wycombe Abbey girls' school to which "He was a good friend"[67] in May 1951, and chaired the Council from 1953 through 1956. He was married for 47 years to Lily Holland. Their only son, J.R.W. Stott, was a long-time Rector of All Souls, Langham Place and Chaplain to Her Majesty the Queen. Her father, King George VIth, had appointed Arnold Stott, Physician to the Royal Household in 1937[66].

Badger had concluded that maybe it was the Belfast blitzes' infected milk, so we blamed the Germans.

FOLLOW UP

During the 1940s and early 1950s, Stott would examine us and recite his 'Ryki' ballads about Rycroft's war and horsemanship and the snakes and wild animals in Rycroft's Number 35 Harley Street consulting rooms. We heard from Stott of Rycroft's successful human corneal grafts[1] later of his use of Waksman's actinomycin D (NSC-3053) to treat certain eye tumors.

On July 1, 1960 my wife[71] became Sidney Farber's intern; we soon were told of Selman Waksman's 1954 arrival at the Boston Children's Hospital with 300 mg of actinomycin D (NSC-3053). The "little vial" was delivered and Waksman and Farber "started work immediately. To our great pleasure," writes Professor Farber, "we quickly found—that this was the most powerful antitumor agent"[72,73]. Within a few months, childhood Wilms' and Ewing's tumors were being cured. For gestational choriocarcinomas actinomycin was combined with Methotrexate, NSCF-740, glutamic acid, N-F-[[2,4-diamino-G-pterdinyl]methyl] methylamino]benzoyl][74]. Farber always gave credit to Gerhard Domagk's[1] group's work on animal tumor treatment with actinomycin C[75].

From 1960, Ted Badger was my caring Boston physician[76]. In 1969 our singles tennis match at The Country Club unmasked his need for an aortic valve replacement. The replacement at the Massachusetts General Hospital was entirely successful and led to a memoir and critique[77,78]. Badger lived another ten years, but would never again play tennis against me[79].

PARTIAL IMMUNITY

Is bovine TB disease protective against subsequent infection with human TB? This question has been debated since Koch's description of the bacterial causes of human and bovine tuberculosis[80]. My father did not seem to mind my boyhood conversations with Eric Arthur Blair at Greystone, Stockton-on-Tees, the home of the O'Shaughnessy's[14]. Laurence Frederick O'Shaughnessy, with whom my father had grown up, was known as Eric O'Shock from an early age. O'Shaughnessy was the famous Eric then, not his sister Eileen's husband, Eric A. Blair. Eric O'Shock's death at the Dunkirk evacuation of the second BEF was mourned by both the Allies and the Axis. He had been Sauerbruch's favourite assistant in Berlin[81].

TABLE 3.

Treatment Of Tuberculosis

YEAR PUBLISHED	DRUG	RESULTS
1937[1,57]	Sulphapyridine (M and B 693)	Limited usefulness
1940[29,31]	Actinomycin	Very toxic; not for paediatric use[17]
1942[41]	Clavicin	Less toxic[17]
1942[41]	Fumigacin	Less toxic but less active[17]
1942[37]	Streptothricin	Delayed toxicity; active against bacteria[17]
1944[58]	Streptomycin	Similar to streptothricin, less toxic[17]

In his 1954 autobiography[17] Waksman reported the isolation of actinomycin in 1940, clavicin and fumigacin in 1941, streptothricin in 1942 and streptomycin in 1943. Publication followed within the year.

Eric Blair in 1942 and 43 questioned me at Greystone about horse herd behaviour. He was writing *Animal Farm* as George Orwell†. We discussed the intelligence ranges of Clover the intelligent mare and Mollie the flighty but beautiful mare. I emphasized the leadership roles of mares and their territorial and herd behaviour. My mother told me not to get too close to this coughing Old Etonian. My father said I was protected by my Ulster infections.

George Orwell died of a pulmonary bleed from his TB on 21st January 1950, having had severe reactions to two successive but aborted courses of streptomycin. Eileen had died on March 29, 1945, and is buried in Jesmond Cemetary near my wife's grandparents.

When I was house physician at Barts to Chest Physician Neville C. Oswald[83], he taught "that middle class doctors and nurses were protected by having had the King's Evil." Is this protection more powerful than BCG vaccination? The Harvard Technology Assessment Group chaired by Professor Fred Mosteller[84,85] could not come to a conclusion on this issue[86].

For the years 2003-2008 in some hospitals with access to the full range of drugs, the hospital mortality in patients admitted with tuberculosis is one in three[87]. In parts of South Africa the incidence of multi-drug resistant tuberculosis (MDR-TB) or extensively drug-resistant tuberculosis (EDR-TB) is 72 per 100,000 health care workers; for the general population it is 6 per 100,000. Nosocomial infection of nurses is rampant[87]. The World Health Organization has reported an estimated 440,000 incident cases of MDR tuberculosis worldwide in 2008[88,89]. The World Health Association's (WHO) twelve recommendations for the control of TB must be implemented[90].

Sixty-nine years after the scrofula diagnosis I have a calcified cervical gland, my sister's neck scars are just visible, and my brother's cervical adenopathy seems to have had complete resolution. They have approved this Medical History.

† Mr. Blair told me the inspiration for Animal Farm's revolt of the animals was a carthorse on Hampstead Heath who went exactly where he wanted despite the wishes of his human leader. In Orwell's introduction to the Ukrainian edition of Animal Farm[82], he wrote that the horse was mistreated. He never mentioned equine ill-treatment to me.

ACKNOWLEDGEMENTS

We thank Professor Douglas E. Eveleigh of Rutgers University for his assistance. H. Boyd Woodruff[18, 28-30, 32,33,37-40] will receive the U.S. National Academy of Sciences 2011 Award for the Industrial Application of Science. Woodruff is being honored during the 148th Annual Meeting for "leading the development of multiple antibiotics, vitamin B_{12} and the avermectins, the latter revolutionizing parasite treatment in livestock and humans."

The authors have no conflict of interest.

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The James Logan Essay Prize

April 2011

James Alexander Logan, a second-year medical student at the Barts and The London School of Medicine and Dentistry, died in February 2001 after a distressing illness of three months duration. His family, friends and interested professionals subsequently set up the James Logan Trust[1] to encourage doctors and others to have the confidence to recognise and treat cancer pain. The trustees were not oblivious of the need for the proper recognition and treatment of pain arising in other conditions but they wished specifically to improve the general management of cancer pain and they felt that confidence and skill acquired in this could be applied in other cases.

Until pain is recognised it cannot be assessed or treated, and the recognition of pain, like the recognition of so many other conditions, depends almost entirely on listening to the patient and accepting what is being said. Once it is acknowledged that pain is present then treatment should follow. The Trust recognises that specialist palliative care teams provide an essential service especially when pain is severe and unrelieved by standard mediation but their existence does not absolve other doctors, no matter how junior or senior, from doing their best to treat pain promptly and effectively. The Trust would encourage every doctor to have the confidence to start a patient on simple pain-relieving medication and to know how and when to increase it according to well established guidelines.[2]

The James Logan Trust has provided funds for an annual prize for the best essay on "The challenges of cancer pain assessment and management" to be submitted by a Queen's University of Belfast undergraduate medical student after the completion of their fourth-year palliative medicine teaching. The University and its Palliative Medicine Undergraduate Curriculum Committee were instrumental in setting up the James Logan Essay Prize and the essays are to be judged by at least two members of the latter committee. The Trust is indebted to the University and to the Committee for their assistance.

The first essays were submitted in the summer of 2010 and the winning entry, written by Mrs Victoria Campbell, is published in this issue. The Trust congratulates Mrs Campbell on her effort and wishes her and the other essayists well in the future.

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1 Charity Commission Number 1102923.

2 WHO Pain Ladder: <http://www.who.int/cancer/palliative/painladder/en/>. Accessed 22

The James Logan Essay Prize

The challenges of cancer pain assessment and management

Victoria Campbell

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Both acute and chronic pain has been well documented as one of the most frequent and distressing symptoms in cancer, and has been shown to adversely affect quality of life.[1-5] While it is difficult to be precise, it has been estimated that pain is present in 36-61% of patients depending on cancer type, stage of disease, and patient setting e.g. in-patient or out-patient.[1] Of those patients with advanced cancer, at least 64% have been shown to experience pain.[6] The magnitude of the problem has been acknowledged by the World Health Organization who first published the analgesic ladder in 1986 in an attempt to establish guidelines for cancer pain management.[7] Yet despite advances in policy, diagnosis and treatment since then, research suggests that cancer pain relief is still inadequate.[3,8-9] This contradicts alternative research which has proposed that effective treatment of pain should be feasible for 70-90% of oncology patients.[8,10] The purpose of this essay will be to review those factors that may be contributing to the cancer pain problem, and also to consider any solutions which have been proposed in the literature.

It is widely accepted that assessment is the first step in the management of pain, indeed a comprehensive understanding of pharmacological and non-pharmacological pain management is of little value if the assessment of pain is inaccurate.[11-12] The current standard approach to the initial assessment of cancer pain includes a detailed history and physical examination, assessment of psychosocial circumstances, and a diagnostic work-up. It is important to consider what may be causing the pain, as well as to ask about pain intensity.[11] The specific challenge of cancer pain

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assessment lies in its subjective and evolving nature. Cancer pain is multifaceted, and clinically may be described as acute, chronic, nociceptive (somatic), visceral, or neuropathic.[5] Indeed a combination of all these subtypes may be present in any given patient at any one time. Furthermore, pain characteristics evolve over time due to changes in underlying pathophysiology.[12] Together these factors make the challenges to cancer pain assessment obvious, and it has been suggested that no individual assessment tool exists that adequately and accurately captures the multidimensional phenomenon of cancer pain.[5,12] This was well demonstrated by de Wit and colleagues who showed, using different assessment methods in the same patient population, that the percentage of uncontrolled cancer pain ranged from 16-96% depending on the method used to quantify it.[13] The absence of a standardised approach to cancer pain assessment not only means that pain is being inadequately treated, but also exposes the limitations of comparing research results in cancer pain management.[11]

In the literature, one of the main pitfalls of cancer pain assessment is failure to properly listen to the patient's complaint of pain, and to establish an accurate measure of pain intensity.[11,14-16] The development of a pain classification system is complicated by the factors mentioned above, however in the same way that the TNM Classification System has been a common language between oncology specialists for some decades, it has been recommended that a useful approach to cancer pain assessment is to use either a standardised visual analogue scale or a numerical scale.[11-12] The problem with these scales is that they are a one-dimensional assessment of pain intensity. In an attempt to develop a multidimensional assessment of pain Bruera and colleagues[17] developed the Edmonton Staging System (ESS) to assess and classify pain on the basis of seven characteristics, including mechanisms of pain, presence of incidental pain, daily opiate use, cognitive function, psychological distress, tolerance, and past history of alcohol or drug addiction. Patients were defined as having a good, intermittent, or poor prognosis for pain control based on a combination of these features.[11] Like other cancer pain classification tools, clinical use of the ESS was limited by problems with definitions of some of the constructs. An evaluation of the ESS in 276 patients found it to be highly sensitive but with poor specificity.[18] In response to its limitations, the ESS was later evaluated by a panel of experts and renamed as the Edmonton Classification System for Cancer Pain (ECS-CP).[19] Despite this, some researchers maintain that there is still no internationally accepted tool for cancer pain assessment.[11]

The literature suggests that inadequate pain management is a function of a number of factors, including misconceptions about the use of drugs commonly used to treat cancer pain, and a lack of communication between patients and clinicians, in addition to the absence of formal assessment procedures as outlined above.[3] With regards pain management following initial assessment, numerous barriers have been documented that prevent patients from receiving effective pain treatment, and challenge clinicians when providing adequate pain relief. These barriers have been divided into patient-related as well as professional-related barriers, and together they contribute significantly to the challenges of cancer pain management.[1,3-5]

Several studies have reported professional-related barriers that hinder cancer pain management. A recent systematic review of these studies found that nurses and doctors reported the following barriers most frequently: a) inadequate assessment of pain and pain management, b) patients' reluctance to report pain or to give a pain score, and c) professionals' inadequate knowledge of pain management.[1] Specifically, misconceptions expressed by health professionals have centred around the use of morphine in the treatment of cancer pain. A study by Elliott and Elliott surveyed 243 physicians and found approximately half to have misconceptions about drug tolerance, believing that an increased need for morphine was indicative of tolerance as opposed to increasing pain intensity. Over 20% had misconceptions about opiate addiction, though fewer oncologists expressed this misconception. Other misconceptions centred around opiate side effects and administration, with many physicians indicating that parenteral administration is the only route available when treating severe cancer pain. Perhaps the most concerning finding was that almost 20% of physicians believed that pain associated with cancer is inevitable and cannot be fully alleviated through treatment.[3,20] Other studies since then have yielded comparable findings.[3] The overestimation of addiction and an over-inflated fear of respiratory depression and other opiate side effects, has regrettably led to widespread under-treatment of pain in cancer patients.[5,21] Physicians themselves have acknowledged education in the area of cancer pain management to be inadequate.[22]

Like some health-professionals, patients and their families can add to the challenge of cancer pain management due to their misconceptions about analgesics and their side effects.[1,3-5] This in turn can lead to non-adherence to treatment regimens and poor communication of concerns about pain to medical staff.[3] Patients may not report pain for a variety of reasons, ranging from a desire not to 'bother' the doctor, to concerns that they are not being a 'good' patient, or a fear that their pain is indicative of disease progression and avoidance of this possibility. They may be reluctant to take their pain medication due to fears of becoming addicted or tolerant. They may also have concerns about side effects, or fear that the medications are 'bad' for their bodies.[3] In 1993 Ward and colleagues[23] surveyed 270 cancer patients to assess their concerns regarding the use of analgesics and the reporting of their pain to medical staff. The patients were given a 27-item questionnaire called the Barriers Questionnaire (BQ) and also the Brief Pain Inventory (BPI) to measure pain intensity. Ward found that many of the patients surveyed expressed some concern over issues relating to pain management, with concerns about addiction receiving the highest mean score. Patients who were older, had lower incomes, and less education had more concerns about pain management.[3,23] Further patient-related barriers were highlighted by a recent systematic review which analysed fourteen studies looking at adherence to analgesics by cancer patients.[1] One of these studies, by Lai and colleagues[24], showed that the stronger patients believed they could control their pain themselves, the less likely they were to adhere to treatment. In addition, the stronger they believed that medication was necessary for their pain, the more they adhered to treatment.[1]

In response to the challenges to pain management raised in the literature, better education has been proposed as a solution.[1]

In addition to health professionals who must be made better equipped to assess and therefore manage pain, patients and their families must be educated on the proper use of pain medications, and concerns regarding their side effects and addiction must be addressed. Only through facilitating open communication between professionals who are confident in their ability to deal with the complex nature of cancer pain and patients who understand and are less intimidated by their pain, may the doctor-patient relationship become one in which pain is best controlled.

The author has no conflict of interest.

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Letters

TRANSVERSE-SIGMOID COLON KNOT: A RARE CAUSE OF BOWEL OBSTRUCTION

Editor,

We report the case of a transverse-sigmoid colon knot, a rare cause of large bowel obstruction. There have been no previous documented reports of a transverse-sigmoid colon knot in the literature. Early surgical exploration in this case prevented progression to strangulation of the bowel and gangrene, which avoided the need for resection.

Fig 1. Coronal CT image showing dilated large bowel loops loaded with faeces.

Case Report: A 63year old lady was admitted to hospital with a 3day history of lower abdominal pain and obstipation. On examination, she demonstrated a distended tender abdomen. Digital examination revealed faecal impaction of the rectum. Blood investigations were normal and abdominal X-ray revealed dilated large bowel loops with some faecal loading. Initially managed conservatively, she proceeded for a CT abdomen and pelvis to ascertain the cause of obstruction. This revealed a very convoluted and faecally loaded large bowel, with two apparent areas of volvulus involving the mid-transverse and sigmoid colon. There was no evidence of free fluid or free air. Without clinical improvement, she proceeded to an exploratory laparotomy which revealed a long and redundant sigmoid colon found to be looping around a very mobile and redundant transverse colon. The caecum, distal transverse and proximal sigmoid colon were grossly distended and loaded with faeces. The entire large bowel was carefully untwisted to relieve the apparent knot and all involved loops appeared congested but viable. No resection of bowel was required. The sigmoid colon and mobile left and right colon were fixed with Vicryl to the abdominal wall. A caecostomy was formed to allow the colon to remain decompressed. Post-operatively, the patient made an unremarkable recovery.

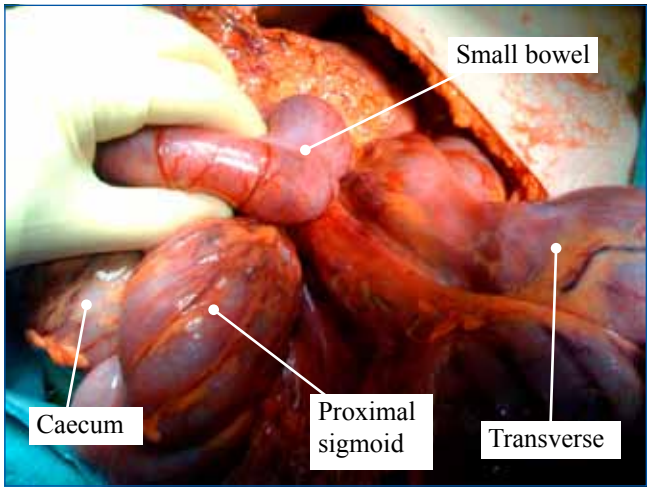

Fig 2. Photograph taken from theatre showing a grossly distended caecum, distal transverse and proximal sigmoid colon as a result of a transverse-sigmoid colon knot.

Discussion: The aetiology for intestinal knotting is unclear. It is likely that the knot is initiated by a hyperactive bowel which winds itself around the pedicle of a passive segment of bowel.[1] On presentation, patients complain of abdominal pain and symptoms suggestive of intestinal obstruction.[2] Preoperative diagnosis is extremely difficult due to the rarity of its occurrence and atypical radiological findings.[2] As an advantage over the plain abdominal X-ray in diagnosing ileosigmoid knotting, computed tomography (CT) can identify medial deviation of the distal descending bowel with a pointed appearance of its medial border.[3] Transverse-sigmoid knotting, however, does not appear to have such characteristic findings on CT imaging.[4]

Closed proximal loops become congested and gangrenous within a few hours. Therefore, aggressive resuscitation, early surgical relief of obstruction and appropriate antibiotic cover followed by exploratory laparotomy are indicated.[3] Usually the knot is tight and so untwisting the knot following deflation of the bowel is only possible when bowel loops remain viable. When friable, there is risk of perforation and septic shock and in such cases en-bloc resection of the gangrenous loops within the knot is highly recommended.

Conclusion: Intestinal knotting is a rare cause of bowel obstruction and despite reports in the literature that describe the clinical features and radiological appearances, diagnosis remains difficult. This report highlights to surgeons that in rarer cases of obstruction, where a clear diagnosis is not given and when conservative measures appear to be failing, prompt surgical intervention can work to reduce complications.

The authors would like to thank their colleagues in the Radiology Department at Altnagelvin Area Hospital for their assistance in preparation of this article.

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WALKING UP SHIPQUAY STREET. A TRADITIONAL WAY TO ASSESS CARDIAC RISK IN DERRY.

Editor,

NICE has recently issued guidance for patients with chest pain of recent onset suggesting exercise stress testing is of little value. Instead, an assessment is made of the nature of the pain then three risk factors in addition to age and gender are used to calculate a risk score. This allocates patients to a range of sophisticated tests including cardiac computed tomography, myocardial perfusion scan and coronary angiography.[1]

Fig 1. Shipquay Street, Londonderry, print (mid 19th Century), Heritage & Museum Service, Derry City Council.

Generations of physicians in Derry have used a somewhat simpler way to assess cardiac risk.

The City of Londonderry was established on the hilly island of Derry by royal charter of James I on 29th March 1613. By 1618, the city was completely enclosed in a stone wall with 4 battlemented gates. Four main streets ran from the gates to meet together in an elevated central area called the Diamond. Shipquay Street ascends from the gate nearest the river Foyle up to the Diamond. Its proximity to the docks ensured that many merchants such as rope makers, coopers and ship chandlers located there in the 1800s. The street is 180 metres in length and ascends 30 metres yielding a gradient of 1 in 6 (17%). [Figures 1 and 2]

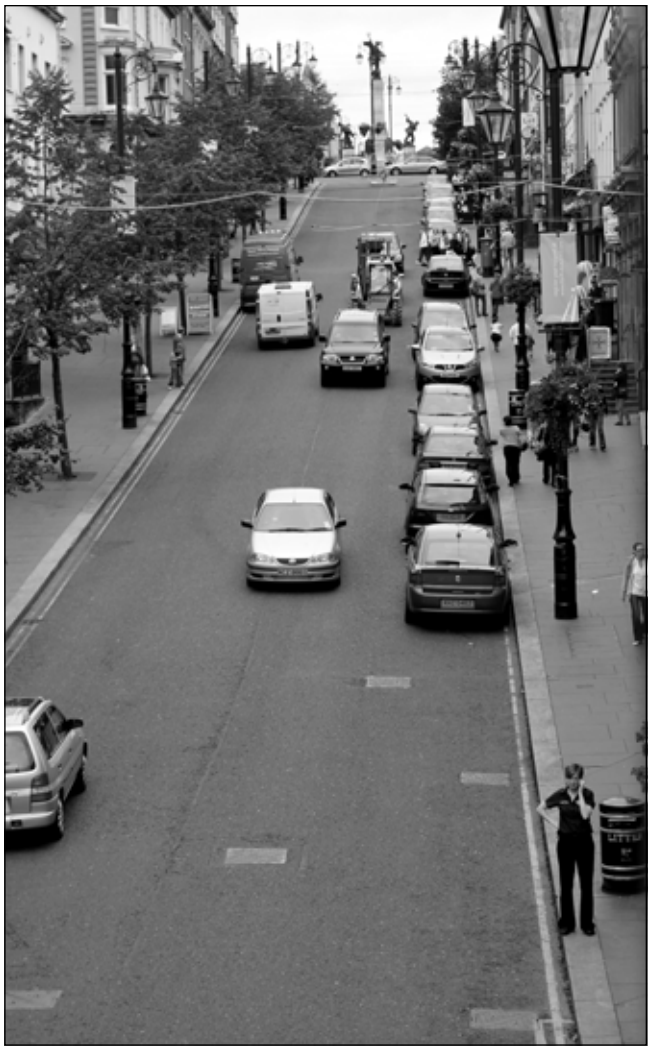

Fig 2. A modern view of Shipquay Street. Photographer, Tony Boyle, Heritage & Museum Service, Derry City Council

Walking up Shipquay Street at a moderate fixed pace (4km/hr) takes approximately 2 mins 40 secs. This matches the speed of stage 2 of a Bruce protocol exercise stress test but at a much steeper gradient. (12% for stage 2 and 14% for stage 3).

The exercise intensity associated with the walk is approximately 8-9 METS (1 MET = metabolic equivalent, an approximation of resting 02 consumption/kg/min). It is recognised that patients able to reach 8 METS have half the mortality of patients unable to achieve 5 METS with further incremental benefit of a 10-15% reduction in mortality for each addition MET over 8.[2]

We asked consecutive Derry residents attending our Rapid Access Chest Pain Clinic if they could walk up Shipquay Street without expecting the pain that led to their referral.

Fifty-five had no pain and of these, 53 (96.3%) completed a satisfactory treadmill test and were discharged. Two patients had unsatisfactory treadmills and underwent further tests: 1 with a positive treadmill underwent coronary angiography then stent insertion to right coronary artery and 1 with an equivocal test had a satisfactory myocardial perfusion scan.

The negative predictive value of walking up Shipquay Street without pain is thus 98% in terms of a final diagnosis of obstructive coronary disease.

We are aware that Derry physicians have asked this question for at least 50 years. It is interesting to note that the NICE assessment of the nature of chest pain includes onset with exertion but if this was adapted to include local landmarks such as Shipquay Street perhaps fewer costly investigations would be required.

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Orla O Kane *General Practitioner*

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The authors have no conflict of interest.

ACKNOWLEDGEMENT

We are grateful to Bernadette Walsh of Derry City Council Heritage and Museum Service, Harbour Museum, Derry for providing images, historical data and physical dimensions of Shipquay Street.

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FIFTY YEARS OF CARDIAC CATHETERISATION IN THE DIFFERENTIAL DIAGNOSIS OF LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION: THE BROCKENBROUGH-BRAUNWALD SIGN.

Editor,

In February 1961, Brockenbrough, Braunwald and Morrow described a new haemodynamic test in the differential diagnosis of left ventricular outflow tract (LVOT) obstruction, based on the haemodynamic profiles of the left ventricle and aorta immediately following an extrasystolic beat[1]. Despite 50 years of multiple technological advances, the observation retains a place in the discrimination of fixed versus dynamic LVOT obstruction.

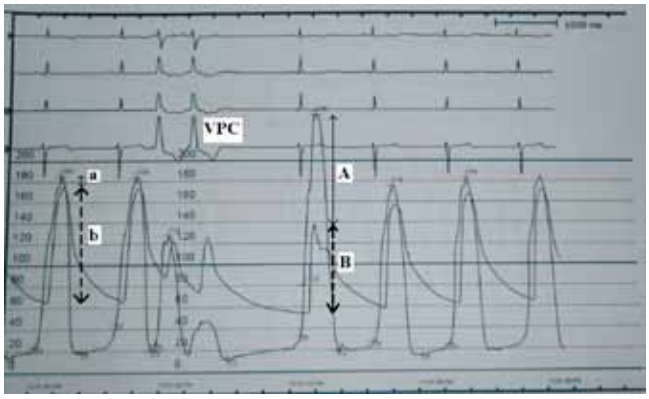

Fig 1. Dynamic left ventricular outflow tract (LVOT) obstruction (the Brockenbrough-Braunwald sign). At rest, a small (10mmHg) LVOT gradient is present (a) with an aortic pulse pressure of 110mmHg (b). Following two extrasystolic beats (VPC) there is a marked increase in LVOT gradient to 105mmHg (A) with a corresponding fall in pulse pressure to 75mmHg (B).

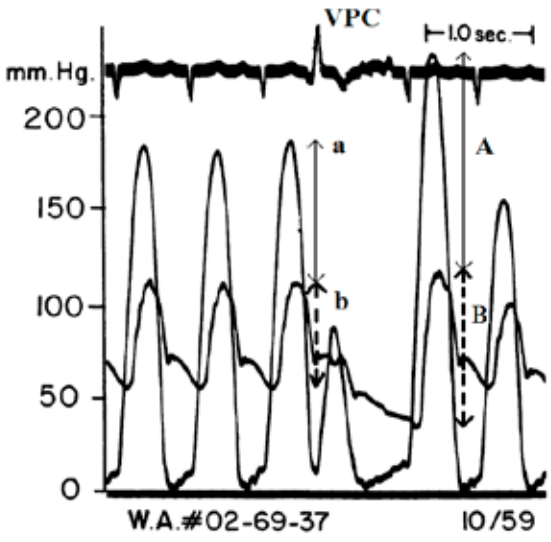

Fig 2. Fixed left ventricular outflow tract (LVOT) obstruction (In this example, aortic stenosis from the original work of Brockenbrough, Braunwald and Morrow (1)). At rest, the LVOT gradient is measured at 80mmHg (a) with a pulse pressure of 60mmHg (b). Following an extrasystolic beat (VPC) there is an increase in both LVOT gradient (A) *and* pulse pressure (B) to 115mmHg and 90mmHg respectively.

A 59 year old man, with hypertrophic cardiomyopathy was admitted for cardiac catheterisation after recent echocardiographic examination had shown a rise in LVOT gradient with progression of symptoms.

Simultaneous left ventricular and aortic pressure tracings revealed a classical Brockenbrough-Braunwald sign (figure 1) in keeping with "dynamic" LVOT obstruction. The sign is characterised by an abrupt increase in peak-systolic LVOT gradient, coupled with a decrease in aortic pulse pressure, immediately after an extrasystolic beat. It is distinct from "fixed" obstruction (e.g. aortic stenosis) where *both* the aortic pulse pressure and LV systolic pressure increase following an extrasystolic beat (figure 2).

Dynamic LVOT obstruction occurs when the ejection orifice is narrowed by increased force of LV contraction[2]. This can occur during catecholaminergic stress, exercise, the use of cardiac inotropes and following an extrasystolic beat (post-extrasystolic potentiation). In the latter case, the reduced effective orifice area leads to a fall in stroke volume and the associated fall in aortic pressure.

Even fifty years after its first description, the physiological understanding of dynamic LVOT obstruction is greatly enhanced by the original work of Brockenbrough, Braunwald and Morrow.

Peter J Scott,

Niall A Herity

The authors have no conflict of interest

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Ulster Med J 2011;**80(2):**111-116

Abstracts

The Ulster Society of Internal Medicine: 82nd -84th meetings, 2009-2010

82nd Ulster Society of Internal Medicine meeting: Friday 20th Nov 2009 at 2pm

ULSTER HOSPITAL

Combination therapy in essential hypertension: effects on insulin action of adding low dose thiazide to ACE inhibitor

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Background: Concern exists regarding metabolic effects of antihypertensive agents. Often more than one agent is required to meet blood pressure targets. Angiotensin converting enzyme (ACE) inhibitors, which are at least neutral in effect on insulin action, are recommended first line for many patients. We have previously shown that addition of low dose bendroflumethiazide to captopril has detrimental effects on insulin action compared with captopril alone in hypertensive type 2 diabetic patients. Our aim was to establish whether similar effects using this combination occur in non-diabetic hypertensive patients.

Methods: A randomised double blind placebo control crossover study was used. Following six weeks run-in, when regular antihypertensive medications were withdrawn and placebo substituted, patients received captopril 50mg twice daily with either bendroflumethiazide 1.25mg (CB) or placebo (CP) for twelve weeks. There was a six week washout between treatment periods. Insulin action was assessed by hyperinsulinaemic euglycaemic clamp following six week run-in and at the end of each treatment period.

Results: There were no differences between treatments in fasting glucose or insulin concentrations. Glucose infusion rates required to maintain euglycaemia were similar between treatments (CP 22.1±2.2 vs CB 22.2±2.2 µmol/kg/min). There was no difference in endogenous glucose production in the basal state (CP 8.9±0.5 vs CB 9.5±0.7 µmol/kg/min; p=0.23) or during hyperinsulinaemia (CP 2.2±0.6 vs CB 1.5±0.3 µmol/kg/min; p=0.30).

Conclusions: In contrast to the situation in type 2 diabetes, ACE inhibitor combined with low dose thiazide diuretic does not adversely effect insulin action when compared with ACE inhibitor alone in non-diabetic hypertensive patients.

Variation in left atrial anatomy in a Northern Irish population: a 64 multi-detector CT study.

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Pulmonary veins (PVs) are an important source of ectopic activity provoking atrial fibrillation (AF). This can be treated by PV isolation (PVI) but knowledge of the number and location of PVs is required for optimal outcome and treating complications. Access to the left atrium (LA) for PVI is facilitated by a "probe patent" foramen ovale (FO).

We studied PV and FO anatomy in 131 patients in sinus rhythm attending for 64 multi-detector coronary CT (64 MDCT) angiography. PV anatomy was graded according to a standard classification [(1)]. FO was assumed to be "probe patent" if there was: 1. a septal aneurysm, 2. separate septal layers or 3. spillage of LA contrast into the right atrium.

55% of the study population were male (mean 56, range 21-81 years) and 45% female (mean 57, range 32-81 years). Overall; 2% had 2 PVs, 16% had 3, 70% had 4 and 12% had 5. PV anatomy associated with high risk of developing AF was seen in 13% (R3a, R4a, R4b, R5 classification). On the left; 20% had 1 and 80% 2PVs. On the right; 5% had 1, 78% had 2 and 17% had 3 PVs.

"Probe patent" FO was seen in 28%; 7% with aneurysm, 13% with separate layers and 8% with contrast spillage.

PVs show significant anatomical variation in Northern Ireland. The excellent spatial resolution of 64 MDCT (0.625mm) facilitates detection of "probe patent" FO. 64 MDCT can provide useful anatomical information to the electrophysiologist performing PVI.

Marom EM, Herndon JE, Kim YH and McAdams HP. Variations in pulmonary venous drainage to the left atrium: implications for radiofrequency ablation. Radiology 2004: **230**; 824 -829.

Case report of Myo- and Hepatotoxicity following ingestion of an alternative remedy

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We report a case of a 26 year old lady who presented with thigh swelling, proximal myopathy and myoglobinuria following ingestion of a herbal remedy prescribed by an alternative medicine practitioner for weight loss. The remedy contained multiple constituents including Agaricus and Kava mushroom extracts.

The serum creatine kinase was 148,000 IU/L with elevated transaminases [AST 2427 U/L; ALT 670 U/L]. She was treated with aggressive fluid hydration. Following cessation of the remedy, serial monitoring demonstrated a prompt decline in the figures quoted above, consistent with the circulating half life of these bio-markers.

There have been no reported cases of concomitant hepatotoxicity and rhabdomyolysis in humans as a consequence of ingestion of alternative therapies containing Agaricus and Kava extracts. Case series have highlighted isolated hepatotoxicity with Kava in humans. Reports stipulate potential myotoxic effects of Agaricus extract in animal studies only[2]. To our knowledge there have been no publicised effects in humans, however other mushroom species have been implicated[1].

This case demonstrates the potential serious side-effects that may accompany alternative remedies particularly in the absence of regulation for these products.

1. Nieminen P, Kärjä V, Mustonen AM. Myo- and hepatotoxic effects of cultivated mushrooms in mice. *Food Chem Toxicol* . 2009 Jan;**47(1)**:70-4. Epub 2008 Oct 14

An unusual cause of haemobilia: pancreatic neuroendocrine tumour

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Haemobilia is a rare cause of upper gastrointestinal haemorrhage which can be difficult to diagnose, source and treat. We present the case of an 81 year old man who presented with epigastric pain, haematemesis, weight loss, pyrexia and obstructive liver blood tests. Abdominal ultrasound identified common bile duct (CBD) dilatation. This was confirmed on MRCP which also raised the possibility of a mass lesion in the distal CBD. The patient subsequently developed melaena associated with a sharp drop in haemoglobin. ERCP identified significant haemobilia associated with a suspected malignant stricture of the lower CBD and a biliary stent was inserted to decompress the biliary system. Mesenteric angiography failed to demonstrate the source of bleeding. Following CT staging, a pancreatic mass was successfully resected by Whipple's procedure. The gentleman subsequently made a good recovery and remains well at two year follow-up. Pathology demonstrated a neuroendocrine tumour of the pancreas as the cause of symptoms.

We offer a review of the available literature and discuss the difficulties in diagnosing and managing non-iatrogenic haemobilia. We suggest that when associated with symptoms of pancreatitis or cholangitis, hepatobiliary malignancy should be considered early in the absence of other clearly identified pathology.

A difficult pregnancy: Arthritis, TNF inhibitors, and infection

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We present the case of a 35 year old woman with severe juvenile idiopathic arthritis and primary infertility. She had required left hip and knee replacements. She achieved disease remission with the soluble TNF receptor Etanercept along with Methotrexate.

She discontinued all drugs including contraception in an attempt to conceive, but was unsuccessful after three years and recommenced treatment. She presented 8 weeks pregnant on Methotraxate 7.5 mg weekly and Etanercept 50mg weekly, which were immediately stopped. At 11 weeks she presented with right hip and knee pain. Ultrasound confirmed effusions of hip and knee, both of which were aspirated and injected with steroid with resolution of symptoms. Culture of hip fluid was positive for MRSA. The hip effusion resolved, swabs from other sites were negative, and she remained well. Antibiotics were not given.

At 27 weeks she presented with a flare of arthritis. Ultrasound confirmed effusions of the right hip and both ankles. These were aspirated and injected with steroid with good effect. All cultures were negative. She was commenced on Prednisolone 10mg/day. She remained well and delivered a healthy baby by elective caesarean section at term. She recommenced Etanercept and Methotrexate 1 month after delivery with further contraceptive advice.

This case highlights a number of issues including the use of potentially teratogenic drugs in women of childbearing age, the role of TNF inhibitors in the management of infertility, TNF inhibitors and infection, the use of clinic based musculoskeletal ultrasound, and the interpretation and management of unexpected laboratory results.

83nd Ulster Society of Internal Medicine meeting: Friday 14th May at 2pm

MID-ULSTER HOSPITAL

Moss Killer's Lung – A vitriolic reaction to a common and garden task

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A 50 year old male lorry driver with an unremarkable past medical history was admitted with a week long history of cough, wheeze and green sputum. He was an ex-smoker and had had no improvement with antibiotics and steroids in the community. CXR demonstrated no acute changes and he had never had these symptoms previously. On admission, he was in severe respiratory distress and required invasive ventilation in the ICU where he remained for a total of nineteen days, with very high airway pressures and copious secretions complicating weaning. Haematobiochemical, autoimmune, vasculitic, viral, atypical pathogen and allergen screening revealed no cause for his respiratory distress. His partner mentioned he had sprayed, without a facemask, a lawn treatment solution containing the active ingredient ferrous sulphate heptahydrate the day before his initial symptoms and then, when raking the lawn a week later, developed florid wheeze.

Ferrous sulphate heptahydrate, or green vitriol, is a compound known from antiquity and functions as a reducing agent in some moss killers. Precautions in avoiding inhalation and skin contact are advised on product packaging. While there are no published reports of inhalational toxicity, individuals who aspirate ferrous sulphate tablets develop cough, wheeze with necrosis and granuloma formation demonstrated on bronchoscopy[1]. Production of cytotoxic free radicals likely underlies the observed lung damage[2].

The case report highlights the need to take a detailed environmental history in those presenting with acute respiratory distress as, in this case, use of a common garden product induced an unusually severe

pneumonitis.

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2. Lamaze R, Tréchot P, Martinet Y. Bronchial necrosis and granuloma formation induced by the aspiration of a tablet of ferrous sulphate. *Eur Respir J* 1994;**7**:1710-1711.

Comparison of efficacy of tenecteplase and reteplase in ST elevation myocardial infarction

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Abstract

Throughout the Northern Trust, two different thrombolytic agents, either reteplase or tenecteplase, are used as part of the treatment of acute ST elevation myocardial infarction. Having found no other comparative studies, this retrospective study was designed to compare the efficacy of the two drugs using rate of follow-on emergency angioplasty as the primary outcome. The study retrospectively recruited 40 patients who had received reteplase and 40 who had received tenecteplase. Of the patients who received reteplase, 5 required emergency angiography. Of those who received tenecteplase, 15 required further intervention. This was a significant difference with a ratio of 37.5%:12.5% ($p=0.01$; significance was assumed to be $p<0.05$). Both groups contained 32 men and 8 women. There was no significant difference in the age distribution of the two groups ($p=0.678$). The secondary outcome was frequency of significant haemorrhage following administration of the two drugs. There was no significant difference found between the two groups ($p=0.09$). A further secondary outcome was 30 day mortality rate. There was one mortality, which had occurred in the tenecteplase group. To conclude, the study found that there is a significant difference between reteplase and tenecteplase, when considering the frequency with which further intervention is subsequently required for each of the two drugs. Patients in the study who received tenecteplase were more likely to require further emergency management than those who received reteplase.

Investigation of subtle changes in haemoglobin may allow earlier detection of colorectal cancer.

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Introduction: Colorectal carcinoma (CRC) may present as iron deficiency anaemia (IDA). Guidelines advocate gastrointestinal (GI) investigation in certain groups of patients with IDA in an attempt to detect CRC early. Some patients may initially have an insidious drop in haemoglobin (Hb) within the normal range. GI investigations at this point may allow earlier CRC detection and improve survival.

Aims: To assess if patients diagnosed with CRC had evidence of iron deficiency and/or a >10% drop in Hb without anaemia at least 12 months prior to diagnosis.

Method: 219 patients with CRC were selected retrospectively from histopathological records between Jan 2003 & Dec 2007. Laboratory data was then collected on each patient.

Results: Median age of patients was 72 years (Range 31-94). 148 patients (68%) had laboratory evidence of anaemia prior to diagnosis of CRC. 36% were microcytic. Iron status was checked in 30 of the 53 (57%) with microcytic anaemia and 43 of the 95 (45%) with normocytic anaemia. Median delay between detection of anaemia & diagnosis was 89 days. 28% of non-anaemic patients had a greater than 10% drop in haemoglobin in the 12 months prior to diagnosis.

Conclusion: The median time from detection of anaemia to diagnosis of CRC was nearly three months. Investigation of iron status was poorly performed in patients with anaemia. A quarter of patients with CRC had a >10% drop in haemoglobin without anaemia prior to diagnosis. Improving investigation of iron deficiency and of subtle drops in haemoglobin may allow earlier detection of CRC.

Long Term Outcome of Percutaneous Coronary Intervention in Octogenarians 2007-2009

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Regional Medical Cardiology Centre, Royal Victoria Hospital

Objective: To determine the clinical risks and procedural outcomes for elderly (age > 80 years) patients undergoing Percutaneous Coronary Intervention (PCI) and compare results with previous analysis in a similar population[1].

Method: A retrospective analysis on all patients greater than 80 years, undergoing PCI at a single tertiary referral centre, between 2007 and 2009. Patient demographics, procedural details and in-hospital complications were obtained from patient notes. 30-day, 6 month and 1 year mortality were obtained from analysis of the death registry. Results were compared with a similar study performed previously from 2003-2005 at the same centre.

Results: A total of 118 procedures were carried out in 106 patients over the two year study period, 2007-2009. This compares with 55 procedures performed over a similar time period 2003-2005. Mean age was 82.5 years, with 35% female cases. Mean TIMI risk score for Acute Coronary Syndromes was 5, overall mean logistic Euroscore was 16.75% (additive score 8.8) and BCPCI (British Colombia Percutaneous Coronary Intervention 30 day mortality) mean score was 7.44%. Actual 30-day, 6 month and 1 year mortality was 2.75%, 7.3% and 10.1% respectively. Cardiac related mortality (as per cause of death on death registry) was 2.75% at 30 days, 4.6% at 6 months and 4.6% at one year. This compares with 21.2% (18.2% cardiovascular) 1 year mortality in the 2003-2005 cohort. The use of radial access for procedure increased from 9.8% in 2007 to 37% in 2008.

Conclusion: The number of elderly patients undergoing PCI is increasing at our centre. The patient group is high risk as per TIMI, Euroscore and BCPCI risk calculators. Despite this, overall outcomes appear better than expected and superior to the previous 2003-2005 cohort.

1. SJ Walsh, K McAuley, PW Johnston. Percutaneous Coronary Intervention in the Elderly. *Ulster Med J* 2007; **76 (1)** 18-21

Comparison of radiation dose in femoral and radial arterial access coronary procedures; the effect of operator experience

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Radial access (RA) coronary procedures are associated with fewer access site complications compared with femoral access (FA). There is controversy regarding greater radiation exposure to both patient and operator using RA. We compared radiation dose during coronary procedures for both access routes and assess the effect of RA experience on radiation dose.

Fluoroscopy time (FT), and Dose Area Product (DAP) were recorded for all RA and FA procedures during 3 phases; default FA, transition phase (FA and early RA) and default RA.

848 FA cases (412 diagnostic, 436 interventions PCI) and 965 RA cases (459 diagnostic, 506 PCI) were assessed. For diagnostics, median FT for RA was longer than for FA (4.43 IQR 2.55–8.18mins vs 2.34 IQR 1.49–4.18mins ($p<0.001$), and associated with higher DAP (RA 1837 IQR 1172–2783μGy.m^2 vs FA 1657 IQR 1064–2376μGy.m^2, $p<0.001$).For PCI, FT was longer for RA: median 12.02 IQR 7.57–17.54mins vs FA 9.36 IQR 6.13–14.27mins ($p<0.001$) - this did not translate into an increased DAP (median FA 3392 IQR 2139–5193μGy.m^2 vs RA 3682 IQR 2388–5314μGy.m^2 (p=NS).

For diagnostic RA, FT fell from the transition phase (n=134) to the default RA phase (n=323); 5.12 IQR 3.07–9.40mins vs 4.21 IQR 2.49–7.52mins (p=0.03). This was not observed for PCI.

Transition from FA to a RA for diagnostics and PCI increased FT. DAP increased for diagnostic RA but not PCI as compared with FA. Fluoroscopy times for RA diagnostic cases reduced with experience.

Cardiac CT measurement of left atrial volume is a useful indicator of diastolic dysfunction.

AJ Howe, SM Hughes, JA Purvis.

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Cardiac CT is considered a static imaging technology unable to measure flow or dynamic parameters. Echocardiographic measurement of static left atrial volume (LAV) is however clinically useful and correlates with markers of diastolic dysfunction (DD). An increased LAV index is associated with risk of acute vascular events.

We prospectively measured LAV and LAV index using a validated technique [1] in consecutive patients attending for routine coronary CT angiography. Age and gender were recorded along with dimensions for calculation of left ventricular mass (LVM) and LVM index. Measurements were taken at 75% of the ECG R-R interval. Contemporaneous echocardiographic parameters of DD were noted if available.

Forty-nine patients were studied. Six had echoes. Mean LAV was greater in males (n=28, 83 mls) than females (n = 21, 72 mls) (p=NS). Mean LAV index was similar in both (40 mls). Statistically significant correlations (* $p<0.05$ and ** $p<0.001$) were seen between LAV and: age (n =49, r =0.39,**), septal wall thickness (n =49, r =0.68,**), LVM (n =49, r =0.76,**), LVM index (n =49, r =0.71,**), E/A ratio (n =6, r =0.87,*).

Measurement of LAV during cardiac CT shows weak correlation with age and fair to strong correlation with LV mass parameters and some echo parameters of DD. Recording LAV during routine cardiac CT may identify patients with DD.

1. Mahabadi AA, Truong QA, Schlett CL et al. Axial area and anteroposterior diameter as estimates of left atrial size using computed tomography of the chest: comparison with 3-dimensional

An unusual case of hypertension and hypokalaemia

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2. Department of Endocrinology and Diabetes, Craigavon Area Hospital, Portadown

A 51yr old man presented with a10 day history of profound weakness and hypotonia and 4 days of diarrhoea. He had a past history of hypertension treated with lisinopril and bisoprolol. He denied alcohol excess. Initial investigations showed a serum potassium of 1.8 mmol/l. and a metabolic alkalosis with pH 7.6 and bicarbonate 50.3mmol/l.

Subsequent investigations confirmed urinary potassium loss (30mmol/l for a prevailing serum potassium of 2.9mmol/l). Urinary pH was 8.5. Renin was 0.3ng/ml/hr and aldosterone 98pmol/l (off interfering medications). Gastrointestinal hormone levels showed a raised gastrin consistent with proton pump inhibitor therapy. CT adrenals was normal.

During follow up he remained well with a varying serum potassium level (2.9–3.6mmol/l) off potassium supplementation. He denied use of non-prescription medication or regular consumption of liquorice. On discussion with his general practitioner it materialised that he had an undisclosed history of kaolin morphine abuse. At the time of admission, he was consuming over 600mls daily.

Kaolin morphine can be purchased without prescription. It contains kaolin 20g/100ml, sodium bicarbonate 5g/100ml, morphine hydrochloride 9.2mg/100ml and liquorice extract 4.5g/100ml. Liquorice has a mineralocorticoid effect due to its content of glycyrrhizinic acid. We believe that the combination of liquorice extract and sodium bicarbonate resulted in the profound hypokalaemia and hypertension in this patient. Two similar cases have been reported of severe hypokalaemia associated with kaolin morphine use, one of which was fatal. This case highlights the importance of a careful medication history and the danger of unmonitored use of kaolin and morphine.

84th Ulster Society of Internal Medicine meeting: Friday 15th Oct 2010, 2-5pm,

BELFAST CITY HOSPITAL

Phenotypic variability in a three-generation Northern Irish family with Sotos Syndrome

Deirdre E Donnelly, Vivienne PM McConnell

Abstract

Sotos syndrome is a relatively common overgrowth disorder, following autosomal dominant inheritance, caused by mutations and deletions in the nuclear receptor Set domain containing protein-1, NSD1 gene. Affected individuals generally have advanced bone age, macrocephaly, characteristic facial gestalt and learning difficulties. Other features include scoliosis, seizures, cardiac defects and genitourinary anomalies. Tumours are a rare occurrence. Genotype-phenotype correlations are unclear, though those with a deletion appear to have more severe mental retardation. Full penetrance is seen, although familial Sotos syndrome is extremely rare. The low vertical transmission rate, which is not fully explained by cognitive impairment, is of great importance, particularly for mildly affected patients. Here we report a 3-generation pedigree with 7 affected individuals shown to harbour the NSD1 missense mutation c. 6115C>T. To our knowledge this is the largest Sotos family to be reported. The phenotype is extremely variable, thus highlighting the clinical heterogeneity that may occur. Detailed study of individuals with NSD1 gene abnormalities will be invaluable for further clarification of the phenotype and may lead to NSD1 gene analysis having prognostic value. Long-term follow up of these rare cases of familial Sotos syndrome should make an important contribution to the clarification of these uncertainties.

Key words – Sotos syndrome, three-generation, familial, phenotypic

variation

Potassium supplementation in patients with increased risk of cardiovascular disease

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2. Regional Endocrine Laboratory, Royal Victoria Hospital Belfast

3. Centre for Public Health, Queen's University, Belfast

There is limited evidence of the effect of potassium (K^+) supplementation on endothelial function with three studies suggesting a beneficial effect in healthy volunteers and mild hypertensives. It is known however that potassium increases aldosterone levels due to a direct effect on the adrenal gland and there is evidence that aldosterone excess is detrimental to cardiovascular health. Studies on the effect of aldosterone on endothelial function have been conflicting. We aimed to determine the effect of K^+ supplementation on 1. endothelial function 2. the RAAS and vascular inflammation.

Forty patients with >10% ten year cardiovascular risk were included in a randomised placebo controlled crossover study with 6 weeks of 64mmol KCl daily/6 weeks placebo and a 6 week washout period. Endothelial function was assessed using global pulse wave analysis (PWA) involving the detection of a change in augmentation index to salbutamol (endothelial dependent) and GTN (endothelial independent) induced vasodilation.

K^+ supplementation improved systolic blood pressure (p=0.013) but did not affect endothelial function or high sensitivity CRP (hsCRP). Plasma renin activity (p=0.048) and serum aldosterone (p=0.001) both increased significantly with K^+ supplementation compared to placebo. Serum K^+ increased with supplemental K^+ vs placebo (4.1 vs 3.9mmol/l; p=0.012) but hyperkalaemia did not develop.

These data show that K^+ supplementation lowered systolic blood pressure as reported previously. Interestingly K^+ supplementation was associated with an increase in both renin and aldosterone suggesting that K^+ may also stimulate the RAAS via the juxtaglomerular apparatus. Despite this K^+ supplementation did not affect global PWA or hsCRP.

Mycobacterium tuberculosis infections diagnosed and treated in the Royal Victoria Hospital, Belfast 2008-2010.

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Northern Ireland has the lowest TB incidence in the UK and Ireland[1]. Traditionally pulmonary disease is the most common clinical manifestation, with a smaller proportion of extra-pulmonary cases. The purpose of this study is to review the current epidemiology and clinical presentation of TB cases to the infectious diseases service.

Retrospective chart review of adult patients attending the infectious diseases service with *Mycobacterium tuberculosis* infection in the last 3 years.

60 cases of MTB infection were reviewed. The site of TB infection was: pulmonary in 43% (26), lymph node 18% (11), miliary 10% (6), and other anatomical sites 27% (16). HIV co-infection was seen in 17% patients (10), and in 7 of these HIV was diagnosed at time of TB diagnosis. 43% (26) were born in N. Ireland. Of those with available drug sensitivities, 7% (3) had isoniazid resistance and 15% (7) multidrug-resistance. 87% patients (52) have completed treatment, 3% (2) died on treatment, and 10% (6) remain on treatment.

When compared with historical data, extra-pulmonary TB and HIV co-infection are becoming increasingly common clinical features[2]. International migration, drug resistant TB, the HIV epidemic, and ease of intercontinental travel mean that TB will undoubtedly remain a clinical and public health concern. Our study reiterates the importance of clinician awareness of TB in this region of low prevalence. The current epidemiology of TB in Northern Ireland suggests that this infection will continue to cause disease which will present to various clinical specialties.

1. Epidemiology of Tuberculosis in Northern Ireland. Annual surveillance report 2006. Health Protection Agency, London: 2006. http://www.cdscni.org.uk/publications/AnnualReports/pdf/TBReport2006.pdf (accessed 16th September 2010)

2. Bonmarin I. Surveillance of Tuberculosis in Northern Ireland from 1992-1998. Communicable Diseases Surveillance Centre, Belfast: 2002.

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The effect of adolescent sugar intake on glucose metabolism in adulthood: a prospective longitudinal, observational study.

Lewis AS[1], McCourt HJ[2], Boreham CA[3], Courtney CH[1], McKinley MC[2], Murray LJ[4], Woodside JV[2], Young IS[2], Hunter SJ[1].

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There is conflicting evidence concerning carbohydrate type, insulin resistance and the development of diabetes.

We examined the effect of sugar intake in early teenage years on glucose tolerance and insulin resistance in early adulthood.

A detailed dietary history was performed in subjects aged 12 - 15y between 1989-1990. At follow-up (1997-1999) 489 patients had an oral glucose tolerance test, from which HOMA-IR was calculated. Univariate analysis was performed to assess the relationship between dietary sugar intake and outcome measures with adjustment for sex, height, weight, BMI, social class, physical activity level, total calorie intake, total fat intake and skinfold thickness.

In early teens mean dietary proportions of carbohydrate, fat and protein were 52±0.2%, 39±0.2% and 11±0.1% and mean total daily sugar intake (expressed as % of total energy) was 22±0.3%. Mean fasting plasma glucose (FPG) in early adulthood was 4.4±0.02mmol/L, median fasting serum insulin (FSI) level was 10.0mU/L (IQR 8.0, 14.0) and median HOMA-IR score was 2.0 (IQR 1.5, 2.9). There was a linear relationship between sugar intake and FPG with a 0.01mmol/L increase for every % increase in dietary sugar p=0.04. There was also a linear relationship between HOMA-IR score and dietary intake with a 2% increase in HOMA-IR for every % increase in dietary sugar (p<0.01).

Higher dietary sugar in early teenage years independently affects longer term glucose metabolism and is associated with insulin resistance.

Rates of acute coronary syndrome post rapid access chest pain clinic attendance

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The aims of rapid access chest pain clinics (RACPCs) are to identify patients at risk of adverse cardiovascular outcomes, and to prevent unnecessary hospital admissions. Recent NICE documentation has suggested that the format of RACPCs should change away from exercise stress tests (ESTs) to computerised tomography.[1] The purpose of this study was to evaluate the RACPC at the Ulster Hospital (UH) and the results that EST produced. From September 2007 to September 2009 2,182 patients attended the RACPC. 1555 were diagnosed as not having ischaemic heart disease (IHD). From September 2007 to July 2010 there were 2703 UH admissions with acute coronary syndrome (ACS). These cohorts were cross referenced using the microsoft programme access. Of the ACS admissions 170 had previously attended the RACPC. The average length between RACPC attendance and admission was 582 days, although 54 patients were admitted within 90 days. Of the 170 admissions 55 were previously diagnosed as not having IHD, with 8 of these patients admitted within 90 days of clinic attendance. The results show that the vast majority of patients who attended the RACPC have been diagnosed and treated properly. However about 3.5% of patients who attended the RACPC and had been diagnosed as not having IHD, developed ACS which is a similar rate to previous studies.[2] The average duration of RACPC attendance to ACS admission was 582 days which raises the question of how long a negative test is valid for, especially as little is known about the rate of coronary disease progression.

1. Cooper A, Calvert N, Skinner J, et al. *Chest pain of recent onset: Assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin.* National Clinical Guideline Centre for Acute and Chronic Conditions, London 2010.

2. Taylor GL, Murphy NF, Berry C et al. Long-term outcome of low-risk patients attending a rapid-assessment chest pain clinic. *Heart* 2008;**94:**628-632.

B12 deficiency without macrocytosis- A case series of difficult to manage skin disease.

Hunter HL, Corbett JR, Department of Dermatology, Belfast HSC Trust, Belfast, UK.

Vitamin B12 deficiency is typically diagnosed following further investigation of macrocytic anaemia. We report 6 cases of difficult to manage skin disease where significant B12 deficiency was identified. In 4 of these cases, there was no evidence of macrocytosis or anaemia, whilst 2 cases showed a raised mean cell volume. In all 6 cases of intractable skin disease there was dramatic improvement upon B12 replacement and simple topical therapies.

This suggests that macrocytosis is a poor indicator of Vitamin B12 deficiency and that a lack of B12 is associated with an impaired skin response to topical therapy. There are no previous reports of skin disease in association with B12 deficiency without macrocytosis and only several reports relating a normal mean cell volume with a B12 deficient state. One study analysed 141 consecutive patients presenting with neuropsychiatric abnormality due to B12 deficiency and found that 28% had no anaemia or macrocytosis.[1]

We suggest that this is an important area for further study since it appears that this could be an under recognised condition. There can be marked, often reversible cognitive and neurologic sequelae. The measurement of Vitamin B12 levels is simple, relatively inexpensive and perhaps more importantly simple and cheap to treat in an ever cost conscious health service. Should this become a routine investigation for patients whose skin disease responds poorly to usual therapies and in other specialties?

1. .Lindenbaum J, Healton EB, Savage DG et al. Neuropsychiatric disorders caused by cobalamin deficiency in absence of anaemia or macrocytosis. N Engl J Med 1988; **318(26)**: 1720-1728.

Decision Making in Stroke Thrombolysis: Is it Straightforward?

Fearon P, Kinnaird M, MacNair S, Fullerton K, Wiggam MI

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Delivery of thrombolysis for acute stroke remains a significant challenge for healthcare providers. Even when patients arrive on time, many are not treated due to restrictions in guidelines based on the eligibility criteria of randomised trials. Our aim was to determine how often treatment decisions in everyday clinical practice were straightforward and within guidelines. Methods: We reviewed records of consecutive patients treated between April 2006 and April 2010. We recorded standard clinical data and all factors affecting the decision making process. Results: 31 patients (19 male) received intravenous thrombolysis - mean age 69y (SD 11y). Mean onset-to-treatment time was 157min (SD 37min). Median pretreatment National Institute of Health Stroke Scale (NIHSS) score was 14 (range 3-23). 3 month outcomes were as follows: mortality, 10%, modified rankin score 0-2, 38%. One patient suffered intracerebral haemorrhage and one developed angioedema. Treatment decisions were straightforward and within guidelines in 6 patients (19%). 10 patients were treated outside guidelines: 4 aged >80y, 4 >3h from onset, and 2 with minor deficit. In the remaining 15 patients treatment decisions were complicated by one or more factors: uncertain of medication (1), consent issues (2), underlying neurological disorder (2), severe hypertension (1), established ischaemic change on neuroimaging (5), improving (1), recent oesphageal biopsy (1), known aortic aneurysm (2), large pleural effusion/likely lung cancer (1), cancer/chemotherapy induced colitis (1), dual antiplatelet therapy (1), recent coronary stent/dissection (1). Conclusions: It is important that clinicians responsible for thrombolysis develop sufficient expertise to facilitate appropriate and rapid decision making in complex situations.

Book Reviews

CARE OF THE CRITICALLY ILL SURGICAL PATIENT 3RD EDITION

Ian D Anderson. Hodder Education. August 2010. £49.99. ISBN 9780340987247

This is the third edition of the very successful CCrISP course manual written by a multi-disciplinary team of surgeons and anaesthetists. The first edition was published in 1999 and the book has been extensively updated for its third edition. However, the original aim of the course continues: that is to encourage trainees to have an understanding of the pathophysiology of critically ill patients, particularly in surgery, and to develop and hone patient management skills as part of a team. The course is now mandatory for the trainee surgeon and this manual is an important adjunct to the course. The lead co-ordinating author is Ian Loftus, a vascular surgeon in St George's Hospital, London, and the Critical Care Tutor at the Royal College of Surgeons of England. He has gathered together a very experienced team of surgeons and anaesthetists.

The course manual covers the main topics important in the management of the critically ill surgical patient. The layout is clear with bullet point boxes and realistic case scenarios. The objectives of this popular course remain, namely to develop an understanding of the theory of the management of critically ill patients, and to develop the practical skills to assess and manage these patients successfully. As is to be expected, there is an emphasis on communication, multi-disciplinary and multi-professional management of these ill patients.

The major topics covered include the assessment of the critically ill surgical patient, airway management, blood gases, cardiovascular problems, various types of shock including haemorrhage, monitoring, renal failure and detailed discussion on fluid, electrolyte balance and sepsis. Pain management, communication and organisational skills are also included.

As is to be expected in a manual of this sort, it is written in a very didactic fashion. Relatively minor critiques would include the observation that some of the figures are small and the font size in some figures is a little too small for easy reading, such as figure 7.2 on page 92. Despite proof reading some typing errors have been included such as page 17 (CVP should be CNS). For a future edition the authors may want to discuss in some more detail the management of hypovolaemic shock, particularly, as it applies to trauma. While I appreciate some of these principles are covered in the equally popular ATLS course, nonetheless, some of the lessons learned from Afghanistan should be mentioned, such as in resuscitation and damage limitation surgery; permissive hypotension, particularly the avoidance of prolonged surgery, acidosis, hypothermia, all of which lead to coagulopathy. These relatively minor criticisms, all of which can be remedied in a future edition aside, I recommend this as an excellent course manual for trainees.

Finally, a significant part of the senior FRCS Intercollegiate Examination in General Surgery is a viva on critical care; more senior trainees would benefit from reading this short manual (only 250 pages) prior to this examination.

Established Consultants will also find this manual of benefit, to scan as a refresher, for their day to day practice and as a useful teaching aid.

Overall, with some minor criticisms as outlined above, this manual can be recommended.

Roy Spence

GETTING INTO GP TRAINING.

Jasdeep Gill. RSM Books Hodder Arnold. 2010. 311pp. £21.99. ISBN 978.1.853.159.541

There is considerable competition for those wishing to enter GP Training. The 2010 cohort consisted of 3,305 vacancies throughout the UK with an applicant to vacancy ratio of 2:1. This little book written by Jasdeep Gill, who at the time of writing was a ST**2** in General Practice, is a must read for Foundation doctors applying for Specialty Training in General Practice. The book begins by looking at the qualities which make a good GP and it is around these competencies that the selection process is founded. The various stages of the Selection process are considered in depth and the applicant : vacancy ratios for the various regions declared. Of the sixteen Deaneries in the UK competition is greatest in London and Northern Ireland .

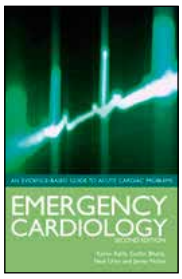
The registration and on line application process is considered along with useful tips on how to avoid rejection at this stage. Icons are used throughout the text to signify top tips, dangers, facts and figures etc. Examples of the Situational Judgement tests which are used in Stage 2 of the process and which test the applicant's ability to apply knowledge and skills to written scenarios depicting professional dilemmas and clinical problems, are described in a useful and extensive question and answer format. In my opinion this text would form excellent test preparation for potential candidates. The revision exercises which deal with all aspects of the assessment curriculum will allow candidates to identify areas of weakness and focus on their learning needs.

The format of the Selection Centres at Stage 3 is also described in detail, along with details of what to expect on the day. The two types of assessment exercises used in the Centres namely the written prioritization and the simulation exercises are described. The simulation exercise involves taking part in role play activities and the written prioritization exercise involves ranking a series of options with regard to priority given a clinical scenario. Advice on how a candidate can demonstrate the key competencies of empathy, communication, problem solving, coping with pressure and professional integrity, all of which are being assessed, are listed. There are several worked examples to consider, and the key points which are important to get across to the assessors are described. The last chapter discusses a list of hot topics relevant to modern general practice and around which many of the scenarios tested at Stage 3 are based.

This is a unique book. It is highly practical, contemporary, well set out and easy to read. The assessment process for general practice is challenging and reading and acting on the advice given in this book would be excellent preparation for a potential applicant.

Keith Steele

EMERGENCY CARDIOLOGY: AN EVIDENCE-BASED GUIDE TO ACUTE CARDIAC PROBLEMS.



Second edition. Karim Ratib, Gurbir Bhatia, Neal Uren and James Nolan. Hodder Arnold. 2010. Paperback 280pp. £22.99. ISBN: 978-0-340-97422-3

The white coat, the definitive symbol of the doctor, has been under assault in recent years. For physicians, white became the new black towards the end of the 19th century, reflecting a new emphasis on cleanliness and antisepsis. Nursing uniforms followed suit as did those of religious orders tending to the sick. Twenty years ago, a medical student or junior doctor would have been chided on the ward for forgetting their white coat. In the new millennium they are likely to be harassed for wearing one

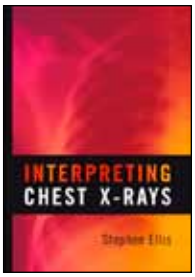
If the white coat has an uncertain future, what is to become of the pocket-sized handbook of emergency medicine? Undeterred, Ratib and colleagues have written a handbook of emergency cardiology aimed at junior doctors, cardiology trainees and emergency department staff. It fits perfectly in a white coat pocket

It opens with a list of abbreviations. Eleven chapters cover the range of inpatient cardiology: resuscitation, acute coronary syndromes, arrhythmias, infective endocarditis, cardiac trauma and more. It goes well beyond emergency cardiology; indeed the inexperienced cardiology trainee would be well-equipped to deal competently with most inpatient scenarios with the help of this book. Of particular value are the appendices: intravenous cardiac drugs, reference ranges for investigations and relevant web addresses. Tables list causes of (for example) ventricular fibrillation and hypertension and summarise clinical scoring algorithms. The 2010 changes to ALS guidelines are not included reflecting the limitation of all printed textbooks – the inability to stay current

Fans of *The Apprentice* will be aware of USP's (unique selling points). The stated USP of this handbook is that it is evidence-based. This could be a problem. Several times a year, long-standing dogmas in cardiology are disproved. It has been proposed recently that CPR may be harmful in out-of-hospital ventricular fibrillation. We don't know. Only a few emergency interventions derive from published evidence. Perhaps "The Practical Guide to Inpatient Cardiology"? The USP: it fits in your white coat pocket!

Carrie Moffitt, Niall Herity

INTERPRETING CHEST X-RAYS



Stephen Ellis. Scion Publishing Ltd. 2010. Paperback 250pp. £24.99 ISBN 978 1 904842 77 4

'Superfluous' would seem a reasonable characterization to any new work uniquely addressing the plain chest film. Ubiquitous for so long and bereaved of any cutting edge technological appeal, reading the simple chest x ray has become a pervasive practice amongst the medical community whilst generating inconvenient disdain by many sub specialised Radiologists. However in providing an uncompromising review of interpretive technique, this book's main strength lies in reaffirming the level of skill and detail required to extract the most from a very cost effective investigation.

Commencing with two succinct chapters on what producing a chest x ray entails and the anatomy thus demonstrated, there follows a pithy resumé of how any image is appreciated in the cerebral cortex. The essential components of the exam are then dismembered, specifically the indispensable review areas and pattern recognition, before applying them to the major disease categories. There are sections on critical care and post operative appearances and a short case study section. The text is erudite but readable and the complimentary schematics are clear.

Unfortunately the elephant in the room is the quality of the images. Reproducing the diagnostic spectrum of black and white contrast unto paper is notoriously difficult, but despite access to online images, it seems impolite not to at least try. The obvious question must be why bother with a hard copy at all when accessing an electronic format is essential anyway. This is particularly disappointing because the selected examples are relevant and informative.

The intended target audience is the diversity of healthcare workers exposed to imaging. Paradoxically in focusing so comprehensively on interpretation, beneficiaries are likely to comprise a much more select group, in particular those required to provide IRMER standard competency over the course of their career. I would have no hesitation in also recommending it as a reference to anyone requiring basic clinical information from this readily available investigation.

In short an accomplished text (and I suspect the author) has been let down by poor image reproduction quality, web access not withstanding. That interpretation of the plain vanilla chest x ray is not a soft skill is confirmed, but the foundations to eventual mastery are provided.

Mark Worthington

So you want to be a **medical student?**

Accepted 30 June 2010

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Being a medical student is necessary to undertake the essential examinations to become a doctor, but also provides an insight into medicine as a career and the social life it brings with it. The exams may be tougher and more frequent than for many other degrees; however, the number of social events and activities are just as numerous.

Medicine has always been a degree with a close-knit community spirit within each year group and even between the different years. This is likely a result of the long hours spent in class together. Medical students are renowned for working hard and playing even harder. Many universities have societies run by groups of medical students to organise social events throughout the year, like three-legged pub crawls, mystery tours and formals. Many medical schools also participate in inter-schools sports challenges and charities that organise a wide range of events, like fashion shows and health clinics. Within each university there is also an even bigger number of non-medical activities and organisations which are available to widen your social circle even further.

When choosing which university at to study it is important to know that there are three main types of courses. The first type, referred to as a traditional course, is purely taught by formal lectures for the first number of years and has separate clinical years, sometimes even at different universities. The second type, an 'integrated systems' based course, still has a significant number of lectures and small group teaching but from the first year has hospital-based clinical attachments. The final type, 'problem based learning', (PBL) uses clinical scenarios to stimulate personal learning and therefore requires a very motivated student.

In recent years the apprenticeship nature of the medical student has become less common, and this is the result of increased student numbers and a change in the organisation of health service provision. Although lectures and tutorials provide a more standardised level of teaching, clinical attachments provide a mentorship aspect, where positive experiences can inspire career aspirations. No matter which type of course you choose you have a minimum of two sets of exams a year and sometimes even as many as four.

Becoming a doctor does come with responsibilities, and a full list of these essential requirements are published in the General Medical Council's document called 'Tomorrow's Doctors' (http://www.gmc-uk.org). The safety of patients is paramount and all medical students will be expected to be able to communicate, work in a team, display a caring, honest and trustworthy attitude when interacting with patients and their relatives. It is crucial to remember that even as a medical student you are privileged with confidential patient information and so you should act appropriately to merit their trust.

The down side to being a medical student is the academically challenging nature of the course, a long hard slog requiring perseverance and unfortunately shorter holidays than most other degrees. However, overall the practical hands-on nature of the course, extensive variety of topics, and start of a career with endless opportunities with a social life that will help support you through the hard and fun times, all make being a medical student a fun few years of life that all of us look back on fondly.

Further information can be found on individual university websites.

THE ULSTER MEDICAL JOURNAL

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3. Scientific measurements should be in SI units (DN Baron. *Units, Symbols and Abbreviations. A Guide for Medical and Scientific Authors*. 5th ed. London: Royal Society of Medicine, 1994). Blood pressure may be expressed in mmHg and haemoglobin concentration as g/dl.

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