THE NEW ZEALAND MEDICAL JOURNAL
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This Issue of the Journal

An audit of referrals to the Southern Cochlear Implant Paediatric Programme
Philip Bird, Andrew Botting, Jacqueline Milburn, Daran Murray, Neil Heslop

Cochlear implants are devices which replace the hearing function of the ear and stimulate the nerve of hearing directly. They are used for adults and children whose hearing is so bad that hearing aids cannot help them. In children with pre-lingual deafness (children who have never heard or have lost the ability to hear before they develop speech and language) it is very important to restore their hearing with hearing aids or cochlear implants as soon as possible. For cochlear implants, there is very good evidence suggesting that the children should have their implants by the age of 1. This study was an audit to check on the ages of referral, especially in the pre-lingual children. We found that the average age of referral was unacceptably high. This means that the children may not perform as well with their cochlear implants as they would do if referred earlier. Just under half the children with significant hearing loss have risk factors which would normally be identified and their hearing tested very early on. Unfortunately our study showed that the children with risk factors were not identified and referred on any earlier than children without risk factors which is of great concern. The age of referral of children with significant deafness should drop as universal hearing screening is introduced but there may be significant problems if testing of children's hearing is not adequately performed in New Zealand.

Trends in the use of minimally invasive surgery in children
Preechapon Pleay Tovaranonte, Spencer W Beasley, Kiki Maoate, Russell Blakelock, Adrian Skinner

This paper summarises the trends in the use of key hole surgery and similar techniques in children (as distinct from adults), and has revealed that a wide range of operations have been adapted to become less invasive. This often leads to less pain after the operation, and shorter hospital stays for these children. Long-term results are probably the same as with conventional open surgery

Juvenile thyrotoxicosis—a South Island, New Zealand experience with long-term outcome
Bevan E W Brownlie, Penny J Hunt, John G Turner

Thyrotoxicosis (overactive thyroid gland) is very uncommon in children, and is usually due to Graves' disease which is an autoimmune disease. Follow-up of these children has shown that antithyroid medication is followed by long-term remission in one-third of patients. The remaining patients needed thyroid destructive therapy (ablation) by surgery or radioactive iodine. This was usually delayed until the late teenage years.

The utility of plain radiography in assessment of upper aerodigestive tract fishbone impaction: an evaluation of 22 New Zealand fish species
Tim Ritchie, Martyn Harvey

Fishbones inadvertently lodged in the throat can result in serious complications. Plain X-ray is commonly employed to search for impacted bones. This study examines the ability of X-ray to detect impacted fishbones, in a benchtop model. The results suggest plain X-ray is insufficiently sensitive to exclude the presence of an impacted fishbone when present for the majority of New Zealand fish species.

Helicobacter *pylori* infection and iron deficiency in teenage females in New Zealand
Alan G Fraser, Robert Scragg, David Schaaf, Patricia Metcalf, Cameron C Grant

Iron deficiency is an important problem in New Zealand children and young adults. A previous study of 8 Auckland high schools showed that 18.3% of girls had iron deficiency. This study assessed the potential role of *Helicobacter pylori (H. pylori)*, a bacterium that can infect the stomach, in causing iron deficiency. 792 female students (median age 16 years) from 7 Auckland high schools had *H. pylori* serology and tests for iron deficiency. The prevalence of positive *H. pylori* serology was highest for Pacific Island students (49.0%), intermediate for Maori (26.7%) and Asian (24.7%) and lowest for European (13.7%). Positive *H. pylori* serology was associated with increased risk of iron deficiency (RR 1.20) (after adjusting for age, ethnicity and school SES decile). This study indicates that *H. pylori* infection is associated with iron deficiency and should be considered as a possible cause when iron deficiency is diagnosed. This study also confirms the significant public health issue of *H. pylori* infection particularly for Pacific Islanders who will carry a burden of upper gastrointestinal disease into coming decades, causing both peptic ulceration and gastric cancer, because of high rates of *H. pylori* infection.

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Severe to profound hearing loss—are we really managing it in New Zealand?

Colin R S Brown

It is 24 years since the first cochlear implant surgery was performed in New Zealand and 22 years since the first child was a recipient of a cochlear implant. This is clearly not new technology, but one which still has the ability to transform the life of a child or an adult. Hearing loss has serious consequences for development of oral language, emotional and social development, educational attainment and employment.[1,2]

Not only is cochlear implant technology the recognised standard of care for most children and adults with severe to profound hearing loss, it is also a cost-effective medical intervention with potential for indirect cost savings in education and community support.[3–5] The factors influencing outcomes in an individual child or adult are myriad, and expectations for children with multiple disabilities or meningitis are lower than when the aetiology is "non syndromic recessive deafness" which is the most common cause of deafness in newborns and young children in New Zealand.

For many children born with a severe to profound hearing loss, a cochlear implant may give them an opportunity to develop normal speech and language, attend mainstream school and engage in a nearly full range of employment opportunities. Long-term studies of children who have received cochlear implants also demonstrate that many are able to use the telephone and some learn musical instruments and other languages.[6,7]

Early diagnosis and treatment is one of the most important factors positively influencing successful outcomes (and cost-effectiveness) in cochlear implant use, hence the concern of Bird et al[8] who demonstrate significant delays in referral to the New Zealand Southern Cochlear Implant Programme for some children, some of whom were turned down as candidates because of their age. Included were children with known risk factors for hearing loss. This is a failure of the medical, audiological and nursing community.

Delivery of cochlear implant services in New Zealand is administered by the Northern and Southern Cochlear Implant Trusts, funded principally through the Ministry of Health (based on a fixed number of children and a fixed number of adults receiving an implant each year) supplemented by piecemeal fund raising. Even though children receive funding priority, on occasions this fixed approach has proved inadequate.

When Waikato District Health Board (DHB) commenced neonatal hearing screening (prior to the development of a National Programme), some children diagnosed at birth with severe to profound hearing loss were unable to receive timely treatment as no allowance had been made for the downstream resultant need for cochlear implants.

Additional fixed funds have since been made available for cochlear implants in anticipation of increased numbers of neonates referred from the National Newborn

Hearing Screening programme, but in the last 2 years most of these funds have been fully utilised even prior to screening "roll out."

Cochlear implants, while demonstrably cost-effective, require a significant up-front investment of approximately NZ$ 50,000 for the initial assessment, hardware, surgery and rehabilitation. Demand for implantation in adults has increased. Performance with cochlear implants has continued to improve with improving technology, and thus people with lesser degrees of hearing loss (but still struggling to hear with hearing aids) are now able to benefit. New hybrid devices (which combine hearing aid and cochlear implant technology) designed for people with mainly high-frequency hearing loss are now also available.

At the present time there are 127 adults on waiting lists for cochlear implant surgery. The term "waiting list" is clearly a misnomer. Sixty to 70 people are added to the "waiting list" each year while only 25 are funded to receive an implant. That is, the waiting list for cochlear implant surgery for adults is growing by approximately 40 per year. Most of the adults on the Southern and Northern Cochlear Implant Programme "waiting lists" will never receive one.

New Zealand insurance companies are not obliged to fund cochlear implants (and therefore specifically exclude them), as they are required to do in Australia where 70% of the implants are funded through private insurance. This is very clearly an important factor contributing to the numbers of New Zealanders on waiting lists who are medically and audiologically appropriate for a cochlear implant, that can neither get one publicly nor through medical insurance. This situation could be changed by an alteration in health policy direction.

It is important to remember, however, that hearing with current implant technology is still not normal and even the best implant users struggle to hear in some situations, particularly in background noise.

In recent years bilateral implantation has resulted in improvements in ability to hear better in these "acoustically hostile" situations.[9] In the UK the National Institute for Health and Clinical Excellence (NICE) guidelines released in January 2009[10] may oblige UK health boards to fund bilateral implants for children for this reason, and bilateral implants in adults who are additionally visually impaired. In New Zealand, some children with families who can afford a second implant have received them. Few adults have done so.

The long-awaited New Zealand National Newborn Hearing Screening Programme is now in the third and final year of its roll-out across the district health boards. The intention is that all neonates will be screened for hearing loss by 1 month of age and babies identified as at risk of hearing loss will receive full diagnostic audiology by 3 months, with intervention if required, by 6 months of age. Intervention may include the use of hearing aids or cochlear implants in addition to education habilitation services.

Estimates that 120–170 newborn children with permanent bilateral hearing loss were likely to be detected through the National Neonatal Hearing Screening Programme were based on historic data collected by the National Audiology Centre (functionally no longer in existence) from voluntary reporting by audiologists.[11] Data also indicate a substantially disproportionate ratio of Māori and Pacific children diagnosed with

hearing loss, who may be more at risk of non attendance for follow-up audiologic assessment.

Data have not been collected since 2005 and this situation is not expected to improve until funding is available for a more comprehensive database incorporating other aspects of child health. The National Screening Programme is therefore compromised in its mission of vigilant follow-up of "missed" babies without a national database, which was recommended by the Advisory Group to the National Screening Unit in 2005.[12]

Enthusiast members of the New Zealand Society of Audiology have recently re-instituted an independent deafness database based on voluntary reporting of new diagnoses, and more meaningful data about the frequency and severity of hearing loss occurrence is expected by the end of the year.

Bird et al point out that the neonatal hearing screening programme will reduce the number of delayed referrals for cochlear implantation. However, stumbling blocks may persist for unscreened children and also for those with a gradual onset of deafness who have normal or nearly normal hearing at birth. As a rule of thumb, we may expect, by age 5 years, approximately double the number children diagnosed with hearing loss that were diagnosed at birth.

The main aetiologies are: (non-syndromic) genetic, congenital cytomegalovirus and meningitis. This means that despite the existence of a newborn hearing screening programme, professional vigilance must be maintained. The days of finger clicking, hand clapping and bell ringing by family practitioners and Plunket nurses to "diagnose" hearing loss should be long gone and all children suspected of hearing loss should be referred to an audiologist. A regular programme of audiologic monitoring of children with identified risk factors, combined with the before school check should help supplement parental and health worker awareness.

In their paper, Bird et al indicate that paediatric electro-physiologic audiology expertise is always available. In fact, there is only a small handful of audiologists with the requisite skill and experience in interpreting diagnostic ABR tests, which are a form of EEG. The National Screening Unit is attempting to address this partly through up skilling courses, but it is simply not realistic to have an expert paediatric audiologist/auditory electro physiologist on each doorstep of 20 DHBs. Diagnostic and management inaccuracies can expect to continue, consequent on small paediatric audiologic caseloads in small DHBs.

Awareness of deafness in the medical community needs to increase/improve. Greater leadership from the Ministry of Health needs to be reflected through: completion of a National Hearing Loss Database; reshaping expert paediatric audiologic support of the Newborn Hearing Screening Programme, and; redirecting policy on cochlear implant and insurance funding if we are to see acceptable outcomes for deaf children, adults and society. The sooner the better.

Competing interests: Dr Brown is a cochlear implant surgeon, a member of the current and previous advisory groups on Newborn Hearing screening to the National Screening Unit and is Chairman of (and a shareholder in) Dilworth Hearing Ltd.

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An audit of referrals to the Southern Cochlear Implant Paediatric Programme

Philip Bird, Andrew Botting, Jacqueline Milburn, Daran Murray, Neil Heslop

Abstract

Aim To audit the age at referral and time to assessment and implantation in children presenting to the Southern Cochlear Implant Paediatric Programme and identify any delay in implantation, particularly in individuals with pre-lingual sensorineural hearing loss.

Methods All paediatric referrals to the Southern Cochlear Implant Programme from March 2003–March 2008 were evaluated retrospectively. The Student t-test was used to compare median time intervals between those with and without risk factors for Sensorineural hearing loss.

Results Seventy five children were referred, 42 with pre-lingual deafness and 33 with post-lingual deafness. The median age of referral was 17 months with a range of 1 to 203 months. Thirty-five children with pre-lingual deafness were accepted as candidates and implanted, 6 were declined as they were too old to receive benefit from cochlear implantation. Of these 6 children who were declined, 4 had not been adequately diagnosed despite having risk factors for sensorineural hearing loss. There was no significant difference in the age of referral in pre-lingually deafened children between those with risk factors and those without risk factors.

Conclusion The age at referral of pre-lingually deafened children to the Southern Cochlear Implant Programme is unacceptably high, particularly in those children who have known risk factors for sensorineural hearing loss.

Cochlear Implants (CI) are devices which replace the auditory function of the inner ear and directly electrically stimulate the cells of the spiral ganglion (which form the cochlear nerve within the cochlea). They are used in both adults and children with severe to profound sensorineural hearing loss (SNHL) where hearing aids provide insufficient amplification for the understanding of speech.

Children with SNHL may be categorised into having either prelingual or postlingual deafness. To optimise language outcomes it is very important to identify and manage prelingually deafened children early, preferably before the age of 6 months.[1]

For those children who require cochlear implantation there is clear evidence that implantation prior to age 2 leads to potentially better results in speech, language and reading skills.[2] With the introduction of neonatal hearing screening in many parts of the world, and thus much earlier implantation, there is steadily accumulating evidence that implantation prior to age 1 year is associated with improved outcomes.[3–8]

At the other end of the spectrum, children over the age of 5 who have not received sufficient sound to develop speech and language are highly unlikely to ever do so because of reduced neural plasticity. In these instances a cochlear implant provides

awareness of environmental sound only, and unless the child has no hearing whatsoever does not provide any significant advantage over hearing aids.

New Zealand is in the process of introducing universal neonatal hearing screening. Prior to this New Zealand neonates only had their hearing tested if they had risk factors for SNHL or if there was parental concern. A risk factor registry can identify up to 66% of those with significant bilateral deafness.[9]

These risk factors include all of the factors predisposing to admission to a neonatal intensive care unit (such as prematurity, hypoxia, low birth weight), maternal infection, positive family history and a number of syndromes which are associated with hearing loss. The biggest single cause of deafness however is genetic, autosomal recessive, non-syndromic sensorineural hearing loss for which there is no "warning". In New Zealand in 2005, 58% of children had no known risk factors for their hearing loss. It is likely that a significant proportion of these children had genetic, autosomal recessive non-syndromic sensorineural hearing loss.

The Southern Cochlear Implant Programme (SCIP) provides comprehensive CI services to the South Island and lower North Island. We are aware of significant delays in some referrals and hence have undertaken an audit to further categorise these. In addition, to try and improve our service to our patients, this study should serve as a baseline prior to the introduction of universal neonatal hearing screening in New Zealand.

Method

A retrospective chart analysis was made of the referrals to the Southern Cochlear Implant Programme (SCIP). The first 5 years of this programme, from March 2003 through to March 2008 were chosen. Data was collected in respect to the age of the child (expressed in months) and the following time points; diagnosis, referral to the program, assessment and then either implantation or observation. The children were divided into two categories, those with pre-lingual deafness and those with post-lingual deafness, based on individual chart review. Those with risk factors for sensorineural deafness were also identified.

Results

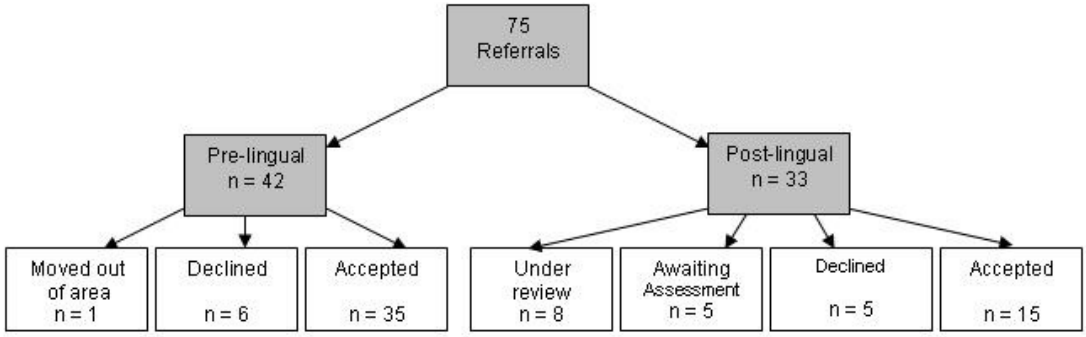
There were 75 children referred over this 5-year period, of which 53% percent were female and 48% male.

Following assessment 50 children (67%) were accepted as surgical candidates, 8 remain under review with progressive hearing loss, 5 were awaiting assessment and 12 have been declined a cochlear implant.

Thirty-three children were identified with post-lingual deafness (44%). Twelve were implanted, while 3 await surgery. Eight remain under review while 5 were awaiting assessment. Five children were declined a cochlear implant.

Forty-two were identified as having pre-lingual deafness (56%). The median age of referral was 17 months with a range of 1 to 203 months. With 6 children over the age of 5 years (5.5yrs, 5.9yrs, 8.5yrs, 8.9yrs, 10.9yrs, 17.4yrs), the average age was much higher, at 32 months. Thirty-five of these children underwent implantation. Seven children with pre-lingual deafness were declined an implant. One child moved away from the region and has had surgery elsewhere, while six children were declined surgery due to their age (Figure 1).

Figure 1. Flow chart of referrals to the Southern Cochlear Implant Paediatric Programme 2003–2008



The 35 children with pre-lingual deafness who received a cochlear implant were referred with a median age of 16 months (mean 18 months), assessed by 18 months (mean 21 months), approved by 20 months (mean 23 months) and implanted by 21 months (mean 24 months).

From the 75 referrals (both post-lingual and pre-lingual) there were 25 children with known risk factors for sensorineural deafness. Ten children were premature, 5 had a family history of deafness, 2 had Jervell and Lange-Nielsen syndrome and 2 had CHARGE syndrome. The remaining 6 children had a diagnosis of: Goldenhar syndrome, meningitis, Beckwith-Weidemann syndrome, Refsum's syndrome, cytomegalovirus (CMV) infection and cerebral palsy. Despite having known risk factors only 13 of these children (52%) were screened for deafness.

Twenty children identified with pre-lingual deafness had known risk factors. Twenty of the 42 children (47.6%) identified with prelingual deafness had known risk factors. Eight (40%) were screened for deafness. Sixteen have been implanted. These children were referred (median age) by 14 months, assessed by 17 months, approved by 18 months and implanted by 19 months. Using the Student t-test there was no significant difference between the ages of referral (P=0.88), assessment (P=0.97), approval (P=0.86) and implantation (P=0.90) for those children with known risk factors compared to those without.

Twelve children have been declined an implant; 5 with post-lingual deafness and 7 with pre-lingual deafness. Of the 7 declined children with pre-lingual deafness 6 were declined surgery due to their advanced age, and 1 child moved out of the area. Four children with pre-lingual deafness and a known risk factor were denied surgery. The risk factors included prematurity (3) and CMV infection (1).

Discussion

This audit demonstrates a number of areas of concern relating to children with significant pre-lingual deafness. These children have insufficient hearing levels to access enough information to develop speech and language. As stated previously, it is highly desirable to implant these children at a young age, preferably by 12 months.

The mean age of referral for this group was 32 months, this figure being distorted somewhat by 6 children who were referred after the age of 5 years. All of these older children were declined cochlear implantation, not on audiologic grounds, but because they were too old to be able to utilise the technology to learn spoken language.

A major cause of late referrals to our Programme is the lack of universal neonatal hearing screening. This problem has been identified by the Ministry of Health and a Programme of Screening is currently being implemented. This should help significantly with early referrals, especially in those children with no risk factors for hearing loss. Of the children with prelingual deafness in our series, 22 of the 42 or 52.4% had no risk factors. This is comparable with the 58% of children with no risk factors in the New Zealand Deafness Notification Database for 2005.[10]

The most concerning aspect of this audit is the lack of screening and late referral of children with known risk factors for SNHL. There was no difference in the referral ages between those children with risk factors and those without. A few children at risk had actually had their hearing tested with misinterpretation of results, only to be re-tested later following speech delay or parental concern. Failure to acquire language had been attributed to other causes in some children.

Many of these children with risk factors have chronic medical problems and profound deafness presents a huge extra burden to them and their family. It is particularly devastating for those children declined surgery due to being referred too late to benefit from cochlear implantation.

The late referrals of children with risk factors may be due to a number of factors. Firstly, lack of awareness may be an issue. Secondly poor resourcing and lack of experience in paediatric audiology is likely to be relevant. Testing young children electrophysiologically and behaviourally requires time, more than one tester, skill and experience. If there are insufficient resources to perform this vital testing, universal screening of hearing may not be the panacea we have hoped for.

There are minor “delays” associated with assessment of suitability for a cochlear implant. Some of the intervals between referral and assessment relate to waiting for consent from families and for relevant information from referral sources (principally Audiologists and Otolaryngologists). Some children were referred and then commenced on a 6–8 week trial of hearing aids locally, prior to assessment by the SCIP Team, which also added to the interval time between referral and assessment. Throughout the 5-year period, funding has been a huge issue for the combined Adult and Paediatric SCIP, but we have generally managed to implant children expeditiously.

It is important to stress that this group of children represent the most severe end of this spectrum of hearing loss. When mild and moderate deafness is included, the average age of detection in New Zealand is 33.9 months.

There will be a small number of children who have severe to profound SNHL who are not referred for consideration of cochlear implantation. Parents who are members of the Deaf (Signing) Community may not wish their own deaf children to undergo cochlear implantation for cultural reasons.

In summary, this audit of referral times to the Southern Cochlear Implant Programme demonstrates a lack of early diagnosis and referral in children who have known risk factors for significant sensorineural hearing loss. This factor plus lack of universal neonatal screening means that there are significant delays to cochlear implantation in children, which is likely to impact significantly upon results. Included amongst these delays are 6 children who were denied any benefits of cochlear implantation because they were referred after the age of 5 years, with no ability to utilise this technology.

Competing interests: None known.

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Trends in the use of minimally invasive surgery in children

Preechapon Pleay Tovaranonte, Spencer W Beasley, Kiki Maoate, Russell Blakelock, Adrian Skinner

Abstract

Aim To determine trends in the scope of use of minimally invasive surgical (MIS) techniques in children as a predictor of future operative workload and operating theatre requirements.

Method A retrospective review was conducted of all paediatric patients less than 16 years of age who underwent minimally invasive surgical procedures at Christchurch Hospital, New Zealand between 1996 and 2007.

Results There were 1693 children who received 1826 MIS procedures during a period in which 11,893 operative procedures were performed. MI case-weights, an indirect measure of the financial burden and technical difficulty of the procedures, represented 29% of the workload of the unit overall. There was a rapid rise of the number of MIS procedures from 1996 to 2000, but since then the scope and volume has changed little.

Conclusion Use of MIS in children increased rapidly until 2000 since which time it has remained relatively constant. Recent additional applications have involved a small number of rare low-volume and more complex procedures. These observations may assist in the planning of theatre allocation requirements for MIS in children.

Refinements in the design of laparoscopic instrumentation and resolution of a number of technical issues have facilitated the application of minimally invasive surgery (MIS) in children, including even the smallest infants. The range of indications for MIS now match those in adults.[1] It has become the preferred technique for many procedures including appendicectomy, for impalpable testis, pyloromyotomy and Nissen fundoplication. Sometimes it has greatly advanced the operative technique, such as for appendicostomy stomas (the ACE procedure), significantly reducing the complexity of surgery and morbidity.[2,3]

The purpose of this study was to determine trends in the use and scope of minimally invasive surgical procedures as they are applied to children.

Method

A retrospective study was conducted of all paediatric patients under 16 who underwent minimally invasive surgical procedures at Christchurch Hospital, New Zealand, between September 1996 and December 2007 inclusive. Operative procedures were identified through the Paediatric Surgery Departmental Audit Database and the Main Operating Theatre Database. Any discrepancies in diagnoses or procedures were clarified through examination of individual medical records, and correlated with the International Classification of Diseases, 10th revision (ICD-10) used by the Christchurch Hospital Patient Management System.[4]

The scope of application of MIS procedures is summarised in Table 1.

Table 1. Examples of the scope of the application of MIS in children

Thoracic procedures
Thoracoscopic lung resection, VATS for empyema, thoracoscopic lung biopsy, thoracoscopic excision of intrathoracic tumours and cysts, and other thoracoscopic procedures (e.g. removal of lung abscesses and diagnostic thoracoscopy)
Abdominal procedures
Laparoscopic appendicectomy, pyloromyotomy, intussusception reduction, Ladd's procedure for malrotation, cholecystectomy, splenectomy, pancreatic procedures, Nissen fundoplication, ACE (appendicostomy), Meckel's diverticulectomy, surgery for congenital anorectal malformations, gastrostomy, drainage of abscesses, adhesiolysis, colonic biopsies, ovarian cyst removal, oophoropexy, salpingectomy, and diagnostic laparoscopy
Urological procedures
Laparoscopy for undescended or impalpable testes, nephrectomy/ heminephrectomy, pyeloplasty, varicocele repair, and others (e.g. cystoscopy with intervention, nephroscopy)
Procedures excluded
Gastrostomy, oesophagoscopy, bronchoscopy and colonoscopy.

Endoscopic procedures such as gastroscopy, oesophagoscopy, bronchoscopy and colonoscopy were excluded due to difficulties identifying them accurately from ICD codes and because they involved techniques already in existence before laparoscopy and thoracoscopy were introduced. Children whose procedure was converted from a laparoscopic to an open approach, were recorded in both the laparoscopic and open categories of our database.

As most paediatric surgical procedures involve minor open procedures, procedure numbers alone provide a poor indication of surgical workload: MIS operations tend to involve more major and more time-consuming procedures in theatre. For this reason, case-weights were calculated to provide an indirect measure of the complexity of procedure, its technical difficulty, theatre time and overhead costs. The case-weight measure has been validated previously.[5]

Case-weight data were only available from 1998 onwards, when fiscal data were recorded electronically. Case-weights were applied to match each procedure for each year. Percentages were calculated from the product of the number of MIS cases by case-weight (referred to as "MIS Workload") in relation to the sum of all case-weights existing on our database ("Total Workload").

Some selected MIS procedures (nephrectomy, appendicectomy, pyloromyotomy, Nissen fundoplication) were compared with their corresponding open approach to provide an indication of when, and the extent to which the MIS approach became adopted.

Results

During the period reviewed there were 11,893 operative procedures performed, of which 1827 involved MIS. There was a general trend towards an increase in all MIS cases until 2001 after which it plateaued off. The highest number of cases was in 2000, when 211 children underwent MIS. Since then the number of MIS cases has fluctuated around 170–180 cases annually (Figure 1). Overall, this has represented 14.2% of the total cases.

Figure 1. Total MIS procedures according to year (*incomplete year)

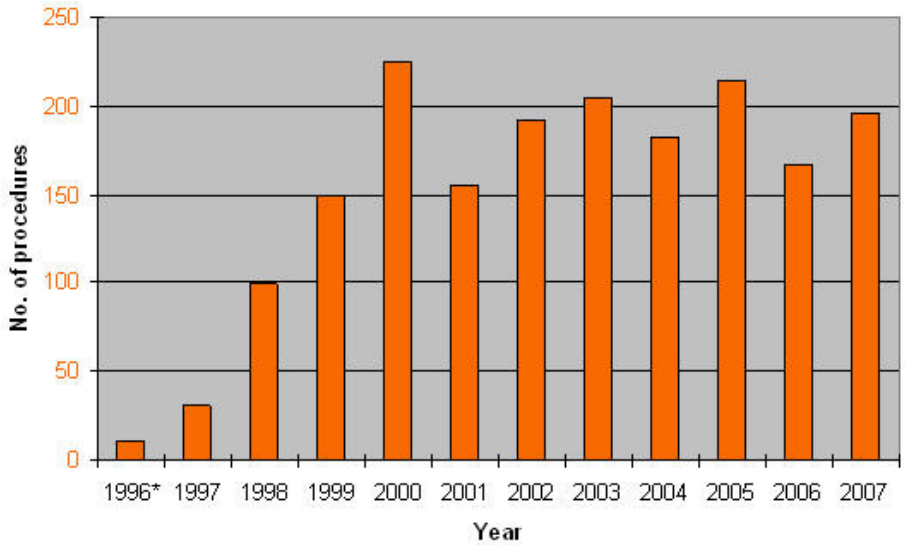
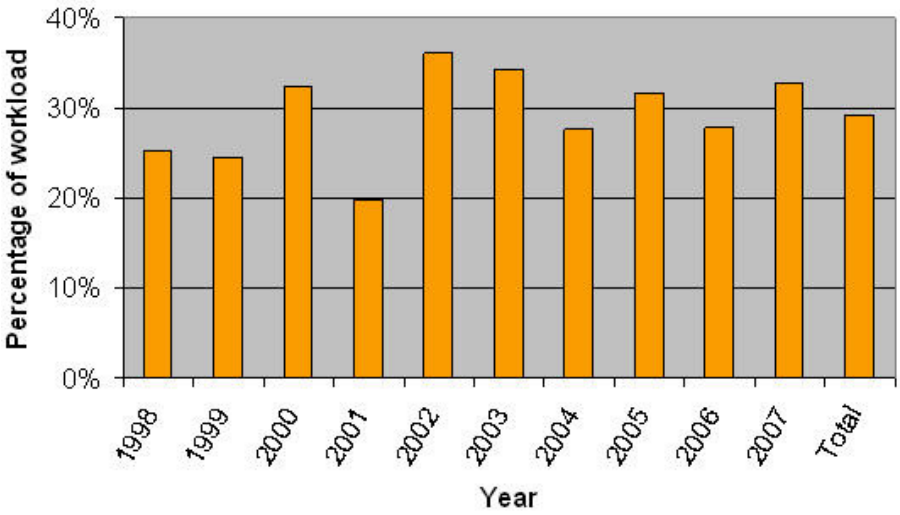


Figure 2. MIS as a case-weight percentage in children presented to Christchurch Hospital during 1998–2007



A summary of case-weight data for each year is shown in Figure 2. The MIS Case-weight Workload peaked in 2002 (36%) and over the last 5 years the MIS Workload became stabilised at about 29%.

Figure 3 shows the body regions in which MIS procedures were performed. Abdominal MIS procedures account for 88% of the total MIS workload. Figures 4–7 show the trends for nephrectomy excluding all malignancies (Figure 4), appendicectomy (Figure 5), pyloromytomy (Figure 6) and Nissen fundoplication (Figure 7).

Figure 3. MIS workload pie chart

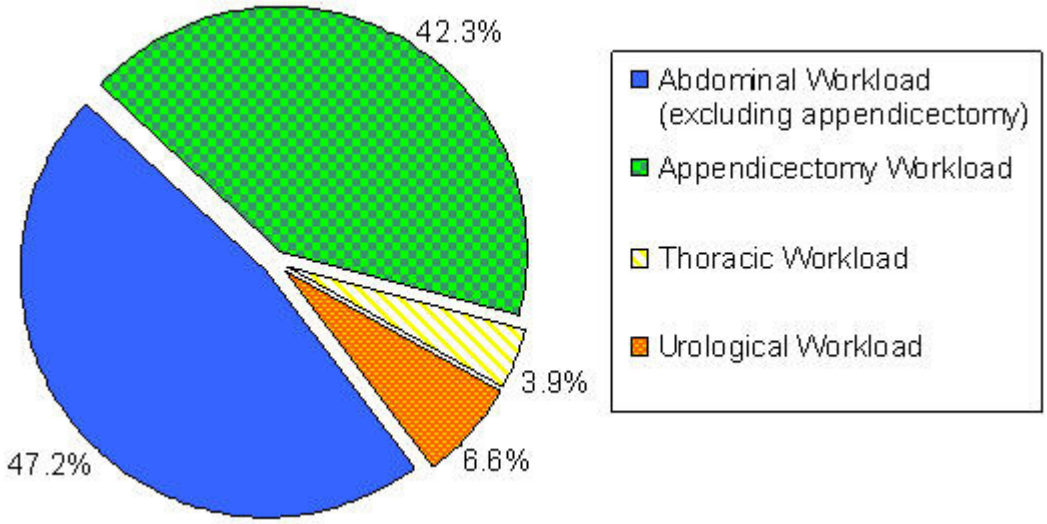


Figure 4. Fundoplication (*incomplete year)

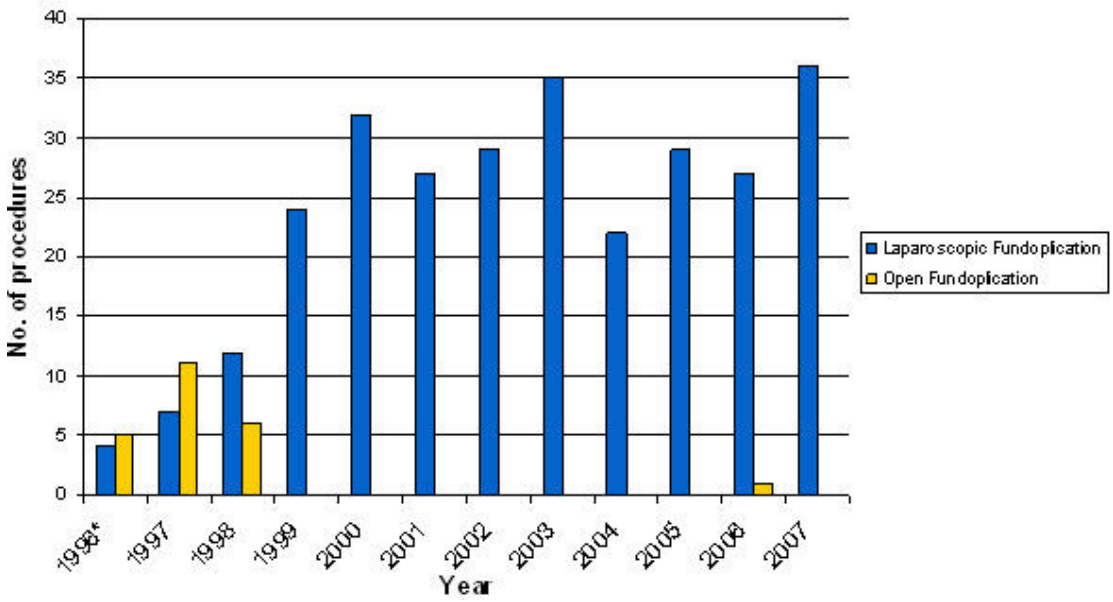


Figure 5. Appendicectomy (*incomplete year)

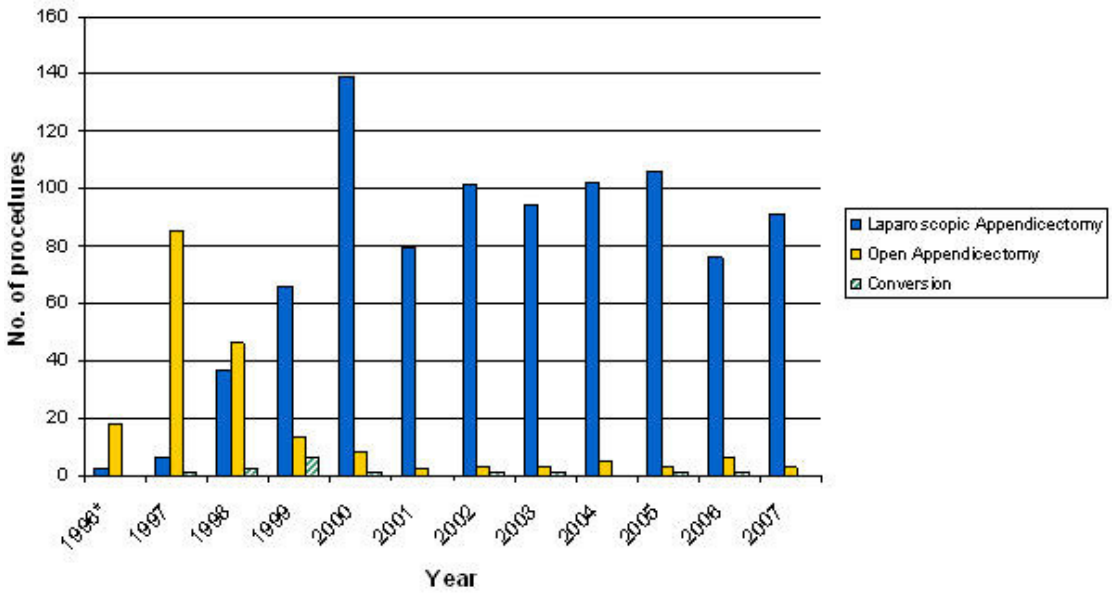


Figure 6: Nephrectomy for benign disease (*incomplete year)

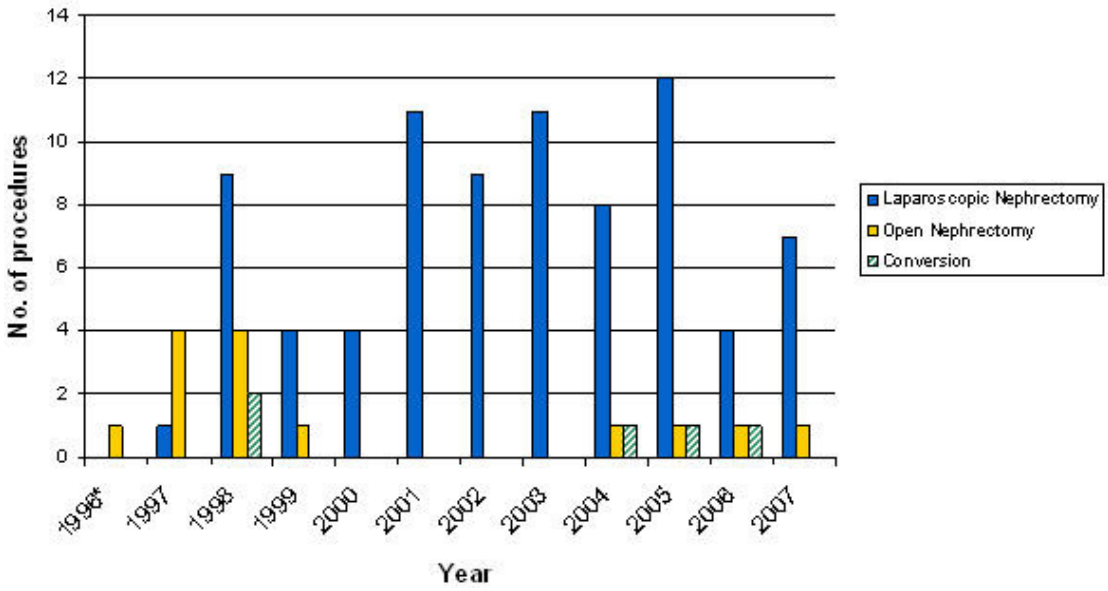
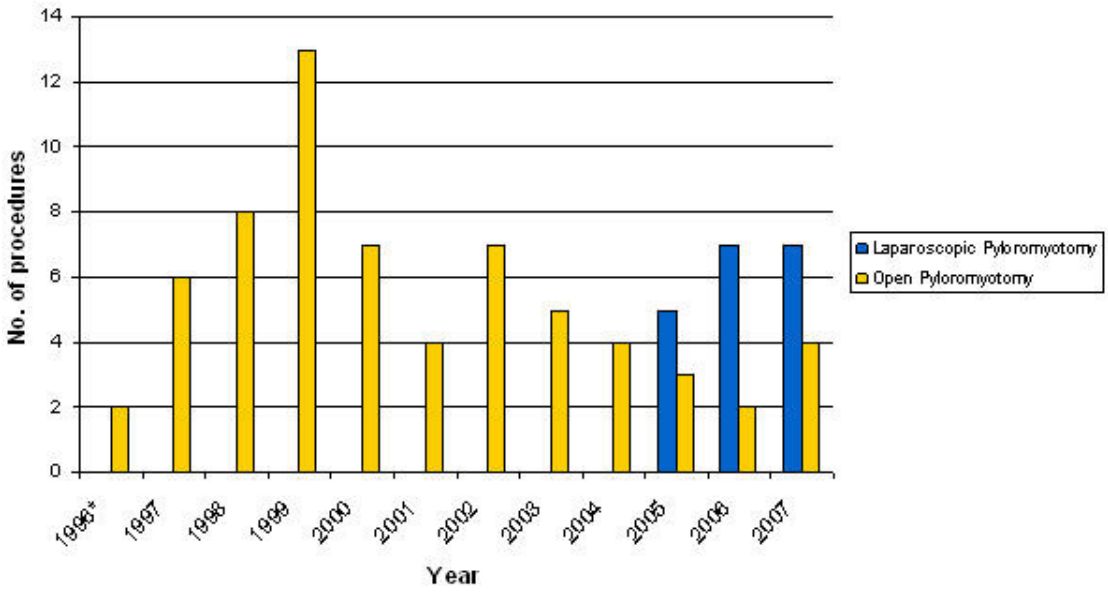


Figure 7. Pyloromyotomy (*incomplete year)



Discussion

The introduction of laparoscopy started in children almost 40 years ago for the management of the impalpable testis,[6] but more recent expansion of the indications for laparoscopy in children has lagged behind that of adults, in part for technical reasons and in part because of the relative rarity of conditions for which laparoscopic surgery was most commonly performed—e.g. cholecystectomy. Once the size and calibre of instruments became more appropriate for children, and light sources improved, the techniques were adopted more quickly.

Nevertheless, many paediatric surgeons worldwide were initially reluctant to acquire laparoscopic skills when they considered themselves already highly skilled in open surgery[7]and laparoscopy in children was perceived as conferring few advantages over open surgery . Our rapid acceptance of MIS compared with many other centres – some of which still perform laparoscopy only infrequently – is in part a reflection of the fact that the paediatric surgical department lies within a general hospital that has a long history of routine laparoscopic surgery in adults.

There was a rapid increase in the number of MIS cases from 1996 to 2000, but later became stable in both total number and as a percentage of volume (Figs 1 & 2). MIS procedures tended to utilise more complex equipment, had greater overhead costs and consumed more operating time for which reason their Case-weight volume was employed, as a crude and indirect measure of the proportion of "workload" they created. Overall, MIS represents almost 30% of the operative workload.

In children MIS is performed for a wide variety of surgical procedures and its perceived applications grow yearly – although most recent new applications have involved relatively rare and complex conditions, for example, anorectal

malformations and oesophageal atresia. In our institution the two most frequent MIS procedures are laparoscopic appendicectomy and fundoplication.

The influence of MIS in the treatment of four procedures is summarised in Figures 4–7. Since 1999 laparoscopy has been the preferred approach to fundoplication in infants and children of all ages, with few requiring conversion. Laparoscopic appendicectomy was also introduced early and rapidly became routine (Figure 5), with few open appendicectomies since 2000. The conversion rate has remained steady around one to two per year. Review of perforated appendicitis in 2000 identified a postoperative intra-abdominal abscess rate of 6% following laparoscopic appendicectomy.[8,9]

The complication rate for perforated appendicitis is decreasing as surgeons become more experienced.[8] Complications tend to occur with less experienced operators, regardless of patient age, operative time, pre-operative duration of symptoms, or the extent of intraperitoneal soiling.[9,10] Laparoscopic nephrectomy or heminephrectomy has been undertaken in 80 children (Figure 6) with an age range of 8 months to 15 years. Mean operative times have decreased from 105 to 90 minutes, indicating a flat learning curve. Conversion to an open procedure (6.3% overall) was due to marked fibrosis, large renal size, difficulty gaining access to the retroperitoneal space and major peritoneal breech.[11]

Laparoscopic pyloromyotomy was introduced more recently in our institution, and does not yet have its own ICD-10 procedure code. In the USA, the procedure became common from about 1997.[7] It has made no difference to outcome.

The main advantages of MIS have been related to better cosmesis (smaller less obvious scars), reduced post-operative discomfort, reduced analgesic requirements and a reduction in average length of hospital stay for procedures such as appendicectomy.[12] Overall, the introduction of MIS has had little other demonstrable effect either on the complication rate or longterm outcomes.

Conclusion

At our institution, MIS in children increased in volume until 2000 by which time most of its applications had been established. Subsequent additional applications have been limited to a few uncommon and complex procedures, such as anorectal malformations and thoracic tumours, affecting total workload little. Knowledge of the recent trends in the use of MIS techniques (now in a “plateau phase”) may assist in planning likely future operating theatre requirements.

Competing interests: None known.

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Juvenile thyrotoxicosis—a South Island, New Zealand experience with long-term outcome

Bevan E W Brownlie, Penny J Hunt, John G Turner

Abstract

Aim To assess our experience in the management of juvenile thyrotoxicosis.

Method Retrospective review of thyroid clinic records of juvenile (<16y) thyrotoxic (JT) patients treated at thyroid clinic between 1972 and 1999. Long-term (>8y) treatment outcome was assessed.

Results During the 28-year period, 34 JT patients were diagnosed and treated—30 girls and 4 boys, median age 13 years (5.6–15.9 y). Thirty-two children had Graves' disease and two had toxic nodular goitre. All patients were initially treated with carbimazole, and no major adverse reactions occurred. One Graves' disease child later developed severe ophthalmopathy. During long-term follow-up, 12 of the 32 Graves' patients remain in remission after antithyroid drug treatment alone, but 4 of these 12 patients are currently receiving thyroxine replacement. Fifteen patients were surgically treated (median age 16 y), and six patients received radioiodine therapy (median age 18 y) including one patient with post-thyroidectomy relapse. The two patients with toxic nodular goitre were treated by thyroidectomy.

Conclusion Juvenile thyrotoxicosis is relatively rare and not always due to Graves' disease. More than a third of children with Graves' disease achieved long-term remission following antithyroid drug therapy, and remaining patients required definitive therapy.

Thyrotoxicosis is uncommon in childhood and is usually due to Graves' disease, which is an autoimmune disease with the hyperthyroidism caused by antibodies stimulating the TSH receptor. Accurate incidence figures are sparse but a nationwide study from Denmark reported an annual incidence of 0.8 per 100,000 for children under 15 years of age, with 96% of thyrotoxicosis due to Graves' disease.[1] A report from Hong Kong however showed a five-fold greater thyrotoxicosis incidence in Chinese children, which may relate to environmental and genetic factors.[2]

These incidence figures for juvenile thyrotoxicosis can be compared with the overall annual incidence for all age groups in New Zealand of 26 per 100,000, with the calculated incidence of Graves' disease 15 per 100,000.[3] More recent studies report increasing thyrotoxic incidence in both adults and children.[4]

The choice of treatment for thyrotoxicosis in childhood remains the subject of much debate. In most countries, initial treatment is thionamide antithyroid medication for 1–2 years, with definitive treatment by thyroidectomy or radioiodine reserved for patients with persistent or relapsing disease, or for patients with serious adverse reactions to antithyroid drugs.[5]

In contrast, North American clinicians are more likely to recommend relatively early treatment with radioactive iodine (RAI).[6] There is now more than 40 years follow up of RAI-treated adolescents from the USA showing no subsequent adverse obstetric outcomes or increased cancer risk.[7]

In this paper, a regional New Zealand experience of 34 patients with juvenile thyrotoxicosis (JT) is reported. These patients were diagnosed over a 28-year period (1972–99), and all patients have at least 8y follow-up. Infants with neonatal transient hyperthyroidism are not included in this report.

Patients and Methods

Thyrotoxic patients aged <16y at diagnosis between January 1972 and December 1999 were identified from Christchurch Hospital thyroid clinic records. The thyroid clinic is a regional clinic for the Canterbury and West Coast districts of the New Zealand South Island with an estimated average paediatric population (< 16y) of 100,000 using New Zealand census figures between 1971 and 1996.

During this 28-year period, 34 children with thyrotoxicosis were investigated and treated at thyroid clinic; 2 of these children had been diagnosed some weeks prior to moving into our district. An additional two children seen in consultation but not managed at thyroid clinic were excluded from this report—a 3y Māori girl with diffuse thyroid hyperplasia, and an 8y girl with McCune-Albright syndrome.

The clinical diagnosis of thyrotoxicosis was confirmed by Christchurch Hospital laboratory investigations including: total serum thyroxine (T_4: normal range 55–140 nmol/L), free thyroxine index (FT_4I: normal range 55–160) and total serum triiodothyronine (T_3: normal range 1.2–2.8 nmol/L) by radioimmunoassay and since 1987 by sensitive thyrotropin (TSH) by IRMA, 99m Tc pertechnetate thyroid scintiscans using a gamma camera, and thyroid antibodies (microsomal (TPO) and thyroglobulin) were measured by haemagglutination (Fujizoki kit).

Results

Investigations

Before treatment, all patients had elevated thyroid hormone levels and those diagnosed since 1987 had TSH suppressed to <0.1 mU/L. The median total T_4 was 247 (range 147–>350), FT_4I 524 (177–885), and total serum T_3 6.5 (3.7–>16). Christchurch Hospital laboratory pre-treatment results were available for 29/34 patients, and the remaining patients had thyroid function tests from private laboratories.

Thyroid scintiscans were available for 32 of the 34 children and one patient had a thyroid ultrasound. Thirty two of the 34 patients had diffuse thyroid hyperplasia consistent with Graves' disease, and in 2 girls the scintiscan showed toxic nodular goitre—a large autonomous nodule, and an 'autonomous lobe with non-homogeneous tracer uptake'. Thyroid antibody testing in patients with diffuse hyperplasia showed 25/32 (78%) to have positive anti-microsomal (TPO) antibody results.

Clinical

Age and gender distribution—The 34 JT children were Caucasian, except for one Chinese girl with Graves' disease. The age at presentation ranged from 5 years 7 months to 15 years 10 months (median age 13y), with only 5 patients less than 10y at diagnosis. There were 30 girls and four boys giving a female:male ratio of 7.5:1. In

the 28y period there was on average one new thyrotoxic child per year for the estimated juvenile population of 100,000.

Children with previously diagnosed medical conditions included: one boy with Down's syndrome, one girl with Type 1 diabetes, a girl with McCune-Albright syndrome ('toxic nodular lobe'), one boy with deaf mutism secondary to congenital rubella and one girl with surgically treated cardiac septal defect.

Clinical features—Emotional lability was the most prevalent symptom with other common symptoms including lethargy, heat intolerance, increase in appetite, weight loss, and tremor. In some patients the emotional changes caused problems with schooling. From case records it was difficult to assess the duration of symptoms but in some children symptoms had been present for at least 12 months. All children had palpable thyroid glands with 5 of the 32 with Graves' disease having large diffuse goitres. One child presented with diabetic ketoacidosis and concurrent new Graves' disease.

Fifty percent of the 32 Graves' disease patients had thyroid eye signs—mild exophthalmos in 25% and lid retraction in 25%. The eye symptoms at presentation were mild, with no patient needing ophthalmological referral. However an 8.5y girl with initially mild exophthalmos developed severe exophthalmos with bilateral orbital nerve compression 4 years later. High-dose oral prednisone 60mg/d successfully preserved vision with the prednisone gradually withdrawn over 3 months, and total thyroidectomy was then performed. The exophthalmos was treated surgically by bilateral orbital decompression 5 years later (patient aged 18y) with an excellent cosmetic outcome.

The two girls with toxic nodular goitre were both diagnosed when seen for other medical problems—the first aged 15y during hospitalisation with asthma when an asymmetric goitre with tracheal deviation was noted and scintiscanning showed a toxic nodule; the second was diagnosed during follow up for McCune-Albright syndrome.

Family history—A family history of thyroid disease was initially noted in 44% of the total JT patient group: the 2 girls with toxic nodular goitre both had a family history of goitre, and 7 of the 32 children with Graves' disease had a family history of thyrotoxicosis , including 2 mothers (one had thyroidectomy for JT) and 1 father.

Three mothers developed thyrotoxicosis some years after their children were treated—including a mother with thyrotoxicosis facticia, which was diagnosed during hospitalisation for medication-resistant thyrotoxicosis, when her son's thyroxine bottle was discovered in her toilet bag. This occurred 10 years after her son's thyroidectomy and she was noted to have an abnormally close mother-son relationship.

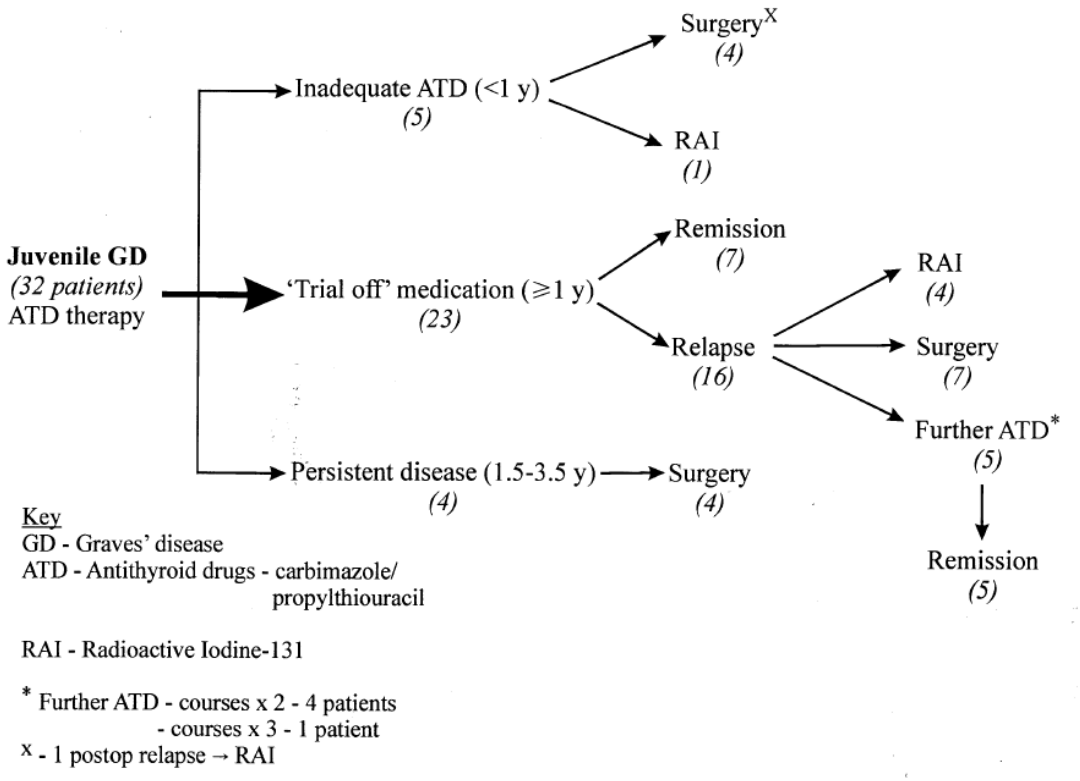
Medical treatment

All patients were initially treated with carbimazole with the dosage tailored to body weight and severity of thyrotoxicosis assessed by FT_4I and T_3 levels. Most patients were initially treated with carbimazole 10–20 mg daily (range: 5–45 mg) with tablets taken twice daily until euthyroidism was obtained—most children were euthyroid after 4–8 weeks treatment.

The carbimazole dosage was then reduced and changed to once daily administration. Three Graves' patients were later prescribed thyroxine with carbimazole to avoid fluctuations in thyroid function, with a subsequent reduction in need for venepunctures. Four patients were switched from carbimazole to propylthiouracil because of rash or urticaria. No patient suffered a serious adverse reaction to antithyroid medication.

The initial treatment plan for the 32 patients with juvenile Graves' disease was to continue antithyroid drug (ATD) treatment for 12–24 months in the hope that the underlying autoimmune disease process would remit. However 5 patients remained inadequately controlled after 6-9 months' treatment and early definitive treatment with surgery or radioiodine was recommended. The subsequent management of the Graves' patients is summarised in Figure 1.

Figure 1. Treatment outcome for 32 children with Graves' disease



The majority of Graves' disease patients completed a satisfactory course of ATD, and were given a 'trial off' medication when they had been euthyroid for some months on low dose carbimazole (2.5–5 mg daily). The median duration of medication was 18 months. Clinical and biochemical assessments were made 6 weeks after cessation of treatment, 6 months later then annually. The thyrotoxicosis relapsed in many patients—mostly within 12 months of stopping medication, and only one patient relapsed later (after 3.5y).

All patients were followed into adulthood, with only one patient lost to follow up (after 8y). Twelve of the 32 Graves' patients (38%) have achieved long-term remission following ATD alone—7 after one course, and 5 after repeated ATD courses. These 12 patients include 2 of the 5 children <10y at diagnosis. The median follow-up of the patients in remission is 19y (range: 8–36y).

At most recent follow up, four of the 12 patients in remission have been commenced on thyroxine replacement therapy many years after the initial diagnosis of thyrotoxicosis—8, 16, 17, and 22y later. Two patients have subsequently developed associated autoimmune diseases—one type 1 diabetes after three years (aged 8.5y), and one coeliac disease after 25 years (aged 34y).

Surgical treatment

Fifteen Graves' disease patients (14 female and 1 male) were treated by thyroidectomy following failed medical treatment, and both girls with toxic nodular goitre were also surgically treated. Eight Graves' patients had early thyroidectomy, as did seven further patients following relapse after courses of ATD (See Figure 1). The median interval between diagnosis and thyroidectomy was 3y (range: 0.5–5y) and the median age at time of thyroidectomy was 16y (range: 8–20y, with only one child < 12y).

In earlier years the thyroidectomies were performed by senior general surgeons, and more recently by an endocrine surgeon with specialist thyroidectomy training. Most patients were treated by bilateral subtotal thyroidectomy, but four were treated by total thyroidectomy. The weight of the thyroidectomy specimens was >60 g in 7 of the 15, including 2 very large goitres weighing 154 and 373 g.

There were no major postoperative complications, with no recurrent laryngeal nerve injuries, but two of the earlier patients have needed long-term treatment for hypoparathyroidism. The median follow-up period post-thyroidectomy was 17y (5–26y) with all subtotal thyroidectomy patients having more than 10y follow up. Thyroidectomy has successfully treated all but 1 of the 15 patients—this patient, treated by less radical thyroidectomy, relapsed 3 years later and was treated with ^{131}I.

A second subtotal thyroidectomy patient had postpartum thyrotoxicosis 12 years after surgery and required 6 months' carbimazole treatment. Currently 5/11 subtotal thyroidectomy patients remain euthyroid without medication, and the remaining surgically treated patients are taking thyroxine replacement.

The two girls with toxic nodular goitre had persistent thyrotoxicosis, and were treated by hemithyroidectomy. The initial (1986) pathology report for the toxic nodule patient was a minimally invasive follicular carcinoma, but on more recent review it has been reclassified as a benign follicular adenoma. The McCune-Albright syndrome patient had very mild thyrotoxicosis, and the surgical specimen was a benign multinodular lobe with cystic changes.

Radioactive iodine (RAI) treatment

Six Graves' disease patients were treated with radioiodine (^{131}I)—the 16-year-old deaf-mute boy after 11 months of suboptimal medical control, 4 patients relapsing following courses of carbimazole, and the post-thyroidectomy relapse patient (noted

above). The median interval between initial diagnosis and RAI was 9 years (range: 0.9–11y), and the median age at time of RAI was 18 y (range: 16–23y). The ^{131}I dosage was adjusted for goitre size and severity of thyrotoxicosis—the median initial ^{131}I dose was 8mCi (296MBq) with range 5–10mCi (175–370MBq). Two patients needed a second ^{131}I treatment (total dosages 13 and 20mCi). Five of the six RAI patients became hypothyroid within 2 years of treatment, and one patient remains euthyroid 15y later.

Discussion

The present series of 34 children with thyrotoxicosis was accumulated over 28 years with an average of one new thyrotoxic child per year. Our population is largely Caucasian and our incidence is consistent with the nationwide Danish figures.[1] In older reports it was estimated that up to 5% of thyrotoxic patients may be in the paediatric age group[8], but in our experience around 1% of thyrotoxic patients initially present when <16 years of age. This 1% figure has been calculated from our recent thyroid clinic database—over a 12y period, 11 children (<16y) were treated from a total of 1119 new Graves' patients.

Most children in our series were female, and in the 12–16y age group which is comparable to other reports.[9–12] A family history of thyrotoxicosis was noted in 20% of our juvenile Graves' patients, which is the same as found in our adult patients.[3] However the genetic effect seems stronger in our children with a higher proportion of first degree relatives—especially mothers. The mother with thyrotoxicosis facticia has been our only patient with this disorder.

Graves' ophthalmopathy infrequently causes clinical problems in children with Graves' disease. Recent reviews however suggest that the incidence of ophthalmopathy in juvenile Graves' is similar to that seen in adults but it is less severe and more likely to remit completely.[13, 14, 15] Our patient with optic nerve compression was an exceptional patient and her exophthalmos led to significant psychological and schooling problems.

Graves' disease patients are more prone to other autoimmune diseases and three of our 32 juvenile Graves' patients developed Type 1 diabetes during childhood. This association with diabetes has been previously documented.[16] No other autoimmune diseases developed in our children, but during long-term follow-up one patient in her fourth decade was diagnosed with coeliac disease.

Our conservative management plan for juvenile Graves' disease is similar to that followed in most European centres.[5] All patients were initially treated with carbimazole with the dosage titrated to keep thyroid hormone levels in the normal range. However in some centres all JT patients are treated with carbimazole plus thyroxine therapy ('block and replace') which may have the advantage of a reduced need for follow-up venesections.

A small number of our patients suffered antithyroid drug side effects, but no major adverse reactions occurred. Some earlier series reported that children were more prone to serious adverse reactions; up to 14% of children in one series.[9] This was possibly due to the greater use of propylthiouracil in the past.

In our study more than a third of juvenile Graves' patients remain in remission following ATD therapy alone. This remission rate is similar to that reported in a recent similar series with long-term follow-up[12] but comparison with some larger series is difficult because they include older adolescents aged 16–20y. Some studies have shown that younger children may be less likely to achieve remission,[17] but this was not noted in our small series.

The optimal duration of ATD is uncertain but it is generally agreed that children need a longer course of treatment than in adults. Some authors have advocated very prolonged ATD in children and have claimed 25% remission for every 2 years' treatment,[18] but the predictions have not been confirmed by subsequent reports.

Long term follow-up of our juvenile Graves' patients who remitted after ATD therapy has unexpectedly shown that four of the 12 patients are now on thyroxine replacement therapy. This spontaneous swing to hypothyroidism has been noted in some previous JT series,[10,19] but this has not been emphasised. In adult Graves' patients the evolution to spontaneous hypothyroidism is better documented, occurring in about 10% of patients, and is thought to be due to either destructive autoimmune thyroiditis or TSH receptor blocking antibodies.[20, 21]

The choice of definitive therapy for Graves' patients remains the subject of much debate, and recent reviews have advanced strong opposing arguments for the more liberal use of radioiodine or thyroidectomy.[6,22] It has been our practice to persevere with ATD medication until the mid-teenage years with the patient contributing to discussions. The choice of definitive treatment should be individualised with surgery recommended for patients with large goitres.

Almost half of our juvenile Graves' patients have been treated by thyroidectomy. The bias towards surgery was in part due to physician preference, but many families were fearful of radiation—fears heightened by the New Zealand Government's adoption of an 'anti-nuclear' stance in 1985.

The surgical management of Graves' disease has changed since the 1970s, when the aim was to achieve euthyroidism, to more radical resection to minimise post-thyroidectomy relapse.[23] Patients should be referred to a surgeon with specialist training to minimise surgical complications, and the risks of hypoparathyroidism or recurrent nerve injury should be around 2%.

A minority of our juvenile Graves' patients have been treated with radioiodine. In earlier years conservative ^{131}I doses were prescribed, but recently higher doses have been used to reduce the need for retreatment. Some North American units have treated very young children with high-dose ^{131}I to ablate all thyroid tissue but this is associated with a higher total body radiation dose.[6,7]

Currently most units avoid radioiodine in children as the thyroid in young children is more sensitive to radiation. The increase in thyroid cancer incidence following the Chernobyl disaster has been most marked in children <10y at the time of radioiodine exposure.[24]

Our series included two children with toxic nodular goitre. In many of the published series there has been no thyroid imaging or measurement of TSH receptor binding antibodies, and it seems likely that not all included cases had Graves' disease. In our

series, one patient had a toxic autonomous nodule, which is 3% of our cohort and similar to the Danish study.[1]

The treatment of choice for toxic nodules under the age of 20y is hemithyroidectomy to provide histology, and radioiodine is best avoided as many patients are left with a residual nodule, and there may be concerns about subsequent new nodules many years later.[25] Toxic multinodular goitre is rare in the paediatric age group and is usually found in the context of McCune-Albright syndrome due to activating mutations.[26, 27]

This report describes our experience in the management of children with thyrotoxicosis. The relative rarity of this disorder (incidence approximately 1/100,000 children) explains the small size of our series. After long-term follow-up more than one-third of our Graves' patients remain in remission following antithyroid medication, and remaining patients had ablative treatment.

Better documentation of treatment outcomes requires prospective multicentre studies of larger cohorts.[28] Future advances in genetic and immunological research may lead to new treatments for Graves' disease and reduce the need for thyroid ablation.

Addendum

Recently 1 of the 12 Graves' patients in long-term remission after ATD treatment has been diagnosed with recurrent thyrotoxicosis—after a 16y remission.

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The utility of plain radiography in assessment of upper aerodigestive tract fishbone impaction: an evaluation of 22 New Zealand fish species

Tim Ritchie, Martyn Harvey

Abstract

Aims To determine the utility of plain radiography for suspected upper aerodigestive tract fishbone impaction in New Zealand fish species.

Methods Tissue densities of the least and most dense regions of the upper aerodigestive tract were measured on a lateral soft tissue X-ray of the neck. Densities of the measured regions were reproduced in two custom manufactured radiological phantoms. Epipleural bones from 22 commonly eaten New Zealand fish species were X-rayed within these phantoms. Forty-one Emergency Department doctors graded the X-ray visibility of each bone using a five point visual analogue scale.

Results Twenty species (90.9%) returned a sensitivity of 95% or greater when viewed within the least dense phantom. The two species with lesser sensitivities within the least dense phantom were Red Cod (90.2%) and Ray's Bream (58.8%). Only one species (Black Cardinalfish; 4.5%) returned a sensitivity of 95% or greater when viewed within the most dense phantom.

Conclusions Bones from the majority of commonly eaten New Zealand fish species are poorly visible when X-rayed in a background of soft tissue density. Given fishbones frequently impact in regions of high tissue density, plain radiography would appear insufficiently sensitive to exclude upper aerodigestive tract fishbone impaction.

Fishbone impaction in the upper aerodigestive tract is an Emergency Department presentation with potentially fatal outcome. Retropharyngeal abscess, mediastinitis, and oesophago-aortic fistula[1] are recognised complications of missed diagnosis. A significant proportion of those who present with the complaint of foreign body sensation however are eventually demonstrated not have a fishbone present.[2–4]

Endoscopy is acknowledged as the gold standard investigation in assessment of potential fishbone impaction,[2–5] in addition to serving as the prevailing method of removing fishbones not directly accessible on oral examination.[2,3,6,7] As endoscopic techniques require specialist referral, soft tissue lateral X-ray of the neck is commonly employed as the first line investigation in cases of suspected fishbone impaction.[8]

An X-ray positive for fishbone reliably indicates the need for endoscopic intervention, having reported specificity in the order of 90%.[3,5] However, controversy surrounds the utility of an X-ray negative for fishbone. Overall sensitivity of X-ray for detecting upper aerodigestive tract fishbone impaction has been shown to be poor.[2,3,5,9]

Several authors have nonetheless suggested inter-species variation in radiologic sensitivity with differing calcium content and bone thickness. As such sensitivity may

prove sufficiently high to be clinically useful in isolated species with highly radiodense bones.[7,8,10–12] There are, however, no published studies documenting bone radiodensity of New Zealand fish species.

Anatomic location within the aerodigestive tract is another factor with potential implication for the sensitivity of X-ray in detection of fishbones. It is not clear whether highly radiodense fishbones demonstrate similarly high radiologic sensitivity across all possible locations of impaction.[7,13–15]

The present study was therefore undertaken to examine the utility of plain radiography in assessment of suspected upper aerodigestive tract impaction of bones from commonly eaten New Zealand fish species. Specifically, the variables of bone radiodensity and location of impaction were evaluated by X-raying bones from a variety of fish species within radiological phantoms approximating tissue density extremes of the upper aerodigestive tract.

Methods

The assistance of staff from a large fish processing plant in Hamilton, New Zealand was sought in determining which species are most frequently consumed by domestic diners. The fishbone most likely to be accidentally ingested in a processed fillet was considered to be the epipleural (pin) bone. Pin bones were obtained from 22 species of commonly eaten fish.

Creation of radiological tissue phantoms—A General Electric X-ray unit was set at 72 kVp, 25 mAs and 180 centimeters to produce an optimally exposed lateral soft tissue lateral X-ray of the neck on Kodak Min-R film. An X-rite 301 densitometer was utilised to catalogue the tissue density of this reference exposure's upper aerodigestive tract. The least dense region was noted anterior to the superior horn of the thyroid cartilage and measured 1.70 optical density units (ODU). The most dense regions were found to be the oesophagus and regions adjacent to the mandible such as the palatine tonsil and the posterior tongue, all of which measured 0.36 ODU.

Two radiological tissue phantoms were created in consultation with the Waikato Hospital Department of Medical Physics. In brief, stacked sheets of A4 paper were X-rayed using the same settings and film as those used for the reference exposure. Leaves were sequentially added or removed from the relevant phantom to achieve blank exposures measuring 1.70 and 0.36 ODU. A single pin bone from each species of fish was then alternately placed in the centre of both phantoms and X-rayed on the same film and at the same settings as the reference exposure.

Data collection—Forty-one Emergency Department doctors interrogated the resulting 44 radiographs under standard conditions (usual X-ray box illumination). Clinicians were asked to grade the visibility of each bone according to a five point visual analogue scale (VAS). Scale descriptors included the following: invisible (0), barely visible (1), somewhat visible (2), quite visible (3) and clearly visible (4).

Statistical analysis—Accuracy of detection, sensitivity, and mean visibility were calculated for individual fish species according to background phantom employed. Chi squared testing was used to compare rates of detection between groups. Statistical evaluation of all variables was undertaken utilising GraphPad Prism software (Version 5, 2007). A p value of less than 0.05 was retained as statistically significant.

Results

Accuracy of detection, sensitivity, and mean visibility are presented for the least dense and most dense tissue phantoms in Tables 1 and 2 respectively. Accuracy is presented as proportion, sensitivity as percent (95% confidence interval [CI]), and visibility as mean VAS score (95% CI).

Table 1: Accuracy, sensitivity, and mean visibility; *least* dense tissue phantom

Fish species	Accuracy	Sensitivity (95% CI)	Mean visibility (95% CI)
Alfonsino	40/41	97.6 (87.1–99.9)	1.6 (1.4–1.9)
Black Cardinalfish	41/41	100 (91.4–100)	3.7 (3.6–3.9)
Bluenose	41/41	100 (91.4–100)	2.7 (2.4–2.9)
Escolar	41/41	100 (91.4–100)	2.5 (2.3–2.8)
Gemfish	41/41	100 91.4–100)	3.2 (3.0–3.5)
Giant Stargazer	41/41	100 (91.4–100)	3.7 (3.5–3.9)
Grey Mullet	41/41	100 (91.4–100)	3.7 (3.5–3.9)
John Dory	39/41	95.1 (83.5–99.4)	1.9 (1.7–2.2)
Kahawai	41/41	100 (91.4–100)	2.7 (2.4–2.9)
King Salmon	41/41	100 (91.4–100)	1.9 (1.6–2.2)
Rainbow Trout	39/41	95.1 (83.5–99.4)	1.7 (1.3–2.0)
Ray's Bream	24/41	58.5 (42.1–73.7)	1.2 (0.7–1.6)
Red Cod	37/41	90.2 (76.9–97.3)	1.3 (1.0–1.6)
Red Gurnard	41/41	100 (91.4–100)	2.3 (2.0–2.6)
Rubyfish	41/41	100 (91.4–100)	3.4 (3.2–3.6)
Snapper	41/41	100 (91.4–100)	3.4 (3.2–3.6)
Tarakihi	41/41	100 (91.4–100)	3.0 (2.7–3.2)
Trevally	41/41	100 (91.4–100)	3.2 (3.0–3.5)
Trumpeter	41/41	100 (91.4–100)	3.3 (3.1–3.6)
Yellowbelly Flounder	41/41	100 (91.4–100)	2.3 (2.0–2.5)
Yellowfin Tuna	41/41	100 (91.4–100)	3.6 (3.4–3.8)
Yellowtail Kingfish	41/41	100 (91.4–100)	3.3 (3.3–3.7)

Table 2. Accuracy, sensitivity, and mean visibility; *most* dense tissue phantom

Fish species	Accuracy	Sensitivity (95% CI)	Mean visibility (95% CI)
Alfonsino	0/41 *	0	0
Black Cardinalfish	39/41 †	95.1 (83.5–99.4)	1.1 (0.94–1.3)
Bluenose	2/41 *	4.9 (0.6–16.5)	0.07 (-0.04–0.2)
Escolar	2/41 *	4.9 (0.6–16.5)	0.05 (-0.02–0.1)
Gemfish	7/41 *	17.1 (7.2–32.1)	0.17 (0.05–0.29)
Giant Stargazer	36/41 ¥	87.8 (73.8–95.9)	1.0 (0.83–1.13)
Grey Mullet	33/41 §	80.5 (65.1–91.2)	1.0 (0.8–1.2)
John Dory	1/41 *	2.4 (0.06–12.9)	0.02 (-0.02–0.07)
Kahawai	1/41 *	2.4 (0.06–12.9)	0.02 (-0.02–0.07)
King Salmon	0/41 *	0	0
Rainbow Trout	2/41 *	4.9 (0.6–16.5)	0.05 (-0.02–0.12)
Ray's Bream	0/41 *	0	0
Red Cod	0/41 *	0	0
Red Gurnard	1/41 *	2.4 (0.06–12.9)	0.02 (-0.02–0.07)
Rubyfish	1/41 *	2.4 (0.06–12.9)	0.02 (-0.02–0.07)
Snapper	1/41 *	2.4 (0.06–12.9)	0.02 (-0.02–0.07)
Tarakihi	3/41 *	7.3 (1.5–19.9)	0.07 (-0.01–0.16)
Trevally	5/41 *	12.2 (4.1–26.2)	0.12 (0.02–0.23)
Trumpeter	18/41 *	43.9 (28.5–60.3)	0.43 (0.28–0.60)
Yellowbelly Flounder	0/41 *	0	0
Yellowfin Tuna	23/41 *	56.1 (39.8–71.5)	0.50 (0.41–0.76)
Yellowtail Kingfish	15/41 *	36.6 (22.1–53.1)	0.37 (0.21–0.52)

* $p<0.001$, † $p=0.494$, ¥ $p=0.055$, § $p=0.003$

Discussion

Twenty (90.9%) of the 22 fish species evaluated in this study demonstrated radiologic sensitivity of 95% or greater when viewed within the least dense phantom. Observed inter-species variation in visibility obtained from the least dense phantom likely reflecting inter-species differences in the bony mineralisation. Only one (Black Cardinalfish [4.5%]) of 22 species returned a sensitivity of 95% or greater when viewed within the most dense phantom. A further two species (Giant Stargazer and Grey Mullet) returned sensitivities of 80% or greater. The remaining 19 species proved either barely visible, or completely invisible, with correspondingly low sensitivities of detection.

A small body of literature has previously attempted to determine the utility of X-ray negative for fishbone, following suspected upper aerodigestive tract impaction. Several studies have demonstrated poor sensitivity of X-ray for detection of fishbones. In three clinical series, sensitivities of 32%, 29% and 25% only were reported.[2,3,5] One study where fishbones were X-rayed within a human cadaveric head and neck preparation demonstrated a similarly low sensitivity of 39%.[9]

The common conclusion drawn by all four studies was that a negative X-ray is insufficient to reliably confirm the absence of a fishbone. Two studies advocated proceeding directly to endoscopy if oral examination proved negative.[2,3]

Additional investigators have demonstrated significant interspecies variability in fishbone radiodensity.[7–12,15] Correspondingly one such study purported prior knowledge of fish species, and therefore bone radiodensity, conferred direct clinical application and produced a catalogue outlining relative fishbone radiodensities for use in UK Emergency Departments.[8] However, X-ray visibility of fishbones within the upper aerodigestive tract is likely to be additionally affected by the anatomic location of impaction.

Several reported series have described the frequency at which fishbones lodge within the regions of the upper aerodigestive tract. The palatine tonsil, posterior tongue and vallecula are common sites of suprahyoid impaction and in one study were respectively found to contribute 23%, 29% and 34% of the total number of impacted fishbones.[5] The infrahyoid region is a site of less frequent impaction. The piriform fossa, larynx, cricopharyngeus, cervical oesophagus and thoracic oesophagus are all sites of potential infrahyoid impaction.[3 5]

As this study noted the palatine tonsil and posterior tongue to be among the most dense regions of the upper aerodigestive tract, it is evident that a considerable proportion of fishbones impact in locations of high tissue density.

Principles of radiology determine that visibility of any fishbone will be greatest when contrasted against a background of least tissue density.[16] Accordingly, fishbones have been X-rayed within chicken legs, taped to the necks of junior authors and placed in a variety of locations within pig and human cadaver head and neck preparations in an attempt to determine the effect of surrounding tissue density upon visibility.

Several of these experimental studies have suggested that surrounding tissue density is of lesser significance than bone radiodensity in instances of highly radiodense fishbones. Consequently, conservative management has been recommended following

negative X-ray post ingestion of a small number of species with highly radiodense bones.[10-12] The remainder of studies assessing effect of location on X-ray visibility of fishbones have been somewhat more equivocal in their conclusions.[7 13-15]

The recommendations of studies suggesting clinical utility of fishbone radio density operate under a variety of assumptions, any or all of which may be proven erroneous. Assumptions include the following: all bones from all individuals of a particular fish species are equally radiodense; fish are identified correctly when caught and sold; and patients will have accurate knowledge of the fish species ingested. The clinical utility of plain radiography in assessment of potential lodged fishbones is likely to be further reduced in when such data is absent or unreliable.

Limitations to this study relate to its en vitro nature. Specifically, whilst fishbone radiodensity appears to contribute significantly to potential visibility on soft-tissue lateral neck X-ray, numerous additional factors may also contribute to clinical utility. Soft tissue signs such as gas or swelling may declare the presence of an otherwise invisible fishbone.[5]

Portions of fishbones impacted in regions of high tissue density may in practice traverse regions of lesser tissue density and therefore produce higher rates of radiological detection than those noted using tissue phantoms of single density only. Orientation of bones may furthermore affect visibility. One study found end on bones to have a higher degree of radiologic visibility than those viewed from the side.[9] Such factors may serve to effect increased rates of detection irrespective of bony radiodensity.

Finally, the present study examines fishbones against a homogenous background. In practice calcifications within normal anatomic structures (thyroid cartilage, hyoid bone) may obscure, or even mimic, the appearance of a retained bone prompting falsely positive or negative diagnoses respectively. The methodologic limitations inherent in this benchtop model preclude assessment of these phenonomen in the present study.

Conclusions

We have demonstrated plain X-ray to be poorly sensitive in detection of bones from commonly eaten New Zealand fish species impacted in regions approximating soft tissue density, largely irrespective of inter-species variation in bone radiodensity. As fishbones frequently impact in regions of high tissue density, plain radiography would appear of low utility in excluding upper aerodigestive tract fishbone impaction.

Clinical evaluation for potential fishbone concealment requires an investigative technique which excludes impacted fishbones with a high degree of sensitivity, regardless of location. In cases of suspected upper aerodigestive tract fishbone impaction, a negative oral examination may therefore be an indication to refer directly for endoscopy.

Competing interests: None known.

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Helicobacter pylori infection and iron deficiency in teenage females in New Zealand

Alan G Fraser, Robert Scragg, David Schaaf, Patricia Metcalf, Cameron C Grant

Abstract

Background Iron deficiency is an important problem in New Zealand children and young adults. Iron deficiency and *Helicobacter pylori* (*H. pylori*) infection are each more common in Māori and Pacific Island ethnic groups.

Aims This study seeks to determine if *H. pylori* infection is associated with iron deficiency.

Methods 792 female students from 7 Auckland high schools (median age 16 years) had *H. pylori* serology and tests for iron deficiency assessed by a combination of serum ferritin, iron saturation and mean cell volume.

Results The prevalence of positive *H. pylori* serology was highest for Pacific Island students (49.0%; CI 38.0–60.0), intermediate for Māori (26.7%; CI 16.9–36.4) and Asian (24.7%; CI 12.6–36.7) and lowest for European (13.7%; 6.0–21.4) p<0.0001. Students with positive *H. pylori* serology had lower mean levels of iron saturation (p=0.013), but not of ferritin (p=0.068), haemoglobin (p=0.08) or mean cell volume (p=0.16), compared to those with negative serology. Positive *H. pylori* serology was associated with increased risk of iron deficiency (RR 1.20; CI 1.08–1.34), but not anaemia (RR 1.01; CI 0.87–1.18), after adjusting for age, ethnicity and school SES decile.

Conclusions This study indicates that *H. pylori* infection is associated with iron deficiency in adolescent females. There are significant differences in *H. pylori* serology amongst different ethnic groups in New Zealand

Iron deficiency is an important problem in New Zealand children and young adults. A survey of girls from 8 Auckland high schools found that 18.3% of girls had iron deficiency and 11.5% had anaemia.[1] Iron deficiency was more common in Māori and Pacific Island ethnic groups. A longitudinal study of Dunedin children (predominantly European) found lower but still significant rates of anaemia and iron deficiency by the age of 21 years (5.8% and 6.7% respectively).[2] The reasons for these ethnic differences remain unclear.

Helicobacter pylori (*H. pylori*) infection is found more frequently in Māori and Pacific Island ethnic groups and this is a potential explanation for the difference in prevalence of iron deficiency.[3,4] There are a number of possible mechanisms by which *H. pylori* may affect iron metabolism. There may be occult bleeding because of gastritis or ulceration, impaired absorption of non-haem iron because of decreased acid secretion or the bacteria itself may be a scavenger for iron thereby competing with the host for dietary iron or ferritin.[5,6]

Results from cross-sectional studies suggest that the impact of *H. pylori* infection may vary between different countries and also vary according to socioeconomic status within a country.[7–12] One previous New Zealand study has shown a significantly lower serum iron in *H. pylori*-infected adults selected from the electoral roll but no difference in serum ferritin or the prevalence of anaemia.[8]

This study sought to determine if *H. pylori* was an explanation for the high prevalence of iron deficiency in female teenage children in Auckland schools that had a high proportion of Māori and Pacific Island students.

Methods

The participants in this report come from a cross-sectional survey, carried out during May 1997 to September 1998, of 2549 Year 11-13 students attending schools in South, Central and West Auckland. The main aim of the survey was to compare cardiovascular risk factors in Pacific Island students with those of other ethnicities. We randomly selected 10 (out of 32) schools with a proportion (>15%) of Pacific Island students and invited all Year 11–13 students at each school to take part. Information on iron and anaemia status was collected from students at 8 of these schools. The results and methods have been reported previously.[1.] The current report on *H. pylori* and iron status is limited to female students (at 7 schools) because of their increased prevalence of iron deficiency and anaemia compared with males.

After an overnight fast, students were interviewed in the mornings in groups of up to 10. At the time of this interview a fasting venous blood sample was collected from each student to measure glucose, lipids, iron indices and haemoglobin. Each student then completed a 15-minute self-administered questionnaire which documented age, gender, ethnicity (self-defined), past medical history, and general lifestyle patterns. The Ministry of Education classification of schools by socioeconomic decile, from 1 (low) to 10 (high), was used to code socioeconomic status (SES).[13] The number of surveyed students at each school, in this report, ranged from 34 to 373.

All blood samples were separated within 2 hours of collection at a community laboratory, and tested for cardiovascular risk factors and iron status. The following methods were used to determine iron status: serum ferritin was measured by microparticle enzyme immunoassay (Abbott Laboratories); iron (transferrin) saturation was derived from serum iron and unsaturated iron binding capacity by a colourimetric method (Roche); C-reactive protein (CRP) was measured by nephelometry (Behring Diagnostics); haemoglobin (using a cyanmethaemoglobin method) and mean cell volume (MCV) were measured on a Technicon H*3. Any remaining serum was stored at -80ºC.

Definition of anaemia and low ferritin—Cut-points from the United States NHANES III survey are used in the current report.[7] Anaemia was defined as haemoglobin <120 g/L for females. Iron deficiency was defined as any two (or more) of the following three: serum ferritin <12 ug/L; iron (transferrin) saturation <14%; MCV <81 fl which was the 5th percentile for the reference group of students in the sample who met all the following criteria: CRP <4 mg/L, haemoglobin g/L >118 (10th percentile), iron saturation >8%, and ferritin ≥10 ug/L. This definition of iron deficiency is based on that used in the NHANES surveys.[7]

The only difference is that we have used MCV as a third test of iron deficiency in place of measuring erythrocyte protoporphyrin, since the latter test was not readily available in Auckland at the time of the survey.[14] *H. pylori* antibody was determined by enzyme immunoassay using commercially available kits which was been validated by comparison with urea breath test.[15]

Data analyses in this report are restricted to 792 (out of 922 surveyed) female students with measured *H. pylori* antibodies, after excluding 61 students with missing information on *H. pylori* status, 44 students with CRP >5 mg/L (to exclude any students with possible acute phase reaction (which affects serum ferritin, iron saturation and and haemoglobin concentration) and 25 students with missing CRP values. Statistical analyses were made using SAS SURVEYFREQ and SURVEYMEANs procedures (Release 9.2, Research Triangle Park, NC, 2005) which corrects standard errors and confidence intervals for any design effect from clustering of students by school. The Rao-Scott modified Chi-Squared test was used. The STATA command binreg was used to calculate unadjusted and adjusted risk ratios. The natural logarithm of ferritin was used in analyses to normalise its distribution.

Results

278 students tested positive for *H. pylori* antibodies, giving a prevalence of 35.1% (95%CI 23.5–46.7). Table 1 shows the prevalence of *H. pylori* for demographic variables. The prevalence of positive serology was highest for Pacific Island students (49.0%), intermediate for Māori (26.7%) and Asian (24.7%) and lowest for European (13.7%) (p<0.0001). The prevalence of positive *H. pylori* serology varied across schools from 24.6% up to 60.9%. The prevalence varied with school SES decile, being nearly twice as high for students in SES decile 1 schools (53.1%) compared with decile 2 and 3 schools (28.6%) (p=0.036), but did not vary with age (p=0.19).

Table 1. Prevalence of positive *H. pylori* serology by level of demographic variable

Variable	N	*H. pylori* positive % (95% CI)	*P value*
Age (years)			
≤15	200	35.5 (21.7–46.6)	
16	283	31.5 (16.8–46.1)	0.19
17	200	36.0 (23.0–49.0)	
≥18	109	42.2 (33.1–51.4)	
Ethnicity			
Pacific	386	49.0 (38.0–60.0)	
Māori	120	26.7 (16.9–36.4)	<0.0001
Asian	162	24.7 (12.6–36.7)	
European	124	13.7 (6.0–21.4)	
School SES decile			
1 (low)	211	53.1 (44.9–61.2)	0.036
2 and 3	581	28.0 (27.0–30.2)	
Total	792	35.1 (23.5–46.7)	

Comparisons of adjusted mean values for serum iron measures and haemoglobin, between students with positive and negative *H. pylori* serology are shown in Table 2. Students with positive serology had significantly lower mean iron saturation (p=0.013), compared with students with negative serology. Mean ferritin (p=0.068), haemoglobin (p=0.08) and MCV (p=0.16) did not vary with *H. pylori* serology.

Table 2. Mean (95% confidence interval) of blood iron measures and haemoglobin, by category of *H. pylori* serology, adjusted for age, ethnicity and school SES decile

Blood variable	*H. pylori* serology		P value
	Positive	Negative	
Ferritin (ug/L)	21.7 (18.5–25.4)	23.8 (21.4–26.6)	0.068
Iron saturation (%)	20.1 (18.7–21.4)	22.0 (20.7–23.3)	0.013
Mean cell volume (fl)	85.9 (85.4–86.3)	86.7 (86.0–87.4)	0.16
Haemoglobin (g/L)	130.3 (129.4–131.2)	131.5 (130.9–132.0)	0.08
N	278	514	

Table 3 shows risk ratios for iron deficiency and anaemia associated with positive *H. pylori* serology, adjusting for age, ethnicity and school SES decile. There was a significantly higher risk of iron deficiency in students with positive *H. pylori* serology (p=0.001), but not anaemia (p=0.88).

The prevalence of iron deficiency ranged from 24.2% (se=5.9) in Māori students, 18.9% (3.1) in Pacific, 12.3% (2.1) in Asian to 7.2% (1.9) in European students (p=0.0049). Mean ferritin levels were not significantly different for Māori, Pacific and Asian students, when compared with European, adjusting for age and school SES (p>0.05).

In contrast, after adjusting for age and school SES, mean iron saturation was significantly lower in Māori (by 6.0%), and in Pacific (by 6.5%) students (p<0.05), but not in Asian students, when compared with European; while mean MCV also was significantly lower in all three non-European groups compared with European students (Māori by 4.4 fl, Pacific by 3.2 fl, Asian by 3.1 fl).

Table 3. Risk ratios for iron deficiency and anaemia, associated with positive *H. pylori* serology († row percents)

***H. pylori* serology**	**Iron deficiency**		**Relative risk (95% CI)**	
	Yes	**No**	**Unadjusted**	**Adjusted for age, ethnicity and school SES decile**
Positive	56 (20.1%)†	222	1.28 (1.19–1.39	1.20 (1.08–1.34)
Negative	74 (14.4%)	440	1.00	1.00
	Anaemia			
	Yes	**No**		
Positive	33 (11.9%)	245	1.06 (0.90–1.26)	1.01 (0.87–1.18)
Negative	56 (10.9%)	458	1.00	1.00

Discussion

This study has shown a significant association between *H. pylori* and iron deficiency, including iron saturation. The magnitude of this effect is small but may be of some clinical importance. There was no association between *H. pylori* and anaemia.

Data from some other population studies has suggested an association of *H. pylori* with iron deficiency but the magnitude of the effect may be small and may depend on the definition of iron deficiency.

A US study using the National Health and Nutrition Examination survey 1999–2000 found a significantly lower serum ferritin in *H. pylori* infected adults (56 compared with 65 ug/L); there was a significant adjusted odds ratio for iron deficiency anaemia but not for iron deficiency (similar definition to this study).[7] A further report from the 2003 NHANES survey has shown similar results.[16]

Several studies have shown a lower serum ferritin with *H. pylori* infection without showing any effect on iron deficiency anaemia. In a large population study from Germany of subjects aged 18–89 years serum ferritin in *H. pylori*-infected individuals was 54.5 ug/dL compared with 63.8 ug/dL in the uninfected subjects. The association did not vary by age, gender or iron intake.[9]

In another population study of 2794 adults in Denmark serum ferritin was lower in men (114 vs 120ug/L, p=0.01) and in post-menopausal women (63 vs 77 ug/L, p=0.02) who were *H. pylori* positive.[10] An small Australian study found significantly lower ferritin levels among women with *H. pylori* infection compared with non-infected controls (59 vs 88 ug/L)[17] In a study of 2080 native Alaskans (78% positive for *H. pylori*) there was a significant association between low serum ferritin and positive *H. pylori* serology, particularly in subjects less than 20 years of age.[11]

Most of these reports have included mainly adult subjects. There is limited data on the possible association in children.[12,18,19] In a study of 688 Alaskan children 38% were found to have iron deficiency and 7.8% iron deficiency anaemia. There was an association with *H. pylori* infection but it is perhaps difficult to make strong conclusions as 86% of children had *H. pylori* infection.[19]

The other form of evidence for a relationship between *H. pylori* and iron deficiency comes from *H. pylori* eradication studies. Most studies have involved small numbers of subjects and have been non-randomised.[20–22] In a small randomised study from Korea, 22 *H. pylori*-positive subjects (mean age 15 years) were randomised to *H. pylori* eradication, ferrous sulphate alone or both *H. pylori* eradication and iron supplementation. Eradication treatment, with or without iron resulted in a significant increase in haemoglobin.[23]

A randomised study of children in rural Alaska showed no difference between treatment with iron supplementation alone and iron treatment combined with *H. pylori* eradication treatment at 14 months follow-up although there was a difference in iron-deficiency anaemia at 40 months follow-up despite a 50% re-infection rate with *H. pylori*.[24,25]

A randomised study of 200 Bangladeshi children aged form 2–5 years showed no additional benefit of *H. pylori* eradication on iron deficiency compared to iron treatment alone at 90 days. The strength of this study was a randomization to iron treatment alone, *H. pylori* eradication alone or the combination. In addition, *H. pylori* status was assessed again at 90 days by urea breath testing and the analysis of children with successful eradication versus persisting infection showed no difference in iron deficiency.[26]

The reasons for these variable results are unclear. It is likely that *H. pylori* has a small effect on iron balance by decreasing absorption or increasing iron loss leading to iron deficiency but that this effect is not large enough to lead to iron deficiency anaemia in most populations. There may be regional differences or unknown factors that determine whether there is a pangastritis (causing a decrease in acid secretion) or perhaps a hemorrhagic gastritis (as has been commonly observed in Alaskans).

An older population may have more advanced *H. pylori*-related changes in the gastric mucosa (although limited negative data in elderly subjects does not support this concept).[28] Several studies have shown that acid secretion does improve after *H. pylori* eradication particularly if there is corpus-predominant gastritis or pangastritis.[28,29] However the impact of optimal gastric acid secretion on iron absorption may have been overstated.

A study of iron absorption in children aged 2–5 years in Bangladesh showed that gastric acid secretion improved after *H. pylori* eradication but iron absorption did not improve after eradication treatment.[30]

H. pylori infection is claimed to be associated with a number of extra-gastric manifestations. Most of these associations have not been confirmed by larger well conducted studies that control for confounding issues such as socioeconomic status. One major example is the debate over the possible association of *H. pylori* with coronary heart disease.[31]

This study shows that *H. pylori* is associated with iron deficiency but this weak effect is unlikely to explain the major ethnic differences in iron deficiency anaemia. Dietary intake of iron appears to be similar in different ethnic groups in New Zealand.[32]

The prevalence rates of *H. pylori* infection in European, Māori and Pacific island children in this study (collected 1997–98) are similar to data reported from samples taken from 11 year old South Auckland school children in 1988.[3]

This study confirms the significant public health issue of *H. pylori* infection particularly for Pacific Islanders who will carry a burden of upper gastrointestinal disease into coming decades, causing both peptic ulceration and gastric cancer, because of high rates of *H. pylori* infection.[4]

Further studies on the reasons for high rates of acquisition of *H. pylori* infection in some ethnic groups are required. Targeted testing and eradication depending on ethnicity may be sensible to prevent later consequences of *H. pylori* infection.[4]

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Pertussis continues to put New Zealand's immunisation strategy to the test

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Abstract

Young children in New Zealand remain at an unacceptably high risk of pertussis. As an indicator of child disease burden hospitalisation rates have increased in each decade since the 1960s. Despite improvements over the past 15 years immunisation coverage (77% at age 2 years in 2005) remains lower than the level of ≈ 95% necessary to control pertussis. For global pertussis control, seven strategies beyond the primary infant series and early childhood booster doses are currently recommended: (1) Reinforce and/or improve infant and toddler immunisation strategies; (2) Universal preschool booster doses; (3) Universal adolescent immunisation; (4) Universal adult immunisation; (5) Selective immunisation of new mothers, family, and close contacts of newborns; (6) Selective immunisation of healthcare workers; and (7) Selective immunisation of childcare workers.

The first of these—reinforcement and/or improvement of current infant and toddler immunisation strategies—is the highest priority for New Zealand and would reduce infant pertussis disease burden. The universal preschool booster (age 4 years) and the adolescent (11 year) booster should remain. Because of low coverage and unknown effectiveness for protection of infants routine adult pertussis immunisation is of lower priority. Of the targeted strategies selective immunisation of healthcare workers is necessary to prevent nosocomial spread to vulnerable infants. All staff who work in neonatal units and other clinical settings where there are infants should receive a booster dose of pertussis vaccine.

Control of pertussis in New Zealand continues to prove elusive. Improving immunisation coverage and timeliness should remain the primary focus of pertussis control in New Zealand.

Vaccines that protect against pertussis have been a component of national immunisation schedules for at least the past 50 years. Despite this, pertussis is one of the vaccine preventable diseases that has proved difficult to control.

Today pertussis remains among the 10 leading causes of death in young children and results in a large disease burden, larger for example than lung cancer or meningitis.[1,2]

As another pertussis epidemic begins in New Zealand it is timely to review our current knowledge of pertussis, the disease that occurs following infection with *Bordetella pertussis*, and consider what action New Zealand should take to protect our young children from this dreadful illness.

Pertussis epidemiology

Pertussis has always and continues to be underestimated as a cause of death and disease. In the pre-immunisation era it resulted in more infant deaths than measles,

diphtheria, poliomyelitis and scarlet fever combined.[3] It is estimated that in the developed world three times more deaths are due to pertussis than are reported. Deaths occur despite intensive care.[4–10]

Underestimation of incident cases of pertussis and how this underestimation varies with age and intensity of surveillance are central to understanding pertussis epidemiology. Most pertussis incidence estimates are based upon passive notification systems which only identify between six and 25% of all pertussis cases.[6,11] The proportion of cases that are notified decreases with increasing age and decreasing illness severity.[6]

Pertussis affects all age groups and in all likelihood has always done so. Pertussis incidence has always been highest during infancy and early childhood.[3,12–16]

Pertussis in very young infants is unpredictable with the potential for rapid deterioration. Approximately 7 out of 10 infants less than 6 months old with pertussis are hospitalised.[17]

Pertussis is endemic in adolescents and adults. Case series of adolescents and adults with cough lasting for 1 week or more have shown that in approximately 20% of such illnesses there is evidence of recent infection with *B. pertussis*.[18] In countries with immunisation schedules that include no booster doses, beyond-infancy pertussis is also endemic in school-aged children.[19]

Transmission

Transmission of *B. pertussis* is primarily by aerosolised droplets. The time between successive pertussis cases varies between five and 35 days with an average of 2 weeks.[20,21] In immunised populations the secondary attack rate within households remains greater than 80%.[22,23] Although many of the secondary infections are asymptomatic they are an important source of infection of incompletely or un-vaccinated children.[22–24]

Bordetella pertussis is a highly infectious organism. Each primary case produces between 12 and 17 secondary cases.[21,25] This is the principle reason why immunisation coverage needs to be higher (≈ 95% by 6 months of age for the primary series) to control pertussis than some of the other vaccine preventable diseases. Immunisation provides greater protection against disease than it does against infection allowing *B. pertussis* to continue to circulate even in populations with high vaccine coverage.[26]

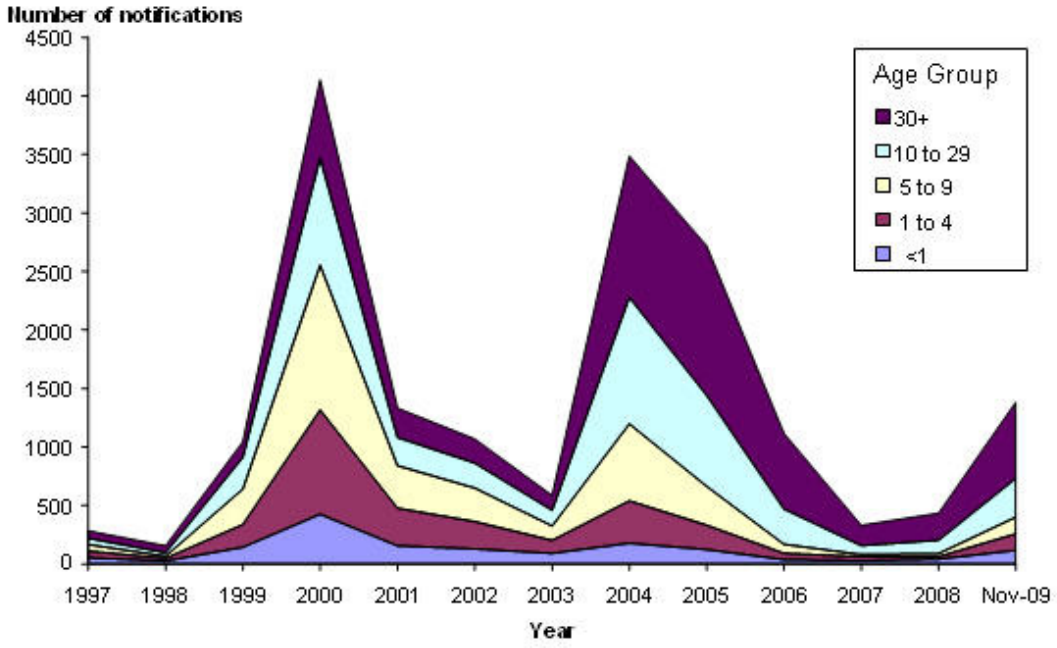
New Zealand epidemiology

Pertussis epidemic peak years in New Zealand have been 1874, 1878, 1880, 1884, 1888, 1892, 1895, 1900, 1904, 1908, 1911, 1914, 1917, 1921, 1926, 1932, 1936, 1941, 1944, 1946, 1949, 1952, 1955, 1959, 1961, 1964, 1967, 1971, 1974, 1978, 1982, 1986, 1991, 1996, 2000 and 2004. There have been 35 inter-epidemic time periods. The mean ± standard deviation interval between epidemic years is 3.71 ± 0.93 years. The duration of inter-epidemic time periods prior to mass immunisation (1873–1944) and since immunisation (1945–2004) are not significantly different (3.89 ± 0.96 vs. 3.53 ± 0.87 years, $t = 1.15$, $P = 0.26$).[27]

The lack of lengthening of the epidemic cycle since the beginning of mass immunisation implies that immunisation has not prevented the endemic circulation of *B. pertussis* in the New Zealand population.[18]

Since pertussis became a notifiable disease in New Zealand in 1996 the annual proportion of notified cases aged 30 years or more has increased from 23% (1997) to 54% (2008) (Figure 1). The more recent increase in reported pertussis incidence in adults is consistent with what has occurred in other developed countries and is primarily due to increased awareness and better laboratory diagnosis.[28,29]

Figure 1. Pertussis notifications in New Zealand by age group 1997 to November 2009



Over the past four decades there has been an increase in hospital admission rates for pertussis. This increase is probably due to a true increase in disease burden.

In comparison with the 1960s, the average annual pertussis hospital admission rate in New Zealand in each decade from the 1970s onwards has been greater. The average annual pertussis hospital admission rate in New Zealand in the 2000s is 50% higher than it was in the 1960s (Table 1).[27] The increase in hospital admission rates has been most marked in those less than one year old (Table 1) but is also apparent for older age groups.[27]

In comparison with the 1960s hospital admission rates have been significantly higher for infants since the 1970s and for all ages since the 1980s. The increase in hospitalisation rates is not explained by the increased capacity to obtain laboratory confirmation of diagnosis in recent years. The polymerase chain reaction as a diagnostic test for *B. pertussis* infection only became available in New Zealand in the late 1990s.[27]

The number of children hospitalised with pertussis who were then admitted to the national paediatric intensive care unit at Starship Children's Hospital has also increased implying that the increased hospital admission rate is not due to the hospitalisation of children with less severe disease.[30]

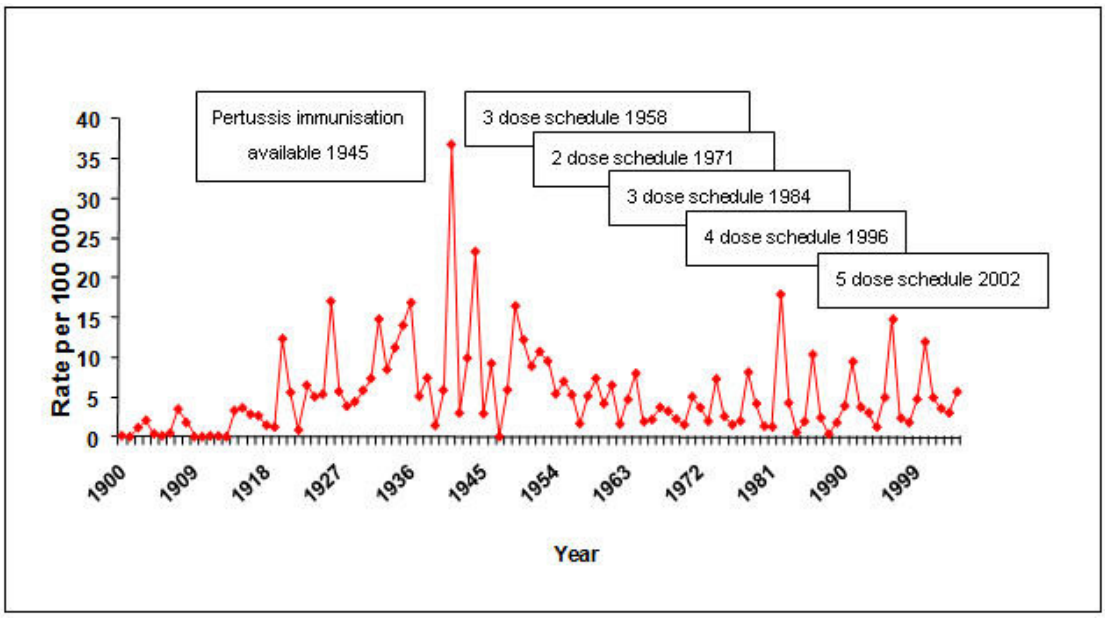
Table 1. Average annual pertussis hospital admission rates in New Zealand per decade and relative to the 1960s[27]

Decade	Age less than 12 months		All ages	
	Rate per 100,000 person-years	Relative risk (95% confidence intervals)	Rate per 100,000 person-years	Relative risk (95% confidence intervals)
2000s	293	2.87 (2.59–3.18)	5.8	1.55 (1.42–1.68)
1990s	222	2.18 (1.98–2.40)	5.0	1.33 (1.23–1.44)
1980s	174	1.71 (1.55–1.89)	4.2	1.11 (1.03–1.21)
1970s	132	1.30 (1.17–1.44)	3.8	1.01 (0.93–1.10)
1960s	102	1.00	3.8	1.00

Based upon these data and current immunisation coverage in New Zealand (see below) it can be anticipated that, without significant increases in immunisation coverage and timeliness, large pertussis epidemics will continue to occur. The upsurge in notified pertussis cases in 2009 indicates that the next pertussis epidemic has begun.

The data in Figure 2 show that we should expect this current epidemic to be of comparable size to recent epidemics.

Figure 2. Annual pertussis hospital discharge rate per decade per 100,000 person years 1900 to 2004[27]



Prevention

As pertussis is difficult or impossible to treat prevention remains the main stay of disease reduction. The principle benefit of antibiotic treatment is a reduction in the risk of spread although, if started within 2 weeks of cough onset, antibiotic treatment may result in some symptom severity reduction.[31] For household transmission to be interrupted prophylaxis must be commenced prior to a second household member becoming symptomatic.[32]

Countries with consistently low pertussis incidence rates have high immunisation coverage rates, which have been sustained over several decades.[33,34] Higher pertussis incidence rates are due primarily to lower immunisation coverage, but lower vaccine efficacy or less than optimal immunisation schedules may also contribute.[4,35–43]

Acellular pertussis vaccines, which have been in New Zealand's immunisation schedule since 2000, were developed primarily because of the adverse events associated with whole cell vaccines. The most efficacious whole cell and acellular vaccines induce protection against clinical disease in approximately 85% of recipients.[44–48]

Pertussis vaccine efficacy in New Zealand

The pertussis vaccines that have been used in New Zealand have been efficacious. The first whole cell pertussis vaccines used, the Lister (pre 1979) and BERNA (1979-86 Swiss Serum and Vaccine Institute) vaccines, were reported to meet WHO standards and to be efficacious in studies performed in the United States and the United Kingdom.[49] The efficacy of the whole cell vaccines used subsequently DT Coq (1989-93 Pasteur Merieux) and Tetramune (1994–1999 Wyeth Lederle) and the acellular pertussis vaccine used since 2000 (Infanrix, SmithKline-Beecham) have been reported.

The reported efficacy in pre-school aged children for three doses of the Pasteur Merieux vaccine was 96% and for four doses of the Wyeth Lederle vaccine 93%.[46,47] Using the same case definition the estimated efficacy of three doses of Infanrix was 84% in children less than 2 years old.[50] The efficacy of Infanrix has been shown to persist to 6 years of age.[51]

Pertussis immunisation coverage in New Zealand

National (1992 and 2005) and regional (1996) estimates that used methods recommended by the World Health Organization provide the most accurate measure of immunisation coverage. Based upon these surveys the percentage of children fully immunised at age 2 years has increased from 60% in 1992 to 77% in 2005.[52-54]

Between these two dates the immunisation schedule was streamlined, dropping one visit in the second year of life and making completion of coverage by 2 years easier. Immunisation coverage at age one year for the primary immunisation series in New Zealand in 2005 (90%) was 102nd of 193 countries globally and 31st of 37 industrialised countries.[55 56] In comparison, Australia (92%) was 86th globally and 27th in the OECD, the United States (96%) was 54th globally and 19th in the OECD and the United Kingdom (91%) was 95th globally and 29th in the OECD.[56]

In the 1992, 1996 and 2005 immunisation surveys coverage has been lower for Maori children compared with non-Maori.[52–54] These ethnic differences have decreased with time. In 1992 coverage at age 2 years was 23% lower for Maori compared with non-Maori, in 2005 it was 11% lower (69% versus 80%).[52,54]

Immunisation coverage for Pacific children has improved. In the 1996 northern regional immunisation survey immunisation coverage for Pacific children at age 2 years was lower than for European/other children (53% versus 71%). In the 2005 national survey immunisation coverage at age 2 years was similar for Pacific children (81%) and European/other children (80%).[53,54,57]

Immunisation coverage varies regionally in New Zealand. Based upon data from the National Immunisation Register for the 12 months ending June 2009 the percentage of children at age two years immunised in each District Health Board varied between 66% and 91%. Large variability between District Health Boards is evident for coverage when comparisons are stratified by population ethnicity and social deprivation.[58]

High immunisation coverage is necessary but not sufficient to control pertussis. The immunisation schedule must start on time and all doses must be given without any unnecessary delay. Delay in receipt of the first vaccine dose in the primary series is one of the strongest predictors of subsequent incomplete immunisation.[59]

The timeliness of immunisation delivery in New Zealand at a national level has not been reported. The National Immunisation Register definition of timeliness is that an immunisation should be given within 4 weeks of the first due date for the 6 week immunisations, and within 6 weeks for 3 month, 5 month and 15 month immunisations.[60]

A recent survey of a random sample of 124 general practices in the Auckland and Midland regions showed that on average only 56% of children less than 2 years old registered at each practice had received all of their immunisations on time.[61] As far as pertussis is concerned the target should be completion of the primary series, 3 doses of a pertussis containing vaccine, by 6 months of age.[16,62–64]

The importance of measuring immunisation timeliness as well as coverage when assessing national immunisation programmes has recently been emphasised.[65] The timeliness of immunisation delivery can be improved, for example, by outreach workers facilitating attendance at immunisation visits.[66]

Immunisation beyond infancy

Without booster doses, the primary immunisation series is insufficient to prevent all disease in infants.[67] This is because the primary series does not provide good protection until all three doses have been received. Prior to then an infant will be at risk of pertussis if exposed to an older child or adult with *B. pertussis* infection. After the primary infant series the first booster dose is not necessary until approximately five years of age.[51,68]

With the recognition that older children and adults spread pertussis to infants the timing of booster doses has been reviewed by many countries in recent years.

Randomised trials have confirmed the efficacy and safety of acellular pertussis vaccine in adolescents and adults. Several countries have scheduled adolescent booster doses with New Zealand having followed the trend with the introduction of an 11 year dose into the schedule in 2006.[69 70 55]

Pertussis control strategies recommended by the Global Pertussis Initiative and their relevance to New Zealand.

Although adequate coverage and timeliness of the infant primary series remains the principle focus of pertussis prevention, additional immunisation strategies are recommended to reduce the risk of vulnerable infants acquiring pertussis from older children and adults.

The Global Pertussis Initiative is a scientific forum established in 2001 to examine the status of pertussis globally and to identify immunisation strategies that will improve control of pertussis. When initiated it included a multidisciplinary team of 37 experts from 17 countries and its membership has since increased.[71]

In 2004 the Global Pertussis Initiative recommended pertussis control strategies beyond the primary infant series and any early childhood aged booster doses (Table 2).[72]

Table 2. Immunisation strategies assessed by the Global Pertussis Initiative and their relevance to reduction of infant pertussis burden in New Zealand[72]

Strategy	Current status in New Zealand	Relevance to ongoing immunisation schedule evolution
Highest priority		
Reinforce and/or improve current infant and toddler immunisation strategies	Improving immunisation coverage identified as the first of 10 health targets in 2007 and as one of the six health targets for 2009/10[73]	• As coverage and timeliness remain too low to control pertussis this is the highest priority of the seven strategies
Intermediate priority		
Universal preschool booster doses at 4 to 6 years of age	Introduced into immunisation schedule in 2002[55]	• Will remain a component of the immunisation schedule for the foreseeable future
Universal adolescent immunisation	11-year dose introduced in immunisation schedule in 2006[55]	• Implementation strategies including education required to increase uptake. • Unlikely to significantly reduce infant pertussis burden unless an adequate adult immunisation programme is in place • Is potentially of greater significance for protecting vulnerable infants from household exposure in New Zealand given the age profiles and crowding of New Zealand households
Selective immunisation of healthcare workers	Has been initiated in some District Health Boards	• Should be offered to all staff; medical, clerical and cleaning • Staff turnover requires this to be a regularly repeated process • High risk of significant disruption of delivery of neonatal intensive care nationally if not instituted in all District Health Boards
Selective immunisation of new mothers, family, and close contacts of newborns	Not currently on immunisation schedule	• Should be considered with birth of child being the trigger point for ensuring all children and adolescents have received scheduled immunisations and boosters are offered to all other household members

Lower priority		
Universal adult immunisation	Not currently on immunisation schedule Immunisation schedule includes adult tetanus-diphtheria doses at 45 and 65 years	• Needs to be introduced for any reduction in infant pertussis burden from adolescent immunisation is to be expected • Booster doses may be required more frequently and starting from a younger adult age • Implementation strategies including education required as uptake of >85% needed to reduce number of infant pertussis cases.[74] • Current incomplete knowledge and delivery issues mean this option is a lower priority at present
Selective immunisation of childcare workers	Not currently on immunisation schedule	• Should be considered but logistics of identifying and immunising all childcare workers are considerable

Reinforce and/or improve current infant and toddler immunisation strategies

By identifying the improvement in immunisation coverage as one of its six health targets for 2009/10 New Zealand has articulated a desire to reinforce and improve current infant and toddler immunisation strategies.[73] As this part of the schedule is delivered through primary care a key component to increasing immunisation coverage will be to develop policy and strategies which enable all primary care practices and providers to deliver immunisation as effectively as those practices and providers who currently do this well.

The Immunisation Research Strategy jointly sponsored by the Ministry of Health and the Health Research Council since 2003 has funded projects which have identified primary care practice and health professional characteristics associated with higher immunisation coverage and timeliness.[75] A currently funded research project is assessing the effectiveness of increased resourcing of practice immunisation delivery on practice immunisation coverage and timeliness. It is anticipated that this and other projects in progress will help reduce the large variance between practices in immunisation delivery and hence enable coverage and timeliness to reach levels where infant pertussis disease burden is decreased.

Universal preschool booster doses at 4 to 6 years of age and universal adolescent immunisation

A universal preschool booster at age four years has been a component of New Zealand's immunisation schedule since 2002.[55] With the demonstration that protection against pertussis persists for at least 6 years following primary immunisation with a three component acellular pertussis vaccine, an 11-year booster dose was added to the schedule in 2006 with the 15-month booster removed at the same time.[51,68]

International expert opinion is that in the absence of adult pertussis immunisation adolescent immunisation cannot be expected to result in a large reduction in infant pertussis.[72] However this booster dose may be of more importance in New Zealand than in some other developed countries given the characteristics of households in New Zealand where infants are at most risk of pertussis.

The risk of hospital admission with pertussis during the first 12 months of life is increased for Maori and Pacific infants.[76] Characteristics of Maori and Pacific households of particular relevance to adolescent pertussis vaccine boosters are that such households are more crowded and are more likely to include both adolescents and infants.[77,78] Poverty produces household dynamics that predispose children to pertussis and also reduces their likelihood of being immunised.[79,80]

Prioritisation of adult and of targeted 'cocoon' immunisation strategies

Four of the seven pertussis control strategies considered by the Global Pertussis Initiative involve immunisation of a specific higher risk group in order to reduce the risk of pertussis transmission to infants. These are universal adult immunisation; selective immunisation of new mothers, family, and close contacts of newborns; selective immunisation of healthcare workers; and selective immunisation of childcare workers. Assuming improvement of current infant and toddler immunisation delivery occurs how can these four be prioritised? This prioritisation can be made by identification of the most vulnerable group of infants and by acknowledgement of the limitations of likely benefit of each of these strategies in the context of the current population delivery of preventive health care.

Universal adult immunisation

Acellular pertussis vaccines are safe and immunogenic in adults.[81] Antibody responses in adults to single doses of acellular pertussis vaccine are at least as large as those generated following a three dose series given to infants.[82-84]

Routine adult immunisation, although a logical next step, requires careful consideration. Without it universal adolescent immunisation is less likely to be effective.[72]

To switch the current doses of adult tetanus diphtheria vaccine scheduled for age 45 and 65 years to a combination vaccine which also included acellular pertussis antigens is simple. Three issues currently raise doubt regarding the effectiveness of such a strategy.

The first issue is coverage. It is estimated that adult coverage of greater than 85% would be required to reduce infant pertussis disease.[74] Accurate data on coverage rates for routine adult immunisation in New Zealand are not available but it is highly unlikely that it is anywhere near this level given that full coverage at age two years in the 2005 national survey was 77%.[55]

Secondly, it is improbable that protection from the 11 year dose would persist through the 34 years until age 45; that this dose would adequately protect to age 65 years; and finally that the 65 year dose would be sufficient to provide lifelong protection. These issues make this option potentially expensive as they imply the need for more frequent adult booster doses, at least every 10 years.

Thirdly, vaccination of adults has not yet been shown to reduce disease burden in infants. Data from a randomised clinical trial demonstrates that a single dose of an acellular pertussis vaccine protects adolescents and adults against clinical pertussis.[69]

Studies which demonstrate that this protection also reduces the risk of transmission to the infant have yet to be reported.

There are clearly too many gaps in our knowledge and in our current healthcare delivery to make universal adult immunisation a sensible option at present.

Selective immunisation of new mothers, family, and close contacts of newborns

As household transmission is the primary source of pertussis in infants it is logical to ensure other household members are immunised against pertussis. Pregnancy presents an opportunity to review the immunisation records of household members and ensure all children living in the household are fully immunised. In the context of New Zealand's insufficient immunisation coverage for scheduled doses of pertussis vaccine, and the excessive burden of pertussis in New Zealand relative to other countries with similar schedules, the emphasis of this pregnancy related immunisation review should be to ensure that all household members receive all recommended doses.

The United States recently recommended administration of acellular pertussis vaccine to all women in the immediate post-partum period.[81] To what extent this will reduce infant pertussis disease burden is not known.

Immunisation with acellular pertussis vaccines during pregnancy is not currently recommended because of a lack of safety and efficacy data. Currently data do not exist that informs on whether receiving acellular pertussis vaccine during the pregnancy poses any risk to the pregnancy or the foetus. Nor are there data on the protection provided to the young infant by transplacental maternal antibodies, or on whether such antibodies would result in any interference with the infants own immune response to the primary immunising series. [81]

Selective immunisation of healthcare workers

Healthcare workers are at increased risk of pertussis and can transmit pertussis to other healthcare workers and to patients.[85] Outbreaks in maternity wards, neonatal units and in outpatient settings have been described.[81] Fatalities occur as a result of such nosocomial spread.[86]

A wide range of healthcare workers have been implicated in such outbreaks including doctors, nurses, students, midwives, and other healthcare staff.[81] Investigation and control measures for outbreaks in healthcare settings are disruptive and costly.[87-89]

Hence, all personnel who work in neonatal units and other clinical settings where they are exposed to infants with respiratory, cardiac, neurological or other comorbid conditions should receive a booster dose of acellular pertussis vaccine. Such unit-based immunisation programmes have already been established in some District Health Boards in New Zealand. For example, since 2008, the neonatal intensive care unit in Auckland District Health Board has offered Boostrix® vaccinations to all staff; medical, clerical and cleaning.[90]

The increased notifications which indicate onset of another of the three to four yearly pertussis epidemics in New Zealand should be used by District Health Boards as a

prompt to offer a booster dose of acellular pertussis vaccine to staff who have not received one in the past 10 years.

Selective immunisation of childcare workers

Childcare workers and teachers are adult occupational groups also considered at increased risk of pertussis.[85 91] This increased risk is due to their exposure to young children, the age group that are the most effective spreaders of communicable respiratory diseases. As New Zealand's current pertussis immunisation schedule is designed to provide protection against pertussis from age 6 months (when the primary series is completed), through until adolescence it is more appropriate for the emphasis to be on the complete and timely immunisation of all children attending childcare, preschool and school.

Conclusion

New Zealand continues to expose its young children to an unnecessarily high risk of pertussis. An infant growing up in New Zealand today has a risk of being hospitalised with pertussis that is three times greater than for an infant in Australia or England and six times greater than for an infant in the United States.[4,76,92,93] Of infants hospitalised with pertussis in New Zealand one in 14 require intensive care.[76]

Recent studies show that one in seven New Zealand infants with pertussis requiring intensive care either die or have subsequent brain or lung damage.[30] Based upon hospitalisation rates and on the number of children per year with pertussis requiring paediatric intensive care pertussis disease burden in New Zealand is increasing.

We know that delay in receipt of any of the three infant doses of pertussis vaccine is associated with a five-fold increased risk of hospital admission with pertussis.[64] Yet we continue to have immunisation delivery that is both mediocre and widely variable. We continue to have lower immunisation coverage for Maori in an era where, in other countries, differences in coverage between indigenous and non-indigenous populations have been eliminated.[94]

If immunisation coverage and timeliness were improved fewer children would die, fewer would be left disabled, fewer would be hospitalised, fewer families would experience all of the direct and indirect costs accrued when *B. pertussis* invades their home, and the societal costs of pertussis to New Zealand would be reduced. For all children receipt of three doses of a pertussis containing vaccine by 6 months of age is the highest priority.

The development of acellular pertussis vaccines has enabled pertussis control initiatives to be expanded to include older children, adolescents and adults. The seven refinements recommended by the Global Pertussis Initiative represent a new generation of pertussis control measures. The implementation of these strategies provides an opportunity to reduce the immunisation generation gap that exists between New Zealand and much of the rest of the developed world.

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Current enoxaparin dosing guidelines have dubious credibility

Hesham Al-Sallami, Sarah Jordan, Ruth Ferguson, Natalie Medlicott, John Schollum, Stephen Duffull

Abstract

Aim To assess the prescribing practice of enoxaparin in comparison to dosing guidelines.

Method A prospective observational chart review of patients who received enoxaparin for the treatment of thrombosis at Dunedin Public Hospital between August 2007 and January 2008. Deviations in dose from guidelines were defined and recorded along with various clinical and demographic data of participants.

Results Fifty-nine patients (62 admissions) were recruited. Dose deviations occurred on 19 (30.7%) occasions. More dose deviations occurred at or close to guideline transition points (total body weight over 90 kg and/or creatinine clearance between 20–40 mL/min).

Conclusion Current enoxaparin dosing guidelines are too simplistic and result in discord between dosing in practice and that approved by Medsafe.

Enoxaparin has largely replaced unfractionated heparin in the treatment of venous and arterial thrombosis. Dosing guidelines are based on patients' weight and renal function. The current dose of enoxaparin approved by Medsafe is 1 mg/kg twice a day based on total body weight (TBW) with a reduction to 1 mg/kg once a day for patients with a creatinine clearance (CLcr) of less than 30 mL/min.[1]

We assessed enoxaparin dosing at Dunedin Hospital and the influence of dosing on bleeding events. We believe that a lack of credibility in dosing guidelines is likely to result in a lack of compliance of prescribing with dosing guidelines. We hypothesise that uncertainty in interpretation of the dosing guidelines will therefore lead to significantly more deviation of dosing from dosing guidelines at or close to transition points.

We define two transition points, their nature depending on whether the guidelines make specific recommendations in their regard. These are the explicit transition that occurs at a CLcr of 30 mL/min a point at which the dose rate is halved and an implicit transition at 90 kg the latter not included in the dosing guidelines but for which there is a growing literature implicating obesity as a risk factor for bleeding.

Since the occurrence of exact transition points is rare we take a value of CLcr between 20 and 40 mL/min and weight >90 kg for the region related to these points. The null hypothesis would therefore be a uniform level of dose deviation over the entire range of renal function and weight which would indicate that no particular regions of these covariate values pose greater therapeutic concern than any other region.

We carried out a prospective observational chart review of all inpatients 18 years and older who received treatment doses of enoxaparin for at least 48 hours between August 2007 and January 2008. Patient demographics were collected and used to calculate the dose and the dosing range for that particular patient. Patients were also monitored for bleeding or bruising while in hospital. The study was approved by the Lower South Regional Ethics committee, the Otago District Health Board, and the Māori Ngāi Tahu Research Consultation Committee.

Fifty-nine consecutive patients (62 admissions) were recruited and followed up until discharged from the hospital. Deviations in dose from the guidelines occurred on 19 (30.7%) occasions involving 15 patients (Table 1). Definitions of a deviation in dose are provided in Table 1.

Table 1. Clinical and demographic characteristics of participants

Characteristics	**Results [N=59 patients; median (range) or number (%)]**
Age in years	67 (22–88)
Females	28 (47%)
Māori	2 (3%)
Height in cm	169 (147–193)
Weight in kg	78 (43.8–150)
Body mass index in kg/m^2	28 (15.3–52)
Characteristics	**Results [N = 62 admissions; median (range) or number (%)]**
Diagnosis	
Acute coronary syndrome	40 (65%)
Venous thromboembolism	17 (27%)
Atrial fibrillation	5 (8%)
Concurrent use of drugs affecting haemostasis	
Antiplatelets	47 (76%)
Oral anticoagulants	23 (37%)
NSAIDs	4 (6.5%)
Others (complimentary medicines)	0 (0%)
Creatinine clearance (CLcr) in mL/min	46 (13.6–113)
Enoxaparin dose and treatment duration	
Dose in mg	80 (40–150)
Dose in mg/kg	1.0 (0.8–1.5)
Number of doses given	6 (3–37)
Treatment duration in days	4 (2–37)
Dose deviation from guidelines	
Dose in excess of guidelines[a]	7 (11.3%)
Excess dose (mg)	1.1 (0–32)
Dose lower than guidelines[b]	12 (19.4%)
Dose deficiency (mg)	2.9 (0.4–15.5)
Type of bleeding[2]	
Major[c]	1 (2%)
Minor[d]	8 (13%)
Excess dose (mg)	3 (0–22.4)
Dose deficiency (mg)	3.5 (2–13)

[a]Defined as >5 mg in excess of a dose based on 1 mg/kg TBW, or a dose given twice daily when CLcr <30 mL/min; [b]Defined as >5 mg less than a dose based on 1 mg/kg TBW, a dose of 1 mg/kg given once daily when CLcr ≥30 mL/min, or a dose capped at 100 mg when TBW >105 kg; [c]Defined as a decrease in haemoglobin by >30 g/L or evidence of an internal anatomical bleeding such as retroperitoneal, intracranial or intraocular; [d]Defined as a bleeding event other than major (e.g. epistaxis, haematuria) or a major bruise that has a surface area greater than 20 cm^2 and is distal to the injection and venipuncture sites.

There were nine bleeding/bruising events of which eight were minor (13%) and one major (2%). Classification of events was based on a previous study.[2] These incidences are similar to those published in the literature.[3–5] The one patient with major bleeding was morbidly obese (wt=150 kg, BMI=52) and received a dose of 150 mg twice daily. This patient's estimated GFR was 58 mL/min, calculated by the ideal body weight (IBW) Cockcroft and Gault equation.[6]

Seven of the eight patients (88%) who had minor bleeding events in this study had CLcr between 30–59 mL/min. Out of the eight patients who experienced a minor bleeding event, three dose deviations were recorded (1 excess dosing and 2 under-dosing). However, the implication of this finding is difficult to deduce due to the low number of events.

We propose that the deviation of the dosing regimens in clinical practice from the guidelines is, at least partly, due to a lack of credibility by clinical staff in the dosing guidelines for enoxaparin. For example, the guidelines recommend that the dose is based on actual body weight with no regard to obesity. Also, a patient with a CLcr of 29 mL/min should receive half the total daily dose compared to a patient with a CLcr of 30 mL/min.

In the case of the obese patient it seems unreasonable that excess fat mass increases the clearance of enoxaparin, a hydrophilic compound.[7] This may have contributed to the popularity of arbitrary dose-capping (at 100 mg) which is considered by some as a safer option.[8] However, dose capping may result in both under- and overdosing as the absolute clearance in the obese patient is higher than in the non-obese but not proportionally to weight.[9] An alternative dosing strategy based on lean body weight (LBW) has been shown to be a safer option.[2]

In the second scenario, the guidelines are patently inadequate at accounting for changes in renal function, where patients who have chronic kidney disease (CKD) 1–3, as defined by the National Kidney Foundation,[10] receive a dose equivalent to that of someone with normal renal function whereas transition to CKD 4 requires a halving of dose. For definition of the CKD stages refer to Table 2.

Table 2. Chronic kidney disease (CKD) classification

Stage	Glomerular filtration rate, GFR (mL/min/1.73 m^2)	Comments
1	≥90	Renal disease with normal GFR
2	60–89	Mild decrease in GFR
3	30–59	Moderate decrease in GFR
4	15–29	Severe decrease in GFR
5	<15	Renal failure

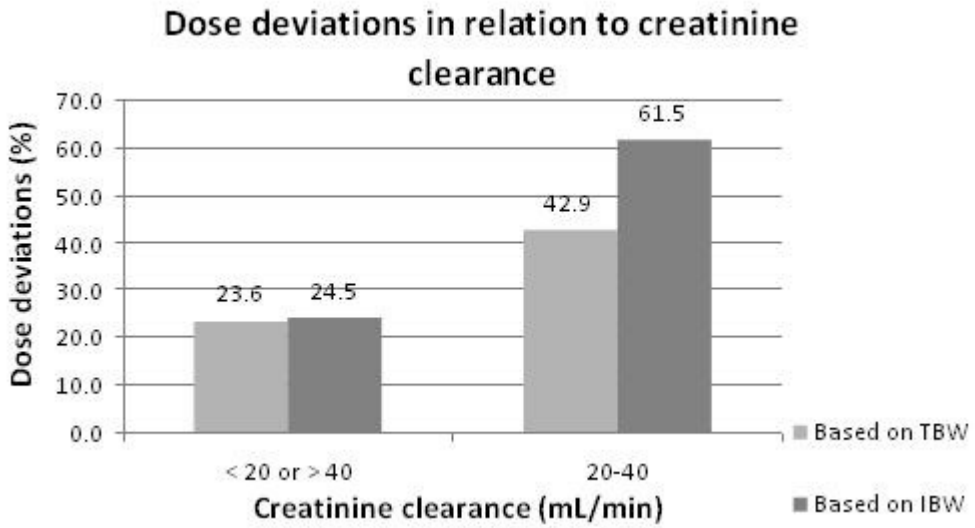
If our hypothesis is correct, then we should expect to see that most deviations in dosing would occur at or close to guideline transition points. The transition points occur at a value of CLcr 30 mL/min and at a weight value of 90 kg where obesity is

likely to be a concern. For renal function we have chosen a range of CLcr from 20 to 40 mL/min.

Values of CLcr outside of this range, i.e. greater than 40 mL/min or less than 20 mL/min are sufficiently normal or abnormal with respect to renal function as to be less likely to engender uncertainty about choice of dose.

We show in Figure 1A that deviations in the dose from guidelines were more common in patients who were close to the transition in the guidelines. The number of dose deviations was not different based on the transition at a weight of 90 kg (shown in Figure 1B). The study was however underpowered for this size of difference. Note, however, that on both scenarios, and irrespective of how CLcr was calculated, more dose deviations occurred closer to a transition point in the guidelines.

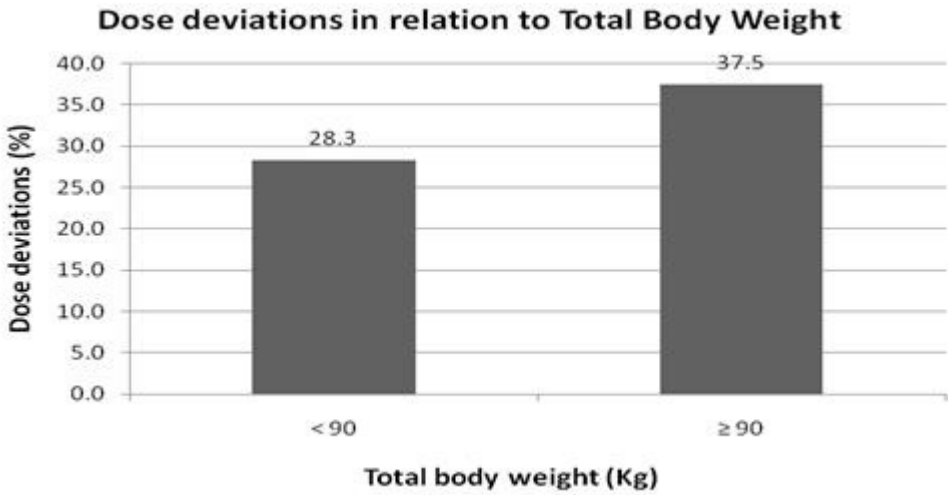
Figure 1A. Frequency of dose deviations in relation to CLcr (mL/min)



Note: CLcr is calculated using TBW (light grey bars) and IBW (dark grey bars). Deviations in the two groups were statistically different when CLcr was calculated using IBW (Chi-squared=6.45, p=0.01) but, despite a trend, not significant when CLcr was calculated using TBW (Chi-squared=1.2, p=0.27).

We believe these results support our hypothesis that the current enoxaparin dosing guidelines, as defined in the datasheet, are too simplistic and result in discord between dosing in practice and that approved by Medsafe. Similarly, LaPointe et al showed that approximately 30% of patients receiving enoxaparin for non-ST-elevation acute coronary syndrome (N=10687) were underdosed.[11]

Figure 1B. Frequency of dose deviations in relation to TBW (kg)



Note: Dose deviations appeared to be higher in patients with a TBW >90 kg but this difference did not reach statistical significance (Chi-squared=0.48, p=0.49).

Alternative dosing guidelines may be more appropriate and this was supported by a randomised controlled trial which showed that individualising enoxaparin dose according to renal function and body composition results in fewer adverse effects.[2] In the individualised arm, a dose of 1.5 mg/kg of LBW^{12} twice daily was used in patients who weighed 100 kg or more. Patients with a declining renal function received a declining maintenance dose based on their CLcr. Dose-individualised patients had fewer bleeding events and composite bleeding and bruising events than those who received conventional dosing. No increased risk of thromboembolic events was noted in either group.

In conclusion, credible dosing guidelines of enoxaparin treatment that take into account individual variability are needed.

Competing interests: None known.

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THE NEW ZEALAND MEDICAL JOURNAL
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Button batteries: the worst case scenario in nasal foreign bodies

Alice K Guidera, Hans R Stegehuis

Abstract

Aim To present four cases of button battery nasal foreign bodies that were referred to an otolaryngology department over a 6-month period.

Methods Four cases are presented and discussed with a review of current literature.

Results Four children aged 2–4 years who were referred to an otolaryngology department over about 6 months were found to have a button battery in their nose. While there was mucosal damage in all the noses the likelihood of a septal perforation developing appears to be related to the time interval between insertion and removal. The two patients who did not develop a septal perforation had the battery removed after about 90 minutes and 3 days. The two patients who did develop a perforation had the battery removed after 4 hours and 24 hours. Battery thickness may also be important as the patient who had the battery removed at 3 days had a 2 mm thick battery whereas the other three all had a 5 mm thick battery.

Discussion As button batteries are ubiquitous it is imperative that consumers and medical practitioners are aware of the risks they pose if placed in the nose, and also elsewhere in the body.

Conclusion As early removal of a button battery is likely to decrease the chances of a septal perforation developing a nasal foreign body should be considered to be a button battery *until proven otherwise*.

A lot of initial assessment and investigation in general practice and the emergency department is based on worst case scenarios. A whiplash injury has cervical damage *until proven otherwise*, a headache with photophobia is meningitis, chest pain is a myocardial infarction, lower abdominal pain in a young woman is an ectopic pregnancy... the list goes on.

Nasal foreign bodies in children often present to both general practitioners and emergency physicians. These are usually innocuous with the majority being plastic objects (particularly beads), foam, paper or cotton.[1] The button battery is the foreign body most likely to have serious sequelae if not removed quickly.[2,3]

While button battery impaction in the nasal cavity is uncommon, four cases have been seen at the Otolaryngology Department at MidCentral District Health Board (DHB) in Palmerston North, New Zealand over a period of only 6 months.

We present these four cases and discuss the initial management of all children presenting with a nasal foreign body.

Case series

Patient 1—A 2-year-old female presented to the emergency department of a rural hospital 2 hours after her 4-year-old brother inserted a "metal wheel" up her left nostril.

Attempts to remove the object were unsuccessful and the patient was referred to the Otolaryngology Department at MidCentral Health for further management the following day.

When the object was removed under general anaesthesia (approximately 20 hours after insertion), the nasal cavity was found to be full of corrosive material and debris and the object was identified as a 5 mm thick 1.5V alkaline button battery (Figure 1; right side).

Figure 1. Typical button batteries

Note: Both batteries are 1.5V and are approximately 10 mm wide. The battery on the left is approximately 2 mm thick and is identical to the battery removed in Case 2. The battery on the right is approximately 5 mm thick and is identical to the batteries removed in the other three cases. The negative terminals are upright.

While we don't know what is in the button batteries these four children put in their noses, we do know many contain zinc and silver oxide in a sodium or potassium hydroxide medium. Other types contain mercury, lithium, cadmium or sulphur. They are all in a metal casing and a plastic grommet forms the seal between the anode and cathode[4].

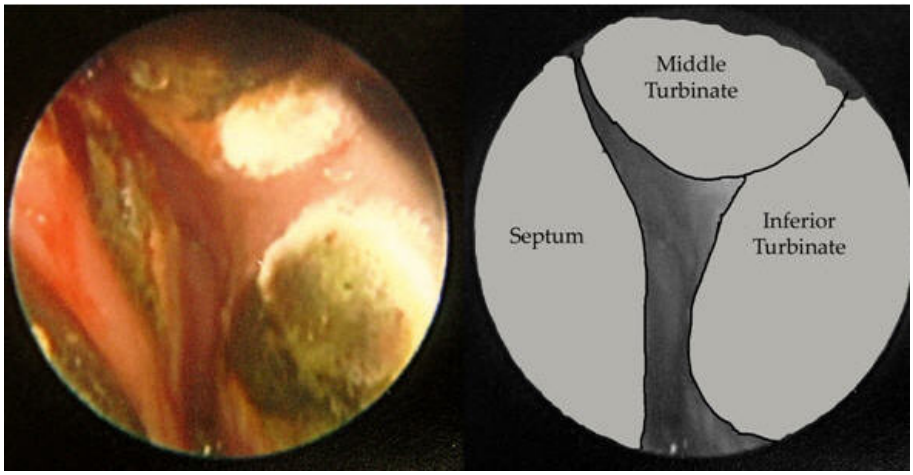
The left nasal cavity mucosa was extensively damaged, with exposed blackened septal cartilage and burns superiorly and laterally along the medial border of the inferior turbinate. The contralateral septal mucosa was also extensively blackened although still intact.

At follow-up after 1 month, a septal perforation was evident despite treatment with antibiotics and saline/bicarbonate nasal douches.

Patient 2—A 4-year-old female presented to her general practitioner 3 days after inserting a button battery into her left nostril. The 2 mm thick 1.5V battery was removed under general anaesthestic. Burns were evident on the superior septum and

the anterior portion of the inferior and middle turbinates (Figure 2). The mucosa on the right side of the septum was intact. The nasal mucosa healed without any apparent permanent sequelae.

Figure 2. Patient 2's intraoperative findings: charred areas are seen on septum and middle and inferior turbinates. The battery, similar to the one shown in figure 1 (left side), had been present for 72 hours

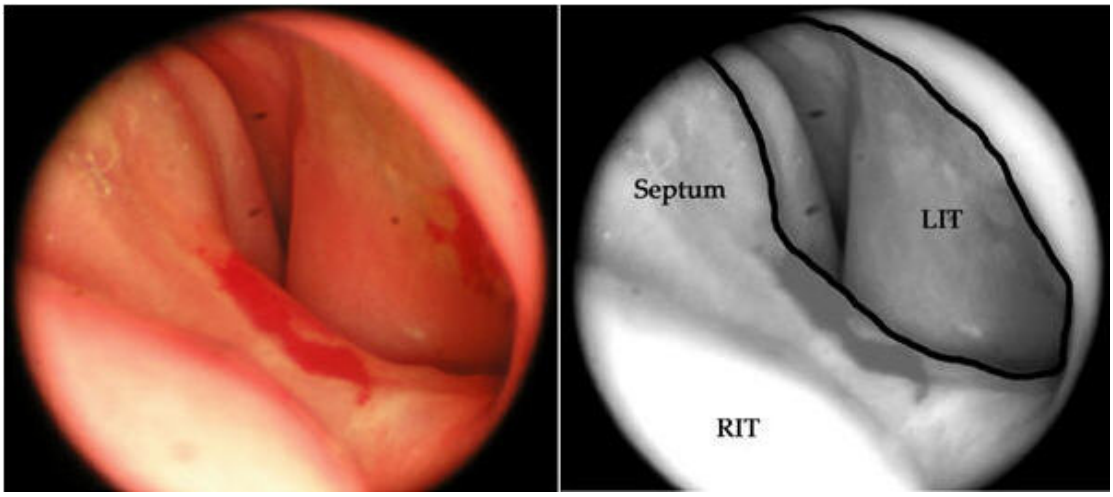


Patient 3—A 4-year-old boy presented to the GP with what was thought to be a ball bearing up his nose. A 5 mm thick battery was removed approximately 4 hours after insertion under general anaesthetic. There was extensive damage to the nasal mucosa on the ipsilateral and contralateral sides of the septum. The surface of the battery was found to be heavily corroded (Figure 3; left-side battery).

Figure 3. 1.5V batteries removed from Patients 3 and 4 as compared to a new battery (right side) of the same size. The battery on the left side (Patient 3) had been in the nose for 4 hours. The middle battery (Patient 4) was removed after approximately 1.5 hours; corrosion is already clearly visible on the casing

An asymptomatic septal perforation developed (Figure 4) which is being managed expectantly.

Figure 4. View through septal perforation (Patient 3) from right nasal cavity to left nasal cavity



Patient 4—A 4-year-old male had been playing with a 5 mm thick 1.5V button battery for 4 days before he put it into his right nasal cavity. The battery was removed after about 1.5 hours in Outpatients (Figure 3; middle battery). Blackening of the anterior portion of the right inferior turbinate and right septal mucosa was already present but the mucosa on the left side of the septum looked normal. There were no apparent long-term sequelae.

Discussion

A septal perforation has occurred in two of the four children in this case series; an incidence similar to that found in previous studies.[2] The likelihood of a septal perforation is multifactorial.

Increased time interval between insertion and removal increases the risk of a septal perforation. Ongoing electrical and thermal burning will occur as long as the electrical circuit is intact and, as the length of time increases, the chemicals released by erosion of the metal shell of the battery may also contribute to further morbidity.

The thickness of the battery may be important, as suggested by the case of the only patient who had a thinner (2 mm rather than 5 mm) battery in their nose—this patient didn't develop a septal perforation even though the battery was in place for 3 days. Of course the charge of the battery is likely to be important too and this may have been the only flat (dead) battery.

The orientation of the battery in the nasal cavity is also reported to be important, with tissue at the anode pole (negative) more likely to be damaged.[2] Hence if the anode pole is against the septum, a perforation is more likely. The size of the nose and the amount of secretions in the nose may also be factors.

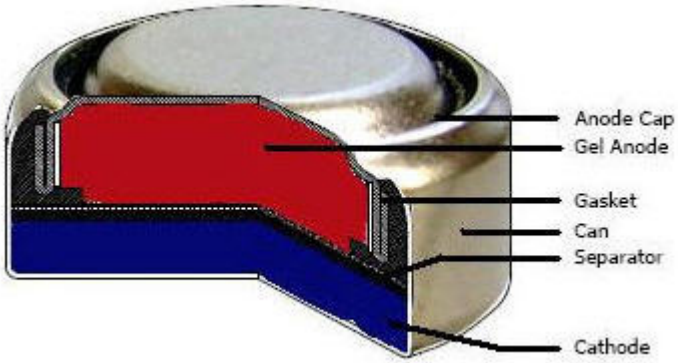
Damage to the nasal mucosa has previously been reported after as few as 3 hours, with damage leading to perforation after 7 hours.[2,5]

This case series shows that mucosal damage can occur as early as 90 minutes, and sufficient mucosal damage to later cause a septal perforation can occur after a time interval of only 4 hours.

Mucosal damage is due to several mechanisms. Firstly, the electrical circuit is completed because the battery is in contact with both sides of the nasal cavity, and the high ionic concentration of the nasal secretions is thought to generate local currents that cause electrical and thermal burns.[2,6,7]

Secondly, erosion of the plastic seal and the layer separating the anode and cathode mixtures results in leakage of battery contents causing chemical burns, particularly at the anode (negative) side.[2] See Figure 5. The battery may also cause pressure necrosis although this is unlikely to play a significant role.[2,6,7]

Figure 5. Cross section schematic of a button battery



Until the advent of button batteries, nasal foreign bodies were generally not considered to be an emergency, with the main concern being the possibility of aspiration if the foreign body went right through the nose.

In practice, most foreign bodies don't go through the nose and if they do they are usually swallowed rather than aspirated. Many nasal foreign bodies present late with a unilateral foul-smelling discharge which ceases when the foreign body is removed.

Button batteries are different in that they almost immediately start to cause tissue destruction that may cause a septal perforation with possible later sequelae such as an effect on the growth of the nose.

While button batteries in the nose are not common they must be considered in order to be excluded. Indeed in a recent review by Glynn (who presented a case series of three button batteries) none were diagnosed prior to removal under general anaesthetic.[8] While Glynn advocates the use of a plain film skull X-ray in the diagnosis of every child presenting with a nasal foreign body, and Lin et al have demonstrated the distinct double contour on plain films that aids in correct diagnosis,[7] we believe an

X-ray will only be appropriate occasionally. Usually the nature of a foreign body is apparent from the history and examination, and after you have seen a few nasal button batteries the copious secretions immediately ring alarm bells.

An X-ray would appear to be worthwhile only if the positive finding of a battery will expedite access to the operating room. General anaesthesia is usually required, although in the 4-year-old in whom the battery had only been present for 90 minutes this was able to be removed in outpatients, presumably because not enough erosion had yet taken place to make it adherent to the tissues.

It is our impression—both from the parental behaviour in some of these cases and talking to friends, medical colleagues, and nurses—that there is very little community awareness of the risks these batteries pose to young children. We hope therefore that this paper will raise both community and medical awareness.

Conclusions

Management begins with a thorough history; reliable witness accounts should be married with a thorough examination of the anterior nasal cavity.

Time in the nose is important. Removal at 90 minutes is likely to mean no permanent sequelae whereas removal at 4 hours can mean a septal perforation. If a nasal foreign body could be a button battery then urgent referral to an otolaryngologist is indicated. A nasal foreign body should be considered to be a button battery *until proven otherwise*.

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Nodular regenerative hyperplasia of the liver secondary to azathioprine in a patient with inflammatory bowel disease

Daniel L Bryant, Carina J Miles, Richard B Gearry

Abstract

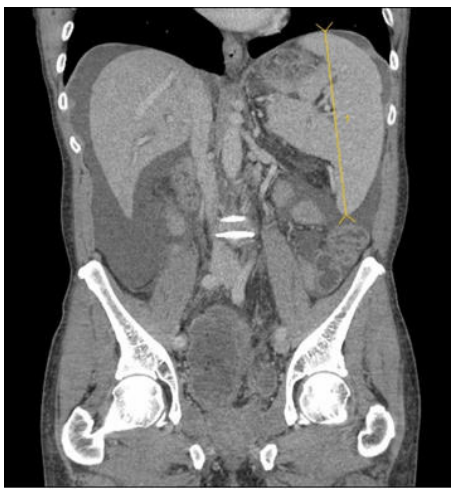
A case of dramatic portal hypertension with massive ascites and splenomegaly is described in a patient with inflammatory bowel disease receiving azathioprine therapy. Liver biopsy confirmed the subtle changes of nodular regenerative hyperplasia and the patient recovered following withdrawal of the azathioprine and commencement of spironolactone. Thrombocytopaenia is an early clue to azathioprine-induced nodular regenerative hyperplasia of the liver.

Case report

The patient, a 54-year-old Caucasian male, was initially diagnosed with ulcerative colitis in 1983. He subsequently failed medical therapy and underwent a panproctocolectomy and ileal pouch anal anastamosis in 1988. Thereafter he developed anal stenosis and perianal disease leading to a change in diagnosis to Crohn's disease with small bowel disease later being confirmed by capsule endoscopy in 2006.

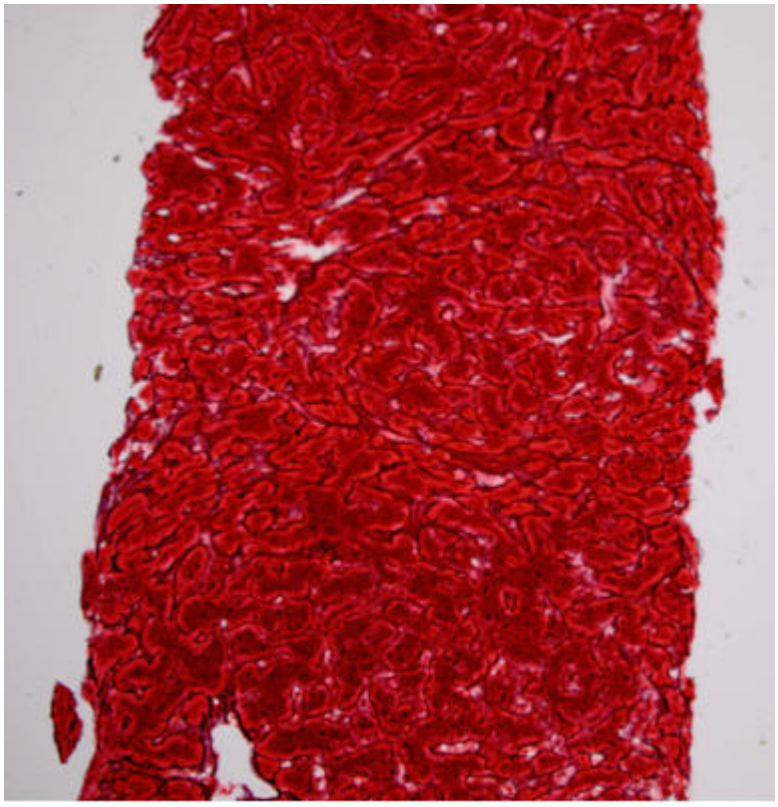
Azathioprine was commenced at this time and due to ongoing symptoms the dose was increased eventually to 3.5 mg/kg over 18 months. The patient subsequently presented in September 2007 with abdominal swelling and a CT scan (Figure 1) revealed ascites and splenomegaly. In retrospect, he had been mildly thrombocytopaenic for 2 months prior to the onset of his symptoms.

Figure 1. Coronal CT scan of the abdomen showing marked ascites and splenomegaly



A trans-jugular liver biopsy was performed. A reticulin stain (Figure 2, 100× magnification) revealing a subtle nodular pattern with some double hepatocyte plates but without fibrosis; all in keeping with a diagnosis of NRH due to azathioprine therapy. No vascular thrombi or portal tract changes were identified. The intervening parenchyma showed focal sinusoidal dilatation and some hepatocyte atrophy suggesting uneven perfusion.

Figure 2. Reticulin stain of transjugular liver biopsy (100× magnification) showing a subtle nodular pattern with some double hepatocyte plates but without fibrosis



The patient was managed with large volume paracentesis, spironolactone and cessation of the azathioprine and his ascites and thrombocytopaenia resolved.

Discussion

The inflammatory bowel diseases (IBD)—Crohn's disease (CD) and ulcerative colitis (UC)—are chronic relapsing-remitting inflammatory diseases of the gastrointestinal tract. Their incidence is rising rapidly in New Zealand for unknown reasons,[1,2] and treatment (particularly medical maintenance of remission) is challenging.

The thiopurines azathioprine and 6-mercaptopurine are frequently used to maintain remission in IBD. Thiopurine therapy[3] and IBD[4] are both associated with hepatic pathology, including nodular regenerative hyperplasia (NRH) of the liver.

It has been estimated that the cumulative risk of developing NRH when receiving a thiopurine for 5 years is approximately 0.5%.[5] NRH is defined as a diffuse distribution of hepatocellular nodules in the absence of fibrous septae.

NRH has been documented as occurring in association with a wide variety of hepatic and systemic diseases.[6] Many of these conditions have a disturbed hepatic blood flow in common and it seems that NRH is a non-specific tissue adaptation to a heterogenous distribution of blood flow.

The clinical features are variable and symptoms, if present, are mainly associated with the complications of portal hypertension such as splenomegaly, ascites and oesophageal varices. This will often lead to delayed diagnosis but thrombocytopaenia will almost always be observed on routine full blood counts which should be performed 3-monthly for patients taking long-term thiopurine therapy.

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THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Systemic lupus erythematosus (SLE) in a paediatric unit

Tilak de Almeida, Rachel Davey, Kamal Solanki, Rafi Raja, Marius Rademaker, Sue Rudge

A 14-year-old Fijian girl was admitted to our paediatric unit via the emergency department. She was referred by her general practitioner with a history of feeling unwell for about 6 months and migratory joint pain involving the large joints for 8 weeks, which affected her mobility.

She had not attended school for more than a week prior to admission. She had swelling of some interphalangeal joints of her fingers (Figure 1). There were papular lesions on the palmer aspect of her fingers (Figure 2), circular discoid lesions (Figure 3) over the upper limbs and a 6 cm × 4 cm area of alopecia (Figure 4) on the vertex of the scalp. She recalled having had a rash over both cheeks previous summer. There were neither oral or ocular symptoms nor lesions.

Streptococcal titres and throat swabs were negative. ESR and CRP were raised. Various antibodies—including anti nuclear antibody, anti-smith antibody, anti double stranded DNA, rheumatoid factor, and anti cardiolipin antibody levels—were all abnormally elevated. Complement levels were low. Full blood count, urine for deposits, and protein creatinine ratio were normal. There was no clinical evidence of other systemic involvement. A diagnosis of systemic lupus erythematosus (SLE) was made.

Echocardiogram and lung function tests were normal. Quantiferon Gold test was done to exclude concurrent tuberculosis prior to considering steroids. She was seen by dermatology and rheumatology teams who took over further care. As she has not had her measles vaccination (live vaccine) she was not started on steroids for her significant symptomatic joint inflammation. She was vaccinated against measles and started on ibuprofen and hydroxychloroquine with the intention of commencing on prednisolone 4 weeks post vaccination.

Figure 1. Proximal interphalangeal joint swelling at the middle finger

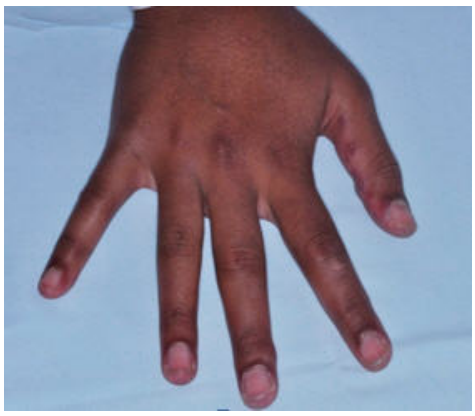


Figure 2. Lesions on the fingers

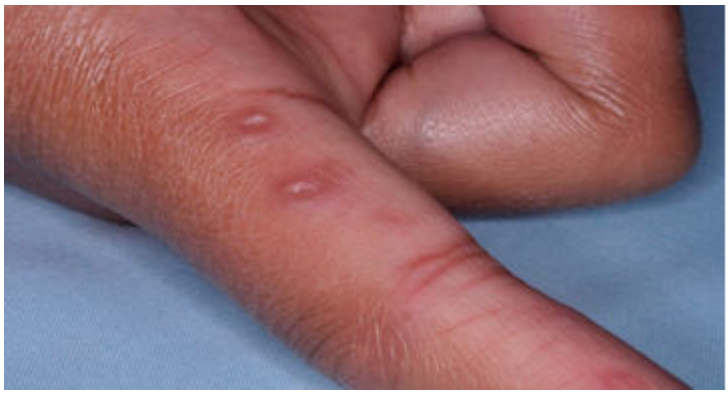


Figure 3. Cutaneous discoid lesions

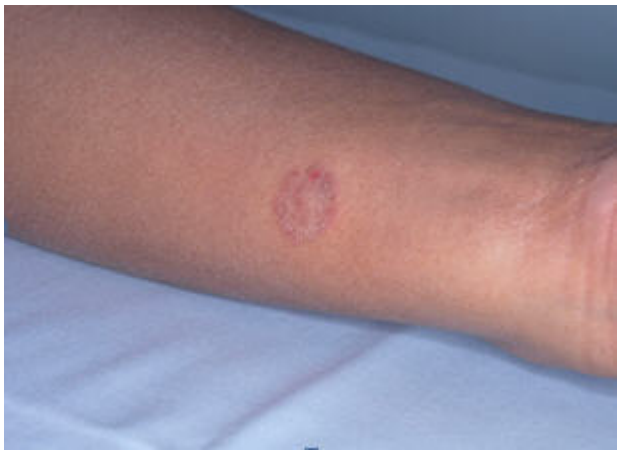
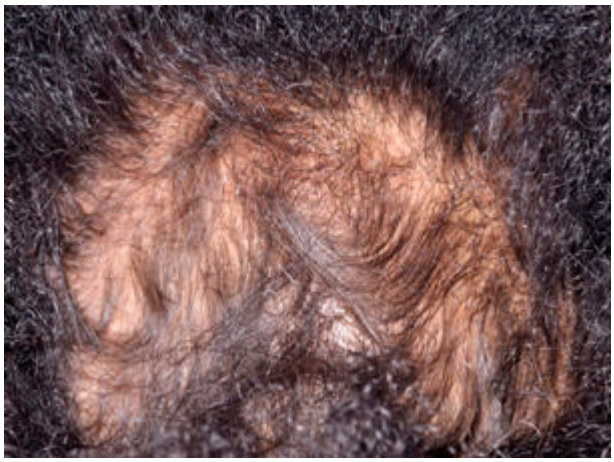


Figure 4. Alopecia



Discussion

SLE is uncommon in general paediatric units. The patient fulfilled the American College of Rheumatology classification criteria for SLE. This is the second patient with SLE admitted to our paediatric unit over the last 10 years. The previous patient presented at the age of 10 years with severe anaemia. She later went on to develop very active cutaneous and rheumatological disease which is being managed with high-dose prednisolone, methotrexate, and infusions of iloprost.

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Acknowledgements: We thank Phil Weston (Unit Leader, Paediatrics) for assistance with the manuscript as well as the dermatology and rheumatology teams for support with the management of the patient.

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THE NEW ZEALAND MEDICAL JOURNAL
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A case of ruptured gastric ulcer in a female aged 64 years

By P. Clennell Fenwick, F.R.C.S.E., F.R.G.S. Read at the February meeting of the Canterbury Division—and published in NZMJ 1910 May;8(34):7–9.

M.O., female, aged 64 years, was admitted into Christchurch Hospital on November 19th with the following history:—She had suffered from indigestion for several years, but had been in good health for some months previous to this attack. On November 11th she was seized with a sudden pain in the "pit of the stomach," shooting into the chest and, throat. She passed a black motion a few hours later, and vomited three times during the next 24 hours. No blood was seen in the motion or vomit.

On admission she was collapsed, the pulse being 102, very thin and thready, temperature 97, face pale and clammy, expression anxious; the abdomen was much distended, resonant in front, dull in the flanks, the resonance in the flanks altered on change of position; great pain was complained of in both flanks, and on pressure on the epigastrium. Dr. Westenra, my colleague, saw the case in consultation with me, and we agreed that there was a perforation of the stomach and advised immediate operation. The patient was very fat, and about 2½ inches of this had to be cut through before reaching the peritoneum. On incising the latter, a gush of foul-smelling liquid escaped. The liver was very large, reaching to the umbilicus, and was covered with thick adherent flakes of lymph. The incision was extended downwards, and the edge of the liver lifted, exposing the stomach, in the anterior wall of which was a perforation the size of a three-penny piece. The peritoneum was curiously oedematous and hung in folds. All the intestines were covered with adherent flakes of lymph. The perforation was closed with three sink sutures, and a fold of peritoneum was stitched over the stomach wound.

Three tubes were inserted into the abdominal wound, one pointing down to the perforation, one upwards in front of the liver towards the diaphragm, and the third passed down into the right renal fossa. A fourth tube was placed in Douglas' pouch through a suprapubic incision. A great quantity of foul liquid was removed. Saline was given by the vein, as the patient was collapsed. For the next four days the patient was given nutrient enemata, and a few ounces of albumin water by the mouth. She complained greatly of faintness. The bowels moved daily, I suppose by the action of the nutrient. No vomiting occurred, and the pain was not severe. The tubes were removed on the ninth day after operation, and the patient appeared well over the worst. There was a constant discharge of black liquid through the tube holes. The amount of fluid by the mouth was increased daily, as the nutrient caused irritation.

On December 5th, 15 days after operation, the patient died suddenly in her sleep, Dr. Crooke performed a post-mortem, and found the whole peritoneal cavity the seat of intense peritonitis, the stomach was water-tight and the perforation wound healed. I think this case unusual with regard to the age of the patient, and the great improvement which occurred despite the continued peritoneal inflammation. There was no intestinal paralysis or vomiting, and death apparently was due to heart failure.

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Proceedings of the Health Research Society of Canterbury Seminar Series, Thursday 22 April 2010

Model-based cardiac disease diagnosis in critical care. J Revie[1], CE Hann[1], D Stevenson[1], JG Chase[1], S Heldmann[2], GM Shaw[3], T Desaive[4], CB Froissart[5], B Lambermont[4], A Ghuysen[4] A Kolh[4], [1]Bioengineering Centre, Department of Mechanical Engineering, University of Canterbury, Christchurch, New Zealand, [2]Department of Mechanical Engineering, TU Darmstadt, Germany, [3]Department of Intensive Care Medicine, Christchurch Hospital, Christchurch, New Zealand, [4]Hemodynamics Research Laboratory, University of Liege, Belgium, [5] Université de Technologie de Belfort-Montbéliard, France.

Inadequate cardiac diagnosis in critical care is a main cause of increased length of stay, cost and death.[1] However, detection, diagnosis and treatment is very difficult, with clinicians confronted by a wealth of confusing, contradictory numerical data. A model of the cardiovascular system[2] can be used to assist medical staff in diagnosis and therapy by matching the model to clinically available measurements. This presentation will explain the application and validation of an 8 chamber cardiac model in identifying drug-induced pulmonary embolism in pigs.

A parameter identification method has been developed based on a minimal number of measurements commonly available in an intensive care unit (ICU). This method allows patient specific modelling of physiological changes to resistances and elastances as a result of disease states and/or therapy intervention. These parameters provide a model-based cardiac diagnosis and a means to test and optimize therapy.

All identified trends were consistent with physiologically expected results for pulmonary embolism including significant increases in pulmonary resistance and increases in the right ventricle expansion index. Contractility and systemic resistance also increased reflecting well-known reflex responses, and the model predicted a decrease in the coupling between right ventricle contractility and pulmonary resistance which matches more invasive measures. All measured variables were captured within expected measurement noise including the left and right ventricle pressures and volumes which were not used in the identification process.

In conclusion, all measurements and trends associated with acute pulmonary embolism in porcine data were accurately captured. The cardiac model in conjunction with an integral-based parameter identification algorithm is capable of replicating a wide range of hemodynamics of the pigs to within acceptable error ranges. These results show the potential for extending the model and methods for testing on human subjects in upcoming clinical studies.

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Patient specific modelling of cardiac muscle activation. **D Stevenson[1], CE Hann[1], J Revie[1], JG Chase[1], S Heldmann[2], GM Shaw[3], T Desaive[4], CB Froissart[5], B Lambermont[4], A Ghuysen[4], A Kolh[4], [1]Bioengineering Centre, Department of Mechanical Engineering, University of Canterbury, Christchurch, New Zealand, 2Department of Mechanical Engineering, TU Darmstadt, Germany, [3]Department of Intensive Care Medicine, Christchurch Hospital, Christchurch, New Zealand, [4]Hemodynamics Research Laboratory, University of Liege, Belgium, [5]Université de Technologie de Belfort-Montbéliard, France.**

The cardiac muscle activation or driver function is a major determinant of cardiovascular dynamics and is commonly used as an input into lumped parameter models of the cardiovascular system. The most common representation of the driver function requires left and right ventricle pressure and volume waveforms which are not typically available. This research identifies a patient specific driver function based only on readily measurable quantities in an intensive care unit (ICU).

Data from a porcine model of acute pulmonary embolism is used to validate the approach. Measurements available are left and right ventricle pressure and volume curves and aortic and pulmonary artery pressures. Population models using geometric properties of P_{ao} are used to estimate the left driver function. The right driver function is estimated by correlating significant features to the left driver function and timings from P_{pa}. To test the robustness of the approach, a 5-fold cross validation was performed and all estimated driver functions are compared to the measured driver functions.

Significant changes in the driver functions were successfully captured over time as pulmonary embolism developed. The method accurately identified all import aspects of the driver functions, such as the upward and downward slopes, inflection points and timings, as well as capturing the general shape. These driver functions allowed patient specific models for the circulation to be developed based on a minimal data set that is commonly used in an ICU.

A method for identifying a time varying patient specific cardiac driver function was developed, using readily available measurements in an intensive care environment. The method was validated on porcine data and demonstrated flexibility in the model to adapt to significant changes in heart rate and ventricle contractility. These results further demonstrate the potential for applying the model and methods in critical care to better manage the cardiovascular system.

Clinical investigations of a synthetic diamond x-ray detector. **GT Betzel[1], SP Lansley[1,2], F Baluti[3], L Reinisch[4], J Meyer[1]. [1]Department of Physics & Astronomy, University of Canterbury, Christchurch, [2]The MacDiarmid Institute for Advanced Materials and Nanotechnology, University of Canterbury, Christchurch, [3]Oncology Service, Christchurch Hospital, Christchurch, [4]Department of Physical and Earth Sciences, Jacksonville State University, Jacksonville, AL, USA.**

Diamond has been considered as a radiation detector material for many years. Advantages of diamond include the following: being a solid-state material, small-volume detectors with good sensitivity should be possible; it has high radiation

hardness; and it is near-tissue equivalent. Detectors based on natural diamond are commercially available for applications in radiotherapy. However, they are extremely expensive and have long delivery times, due to the scarcity of suitable high-quality natural diamond crystals. Recently, the synthesis of diamond, particularly by chemical vapour deposition (CVD), has resulted in more consistent, high-quality material. We have recently demonstrated x-ray detectors fabricated from commercially-available CVD diamond films.[1,2]

We have performed typical clinical measurements using such a detector in a 6 MV x-ray beam from a treatment linear accelerator. The output of the diamond detector compares well to that of a standard ion chamber used during linear accelerator quality assurance measurements such as tissue maximum ratio and output factor measurements. The small dimensions of the diamond detector result in high spatial resolution during off-axis profile measurements, particularly when the detector is held in an edge-on configuration. This is particularly apparent when narrow beam profiles are used. Results show the potential for these CVD diamond detectors.

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2. Betzel G, Lansley S, Baluti F, Reinisch L, Meyer J. Operating parameters of CVD diamond detectors for radiation dosimetry. *Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment*. 2010;614(1):130-136.

Comparison between conventional arc therapy and 2-step intensity-modulated arc therapy (IMAT).

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2-step intensity-modulated arc therapy (IMAT) is an advanced radiotherapy technique.[1] The aim of this technique is to reduce the planning and delivery complexity while keeping the dose coverage and organ sparing at acceptable levels. In conventional arc therapy the target is continuously irradiated throughout the gantry rotation, resulting in beams with a single intensity level at each angle. 2-step IMAT complements the conventional treatment with a second gantry rotation in order to achieve a two-level intensity modulation, resulting in highly conformal plans.

2-step IMAT was implemented into the *Prism* treatment planning system using the Common Lisp programming language. The beam segments corresponding to the first and second gantry rotation were automatically generated based on the 3D-anatomy information of the patient. The beam weights and segment widths optimization was performed in MATLAB.

Both a phantom with a horseshoe-shaped target surrounding a critical organ and a paraspinal tumor case were used to generate 2-step IMAT plans. The target dose uniformity under 2-step IMAT was compared with conventional arc therapy. The

results showed a substantial improvement with 2-step IMAT after the beam weights and segment widths optimization.

The employment of the rotational technique conserves the delivery time of 2-step IMAT. The two-level intensity modulation results in superior plan quality while keeping the planning complexity at a minimum. This work has demonstrated the dosimetric advantages of 2-step IMAT over conventional arc therapy. Future work will compare the plan quality of 2-step IMAT to intensity-modulated radiotherapy with fixed gantry angles.

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1. Bratengeier K. (2001) Applications of Two-Step Intensity Modulated Arc Therapy. *Strahlentherapie Und Onkologie*; 177:394-403.

A comparison between the HOMA and the quick DIST for in-expensive insulin sensitivity identification. **PD Docherty[1], JG Chase[1], TF Lotz[1], L TeMorenga[2], JI Mann[2], KA McAuley[2], JE Berkeley[3], CE Hann[4]. [1] Centre for Bioengineering, University of Canterbury, Christchurch, [2] Edgar National Centre for Diabetes Research, University of Otago, Dunedin, [3] Department of Medicine, University of Otago, Christchurch.**

The quick DIST (DISTq) is a development the fully-sampled dynamic insulin sensitivity test (DIST) that provides a real-time, low-cost alternative for the identification of insulin sensitivity (SI). DISTq enables identification of SI with only limited glucose data by estimating a participant's kinetic insulin response with population assumptions developed from prior fully-sampled DIST tests. Its low cost implies it may be a suitable alternative to the homeostasis model assessment (HOMA) for screening or monitoring interventions.

The aim of the study was to assess the accuracy of the DISTq vs HOMA and the fully sampled DIST

Kinetic insulin and sensitivity values from 218 fully-sampled DIST tests were identified. These metrics were used to produce smooth population parameter estimations that enable simulation of insulin response as a function of the participants SI and anatomical data. SI can thus be identified using only sampled glucose values. The HOMA-IR metric and full DIST SI were also assessed for each test.

The correlation between SI values from the fully-sampled DIST and DISTq (R=0.83) was far stronger than the correlation between the fully-sampled DIST SI and the insulin resistance value from the HOMA (R=-0.33).

Although the common model-based identification method would exaggerate the correlation between the DIST and DISTq, the considerable difference in correlation implies that the DISTq is a more capable surrogate to fully-sampled tests than HOMA. Furthermore, DISTq is real-time capable, and enables a hierarchy of screening tests if higher resolution is desirable. Thus, if a DISTq result is near a diagnosis threshold, the existing samples can be assayed for insulin and a higher resolution fully-sampled DIST result is obtained without the need for another test.

A viscoelastic model of respiratory lung tumour motion. **A E Cavan[1†], P L Wilson[2] and J Meyer.[1] [1]Department of Physics and Astronomy, Private Bag 4800, University of Canterbury, Christchurch 8140, New Zealand. [2]Department of Mathematics and Statistics, University of Canterbury, Christchurch, New Zealand.**

Respiratory induced motion of lung tumours limits the accuracy with which radiotherapy treatment can be given. To increase treatment efficacy this motion must be compensated for. We modelled the correlation of an external abdominal marker and the tumour motion, using a one-dimensional spring-dashpot model.

Three viscoelastic systems (a spring and a dashpot in series, parallel, and a combination), were developed using a basic simulated breathing pattern. Application to clinical data sets determined the parallel configuration (Voigt model), to provide the best model of tumour motion. This model was then applied to 60 clinical data sets of lung tumour and abdominal marker motion from ten patients for up to ten treatment fractions each. The root mean square error between the model and the actual tumour motion was calculated for each data set, as a measure of the efficacy of the model.

The Voigt model achieved an average root mean square error of 0.95 mm in the superior inferior direction. The model displayed good consistency over extended treatment periods and the determined model parameters were patient specific. The model was capable of handling baseline, frequency and amplitude variations of the input data, as well as phase shifts between abdominal and tumour motion.

This study has shown that the internal motion of a lung tumour can be predicted by external motion of an abdominal marker, using a viscoelastic model. The success at dealing with irregularities in the breathing pattern is comparable or better than previous models. Extension of the model to a full three dimensional, predictive system could allow clinical implementation, to increase accuracy of radiotherapy treatments.

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Characteristic arterial spin labeling MRI perfusion abnormalities in early, treatment-free Parkinson's disease. **TR Melzer[1,2], R Watts[1,3], MR MacAskill[1,2], J Pearson[4], L Livingston[1,2],C Graham[1,2], R Keenan[5], A Shankaranarayanan[6], DC Alsop[7], JC Dalrymple-Alford[1,8], TJ Anderson[1,2]. [1]Van der Veer Institute for Parkinson's and Brain Research, Christchurch, New Zealand, [2]Department of Medicine, University of Otago, Christchurch, New Zealand, [3]Department of Physics and Astronomy, University of Canterbury, Christchurch, New Zealand, [4]Department of Public Health and General Practice, University of Otago, Christchurch, New Zealand, [5]Christchurch Radiology Group, Christchurch, New Zealand, [6]GE Healthcare, Menlo Park, California, United States, [7]Beth Israel Deaconess Medical Center, Boston, Massachusetts, United States, [8]Department of Psychology, University of Canterbury, Christchurch, New Zealand.**

Arterial spin labeling (ASL) is a non-invasive, *in vivo* magnetic resonance imaging technique that quantitatively measures cerebral blood flow (CBF) without the use of an exogenous contrast agent.[1] Radiotracer studies by others[2] have identified abnormal metabolic/perfusion patterns associated with a number of diseases including Parkinson's disease (PD); these patterns show promise as disease biomarkers. In this study we used ASL MRI-derived perfusion images from early, treatment-free PD subjects and healthy, matched controls to identify a characteristic PD-related network of abnormal blood flow.

Twenty-four Parkinson's patients and 19 controls completed neuropsychological examination and 3T MRI scans. ASL MRI was used to acquire images of CBF for each individual; these images were normalized to a probabilistic elderly template and smoothed prior to analysis. Principal component analysis (PCA) of the entire data set was used to identify perfusion covariance patterns. The expression of the first seven components was entered into a stepwise logistic regression to determine components that contributed significantly ($p<0.05$) to the differentiation of PD from controls. The optimal linear combination of the significant components then generated a PD-related perfusion network.

The PD-related pattern was characterized by decreased perfusion in PD versus controls in bilateral posterior parietal-occipital regions and posterior medial and frontal cortices. Preserved perfusion occurred sub cortically and in anterior cingulate. ROC of the expression of the PD network yielded an area under the curve of 0.83. Leave-one-out cross validation showed a classification accuracy of 72.1%.

The newly identified, ASL-derived PD perfusion pattern demonstrates the potential of PCA network analysis to identify imaging markers of underlying physiology even early in the progression of PD.

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THE NEW ZEALAND MEDICAL JOURNAL
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Why do South African doctors migrate?

This paper concentrates on Australia but its findings probably apply to other countries which find themselves hosting South African doctors—notably, UK, USA, Canada and New Zealand. Apparently there are about 2200 such doctors in Australia and the authors sought information about the motivation for the migration.

469 of 653 email contacts responded and 93% were motivated by the desire to leave South Africa rather than by Australian inducements. Of those migrating prior to 1990 over 80% did so because of apartheid, concern for the future and safety. After 1990, over 60% nominated violent crime, safety, children's future and the South African political situation as their motivation. Understandable, and very helpful to the host country. But very unhelpful to the citizens of the Republic.

Med J Aust 2010;192:228–90.

Should subjects with a low ankle brachial index (ABI) be encouraged to take low-dose aspirin?

The ABI which is the ratio of systolic pressure at the ankle to the arm, is used in the diagnosis of peripheral artery disease affecting the legs. Also, a low ABI is associated with concomitant coronary and cerebrovascular disease.

In this Scottish study the value of low-dose aspirin as a cardioprotective agent has been evaluated in a cohort of men and women (aged 50–75yrs) who had a low ABI but were free of clinical cardiovascular disease. 3350 people were found to fit these criteria. They were randomised to 100mg of enteric coated aspirin or placebo. After a mean follow-up of 8.2 yrs it was demonstrated that aspirin did not diminish coronary artery events or stroke incidence or all-cause mortality. However, haemorrhage requiring hospital admission was worse in the aspirin cohort (Hazard Ratio 1.71). Good idea, well conducted trial but disappointing results.

JAMA 2010;303(9):841–48.

Thromboprophylaxis after knee replacement—apixaban versus enoxaparin

Post operative venous thrombosis after major joint surgery is a serious problem. It is commonly addressed by the use of subcutaneous perioperative low molecular weight heparin, eg enoxaparin. Apixaban, an orally active factor Xa inhibitor, has the advantages of fixed daily dosing and low potential for drug interactions. But is it better than enoxaparin?

This randomised trial compares treatment with oral apixaban 2.5mg twice daily (n=1528) against subcutaneous enoxaparin 40mg once daily (1529) in patients undergoing elective total knee replacement surgery. Apixaban was started 12–24hr after wound closure and enoxaparin 12hr before surgery; both drugs were continued

for 10–14 days, when bilateral ascending venography was scheduled. The primary outcomes—venous thrombosis, non-fatal pulmonary embolism and all-cause deaths—significantly favoured the apixaban cohort. Risk of bleeding was not significantly different in either treatment arm.

Lancet 2010;375:807–15.

New effective oral treatments for relapsing multiple sclerosis

Systemic treatment with intramuscular interferon beta-1a and other immunosuppressive agents have been shown to reduce relapse rates in multiple sclerosis. Three recent papers in the NEJM report on the use of oral agents. In one trial, oral fingolimod improved the relapse rate, the risk of disability progression, and end points on MRI when compared with a placebo. In another, oral fingolimod proved superior to intramuscular interferon. The third paper compared oral cladribine with placebo and cladribine was significantly superior clinically and as judged by MRI. Fingolimod and cladribine both suppress lymphocyte function and it is presumed their success is due to inhibition of lymphocyte induced neural damage.

The down side is the adverse effects profile. As expected infection, particularly viral, was a problem, fatal in some cases, with both oral agents. Fingolimod also caused cardiac arrythmias. All three trials were regarded as successful—viz active oral agents lowering relapse rates. But all three concluded that the benefits need to be weighed against the risks.

N Eng J Med 2010;362:387–401, 402–15, 416–26.

Breast cancer mortality in women receiving tamoxifen and paroxetine

Women who have tamoxifen as part of the management of breast cancer may also take paroxetine, either for depression or amelioration of tamoxifen-induced hot flushes. Does this matter? In theory yes as tamoxifen is converted by cytochrome (CYP2D6) to its active metabolite endoxifen and paroxetine is a powerful inhibitor of CYP2D6, a reaction which is irreversible. Obviously this could lead to ineffective anti-oestrogen effects.

In this study, 2430 females aged 66yrs or more who had breast cancer treated with tamoxifen and paroxetine or other selective serotonin reuptake inhibitor (SSRI) antidepressants were reviewed retrospectively over a 13yr period. A significant increase in mortality was noted in the paroxetine cohort. Fluoxetine which has similar inhibitory effects on CYP2D6 did not seem to be associated with increased mortality. The authors comment that this may be associated with small numbers in the fluoxetine cohort and not necessarily indicative of safety with coadministration of this SSRI and tamoxifen.

BMJ 2010;340:c693.

THE NEW ZEALAND MEDICAL JOURNAL
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Why did so many women develop cancer?

The correspondence in this *Journal* regarding Linda Bryder's book *A History of the 'unfortunate experiment' at National Women's Hospital* serves a number of important functions.[1] First, it assists in focusing opinion on the scientific validity of Associate Professor Green's research into the natural history of carcinoma *in situ* (CIS) of the cervix. Second, it provides an opportunity to raise relevant issues which have not previously been reported. This is illustrated by Dr Bill McIndoe's failure to communicate his concerns regarding Green's flawed 1974 paper which was published in this *Journal*.[2]

Green's previous papers had been published in international medical journals and few if any readers would have been familiar with the emerging information and tensions within National Women's Hospital (NWH). The publication of Green's 1974 paper caused McIndoe considerable distress. He drafted a lengthy response outlining the details of the women who had developed invasive cancer and who had been excluded from Green's paper. However, he did not submit it for publication. Had he done so, the wider medical community may have responded (not that would I have confidence on this issue) and alarms may have been raised for others in New Zealand to speak out. If this had happened it may have prompted the 1975 internal NWH "whitewash" committee to take more definitive action.

Dr Overton states that "debate over [Bryder's] book has unfortunately centred on criticism of Professor Bryder". This is not so, the criticism is not personal, but on the evidence and conclusions she has reached. Professor Bryder and Dr Overton are advocates for that sector of the medical profession who remain aggrieved by the outcome of the Cartwright Inquiry. I am an advocate for the patients.

Dr Overton's analysis has focused on the treatment received by the two groups of women described in the 1984 McIndoe et al. paper but not on the adequacy of treatment.[1,3] The object of writing our paper was to describe the natural history of CIS, provide alternative results to those previously published by Green and to further alert the medical authorities. This paper which "blew the medical whistle" on the 'unfortunate experiment' was an analysis of a cohort of women with CIS who had been followed prospectively as a consequence of the NWH Medical Committee's approval for Green's study of the natural history of CIS, entailing withholding treatment of curative intent.

We used similar techniques to Green, describing a group of women with CIS, who, irrespective of their treatment had cytology abnormalities consistent with continuing disease (showing that they had failed to receive adequate treatment). This group of women who illustrated the natural history of CIS was compared with a group of women who irrespective of their treatment, had normal cytology follow-up and who therefore did not represent the natural history of CIS. The women with continuing abnormal cytology were 25 times more likely to develop invasive cancer.

In the context of cancer or precancer the adequacy of treatment is paramount. Doctors and patients recognise that inadequate excision of cancer or precancer significantly increases the risk of recurrence of the disease.

It is a pity Professor Bryder and Dr Overton's supporters have not done their homework. Bryder cites the endorsement of Professor Sir Ian Chalmers who admits to having never read the Cartwright Report and Professor de Costa has failed to respond to this question. Professor Seber and Dr Mullins have failed to publish their 1990 "independent analysis" at all. In fact I understand that it was rejected by the *Lancet*.

If there was never an 'unfortunate experiment' as Professor Bryder and Dr Overton claim, can they explain why so many women with CIS in NWH developed cancer? If one ignores the groupings in our 1984 paper and bearing in mind the vast majority of women with CIS in NWH were treated adequately, why did one in 20 develop cancer? With adequate treatment, the proportion that will go on to develop invasive cancer should be approximately one in two hundred after 10 years.[4] Failure to adequately answer this question totally undermines the credibility of the book.*

(* The correct answer is: because so many women with a known precancerous abnormality were either not treated or inadequately treated.)

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Response by Linda Bryder

As an historian I am not an advocate of any group, disaffected or otherwise, but rather assess the evidence. My research enables me to make a number of observations regarding Professor Jones's latest offering.

The 1975 Committee, which Professor Jones refers to, was not a 'whitewash' but rather a serious attempt to review the evidence. The members were well aware of the disputes between Green and McIndoe and McLean; another publication by McIndoe would not have altered their deliberations.

Professor Jones does not tell us how Green's 1974 paper was 'seriously flawed'. He does say that in dividing the patients into groups according to persistent disease for the 1984 paper they adopted a similar approach to Green; the similarity was that

Green too was reviewing patient data, drawn not from his own patients but from all patients with CIS at the hospital.

Professor Jones writes dismissively of Mullins and Seber's 'independent review'. Yet Mullins and Seber were not related to the hospital which qualifies them as independent reviewers. By contrast the same could not be said of the1984 paper, described by the 2008 *Lancet Oncology* article, of which Jones was an author, as an 'independent review'; all three authors of the 1984 paper had worked at National Women's and with Green for many years. The third contributor to Mullins and Seber's review, Dr Graeme Overton, has confirmed after speaking with Mullins that their review was never sent to the Lancet nor was there ever any intent to publish it.

There continues to be a strange logic in the discussion of the 1984 paper. When Jones writes of the women who 'irrespective of their treatment had cytology abnormalities consistent with continuing disease (showing they had failed to receive adequate treatment)', one has to ask the question, 'How could doctors have ensured they received "adequate treatment" if the results were "irrespective of treatment"'? The point is, as Jones writes, women with continued abnormal cytology irrespective of treatment were 25 times more likely to develop cancer than those whose smears had returned to normal.

Curiously Professor Jones writes in his final paragraph, discussing the supposedly high rates of cervical cancer at National Women, that 'if one ignores the "groupings" in the 1984 paper'... But if one ignores the groupings then there was no experiment—the 'experiment' was supposed to have been based on treating some women differently, with 'Group 2' patients receiving 'limited or no treatment '. (This premise was of course false in any case as Group 2 received 228 major treatments according to the1984 paper, as Dr Overton noted).

Professor Jones demands an answer to the question 'Why did so many women with CIS at National Women's Hospital develop cancer?' In order to answer this question one needs to place the hospital in its international context. The 1984 paper showed that 41 out of 948 women who presented at National Women's Hospital with a positive cervical smear over 21 years, between 1955 and 1976, developed cervical cancer and 12 died of the disease.

Was this worse than other institutions? At the Inquiry, the expert witness from Norway, Professor Per Kolstad, stated that in relation to treatment of cervical cancer, National Women's compared very favourably with other institutions. The International Federation of Gynecology and Obstetrics (FIGO) ranked National Women's among the top three in the world in the treatment of cervical cancer according to 5-year survival rates in 1981. National Women's Hospital clearly did better than most.

What's most interesting about the article cited by Professor Jones (Soutter et al) is the authors' conclusion that the risk of developing invasive cancer following treatment for CIN, regardless of the type of treatment, remains higher than among the general population for at least 10 years after treatment. In other words, there is still no certainty that 'adequate' treatment of CIN will avoid subsequent cancer.

Professor Jones claims that he is not being personal. Supporting the suggestion that I was possibly engaged in 'deliberate obfuscation' and stating that my 'response to

criticism has often been to reply with further factual errors', as he did in his February letter in this *Journal*, is tantamount to saying that I am a liar and is about as personal as it gets.

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THE NEW ZEALAND MEDICAL JOURNAL
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Simple suggestions to improve New Zealand Ethical Committees

There has recently been a good deal of long overdue debate on the clinical research ethics review process in New Zealand.[1–3] This has led to a Health Select Committee inquiry into the ethics review system, which has recently requested submissions from interested parties.[4]

There is widespread agreement amongst researchers that the ethics review system must be substantially changed as it is currently frustrating researchers, wasting their valuable time, and perhaps worse of all, preventing researchers from testing their ideas because they do not have the time or willpower to get a study approved.

As medical researchers for between 11 and 30 years and ex-members of New Zealand Ethics Committees we make the following observations, and suggestions as to how they may be corrected with no loss of ethical integrity.

Problem	Solutions
Lack of expertise	Although there is a requirement for two health researchers on each committee, there is often no one with hands-on experience of clinical trials.
Overly bureaucratic	We should have smaller committees. The international standard is 7 members, but New Zealand committees have 12 members. The more members there are, the more comments researchers have to deal with as many members feel that they have to find "issues" to justify their membership.
	No need to have Justice of the Peace sign-off.
	No need to consult Māori for every study. This would be a sensible requirement for research limited to the Māori community, but since 1999 Ethics Committees have insisted that researchers "consult with Māori" for every application. This is often expensive and is unnecessary as there is a requirement for Māori members of each committee, who must surely be there to assess the application from a Māori viewpoint anyway.
	No need for Locality Assessment forms.
	Separate, 1–2 page application system for very simple studies with minimal chance of harm for participants eg. surveys.
	Emphasis of application to change from study minutiae to the actual ethical issues of the study ie. potential harm to participants.
	No need for interpreters to be available for every study if it is highly unlikely that they will be needed.
	Approval by any New Zealand committee should enable that research to be undertaken anywhere in the country, except under the very rare circumstances that there are important local issues to consider.
Unnecessarily complicated application form	Online applications, rather than posting 13 or more applications which can involve hundreds of photocopied pages.
	Researchers to be able to state "refer to attached protocol" rather than having to "cut and paste" all the details into the application forms.
	Form can be reduced in size by over 50%.
Slow	Committee lead reviewer for each study should email the researcher to clarify any potential ethical problems before the meeting.
	Letters should be emailed to researchers within 3 days of the meeting, with a hard copy posted. 3 day turnaround for all other routine matters, including final approval after committee questions have been answered.
	Increase in Ethics Committees funding for more administrative staff to speed up the process and to prevent the frequent delays due to an administrator being sick or on holiday.

The above suggestions could be easily introduced and would help to turn the current ethics review system from a major hurdle for researchers to more of a “sign-off” process, as it should be for the vast majority of applications which have no important ethical issues.

There is no reason why a simpler system should diminish the quality of the ethical review. On the contrary, a simpler system will enable the committees to focus on the ethical issues (if any) rather than on the minutiae of the complicated application process.

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THE NEW ZEALAND MEDICAL JOURNAL
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Effect of using the title 'Dr' on perceptions of complementary and alternative medicine

Some complementary and alternative medicine (CAM) practitioners use the honorary title of Doctor in the course of conducting their practice.[1] However, we could not locate research investigating whether this affects how they and their practice are perceived by potential clients.

Using a short tool consisting of a generic scenario followed by five questions, we therefore conducted a brief pilot-study to explore whether use of the title 'Dr' by acupuncturists, chiropractors, and homeopaths affects how potential clients perceive both practitioner and practice. The generic scenario was as follows: "[Fictitious name of a male practitioner] has worked as a [field of practice] for approximately 20 years since successfully completing his training. On average he sees around 20 patients every week for a variety of problems, such as asthma, allergies, and back-pain." The scenario could thus apply to each of the three practices by inserting a different practitioner name and field of practice.

After reading the scenario, participants answered five questions:

1. What do you think is [practitioner's name] level of expertise?
2. If you thought he could help you, how willing would you be to pay for treatments by [practitioner's name]?
3. Do you think the treatment offered by [practitioner's name] is scientific?
4. Compared to being treated by your usual medical doctor, how likely is [practitioner's name] treatment likely to be helpful?
5. How much do you think it would cost to see [practitioner's name] for treatment or advice? Response options for question 1 ranged from *Low expertise* = 1 to *High expertise* = 10, and for question 2 to 5 from *Not at all* = 1 to *Very much* = 10.

Participants (69 males, 31 females, and 4 who did not state gender) were recruited (having first recorded the study with our University's Ethics Committee) either in classes or on campus at a New Zealand University. The experimental manipulation [between-subjects] was that approximately half of the participants were asked to complete all three scenarios and questions with the title of 'Dr' inserted before the practitioners' given and family names (experimental condition, $n = 53$), whilst the remaining participants read all three scenarios and questions in which only the practitioners' given and family names were provided (control condition, $n = 51$). Participants were randomly assigned to either condition and were blinded regarding the experimental manipulation. The order in which practice type was presented was randomised.

For all three practices, we found evidence that practitioners using the title "Dr" were perceived as more expert. For all three practices, participants would be more willing to pay for treatment when the practitioner used the title of 'Dr'. However, only

chiropractic and homeopathy were perceived as more scientific and more likely to be of help when the practitioner used the title of 'Dr'. There was no evidence that the expected cost of a consultation was affected by use of title. Mean responses and test results by question and practice may be inspected in Table 1.

Table 1. Mean responses and test statistics for questions 1–5

Therapy type	Question	No Title		Title		Test of difference (repeated measures t-test)	
		M	*SD*	*M*	*SD*	*t*	*Sig*
Acupuncture	Expert	7.31	1.74	8.23	1.74	7.16	<.01
	Pay	5.80	2.30	6.75	2.06	4.95	<.05
	Science	5.88	2.09	6.43	2.42	1.54	.22
	Help	5.57	2.20	6.21	2.28	2.11	.15
	Cost	6.80	1.88	6.77	1.62	.01	.92
Chiropractic	Expert	7.32	1.56	8.47	1.15	18.33	<.01
	Pay	6.06	1.79	7.64	1.89	18.95	<.01
	Science	6.26	1.60	7.53	1.75	14.68	<.01
	Help	6.06	1.93	7.42	1.81	13.49	<.01
	Cost	6.88	1.64	7.47	1.69	3.24	.08
Homeopathy	Expert	6.53	1.63	7.94	1.65	19.38	<.01
	Pay	5.14	1.73	6.60	1.99	15.98	<.01
	Science	5.12	2.04	6.09	2.43	4.92	<.05
	Help	4.65	1.82	5.89	2.11	10.26	<.01
	Cost	5.86	1.91	6.57	1.85	3.65	.06

Whilst there may be some advantages associated with using the title of 'Dr', it would be interesting to investigate whether they lead to increased numbers of consultations and whether there is a placebo effect of the title 'Dr' on treatment outcomes.

We note three potential limitations of this pilot-study: i) many of the participants in our survey may have frequent contact with people who use the title of 'Dr' and therefore they may hold views about doctors and non-doctors that differ from those held by other populations; ii) as all of the fictional practitioners in this study were male, a different pattern of results may be found for female practitioners; and iii) we investigated perceptions of practitioners with 20 years' experience, thus a different pattern of results may be found for practitioners at other stages in their careers.

Although using the honorary title of 'Dr' may positively influence the way in which both practitioner and practice are perceived, we suggest that potential clients should be aware that use of the honorary title of 'Dr' by some CAM practitioners may not in itself be a valid indicator of treatment effectiveness.

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THE NEW ZEALAND MEDICAL JOURNAL
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Chaos at the cash register

Whatever complicated subsidy arrangements are set up to help pay general practitioners for their services, the patient will naturally focus on the fee that s/he pays directly.

That fee now shows astonishing variations. For a single consultation, and depending upon the age of the patient, it can be only a few dollars, or it can range up to $60 for an adult. It relates to where you happen to live, and to the doctor whom you choose.

Let us turn back the pages. The most common direct fee in 1960 was about 5 shillings, the equivalent of 50 cents. Any doctor now asking $50 for an ordinary consultation is charging 100 times the going rate of 50 years ago. I know of no other financial transaction that has undergone such a precipitous rise. There is general agreement that all monetary inflation is bad, and that high inflation is disastrous. Over the period I have chosen, inflation has bled the dollar down to one-thirtieth of its value, and that is shocking enough, but a 100–fold increase in the direct medical fee invites scrutiny.

We are repeatedly reminded that the government, spellbound by the notion that good primary care keeps people out of hospital, has poured millions into general practice. Where, then, did it all go? Mysterious forces introduced without proper consultation both the Primary Health Organisations (PHOs) and the capitation system for partial payment of general practitioners. The PHOs and the capitation method of payment were totally unnecessary and it now looks as if they have become powerful cost inflators. What does the Royal New Zealand College of General Practitioners cost both intending and current members? If it doesn't tell us, we shall never know.

Faced with a large direct fee, the patients are now orchestrating the consultation. They are doing their Internet researches before they go and see the doctor. They prepare a list of questions and that takes up a good deal of the paid time in the consultation room. Some are telling their doctor to look at them rather than the monitor linked to the computer, and, if they think they can type the information into their records faster than the GP, they are offering to do so. They want to maximise the return on their money, and stress levels are rising all round.

If GPs believe that all their capitated patients consult them for all their minor ailments, they should go along and sit in in the Casualty Department of the local hospital. A lot of people won't go anywhere else.

The most objectionable feature of the wretched capitation system is the additional fee charged to the hapless patient who, unable to see his or her own doctor because they aren't there, goes and sees the GP down the road. The penalty for this infidelity can be as much as 50% added on to the cash fee charged by the "casual" doctor. The historical arithmetic I have used for doctors' fees would, if applied to motor vehicles, price the humblest family sedan at well over $100,000. Long before that point was reached somebody, somewhere, would have had something to say about it.

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Is evidence-based medicine a sham?

It would be reasonable to expect that in support of the concept of evidence-based medicine, that all relevant evidence had been assessed, but it seems that the information relating to blood rheology has not been included.

In addition, the idea that all relevant evidence has been assessed has been called into question by Greenberg[1] who wrote, "How citation distortions create unfounded authority: analysis of a citation network." In introducing the concept of "citation bias" he noted, "Unfounded authority was established by citation bias against papers that refuted or weakened the belief .... the marked expansion of the belief system by papers presenting no data addressing it; and forms of invention such as the conversion of hypothesis into fact through citation alone."

As the network included 242 papers, this means that neither peer review nor editorial oversight recognised the citation bias.

An important aspect was the citation bias against papers that refuted or weakened the belief, as there are good reasons to believe that this could explain why papers dealing with the topic of haemorheology have been ignored in the development of the current concepts of the causes of the major health problems such as cardiovascular disorders, cerebrovascular disorders, diabetes and hypertension.

The extent of the relevant but disregarded literature can be assessed by the results of PubMed searches for "cardiovascular disorders and blood viscosity" 4323 titles; "cerebrovascular disorders and blood viscosity", 782 titles; "diabetes and blood viscosity", 768 titles; "hypertension and blood viscosity", 848 titles. Given the very large amount of information concerning these disorders which has not been used in evidence-based medicine, what is the logic behind the term?

This apparent rejection of the research results by many devoted investigators demeans their activities. The reluctance of major journals to publish information about blood rheology, has been shown by an email from the deputy-editor of the *British Medical Journal (BMJ)*, which stated, "We won't be posting any more rapid responses from you that mention blood viscosity or rheology."

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Health-related quality of life and its growing importance in clinical practice

With improving socioeconomic conditions and quality of medical care, patients around the world are becoming more concerned about the impact of disease on their daily life and social interactions. It is particularly important for chronic diseases like diabetes and hypertension that the impact of disease should not only be judged by its mortality but also by its social impact and disability. Unfortunately physicians are often being too concerned about the disease and treatment tend to overlook patients' perception about their illness and their threshold for tolerance of discomfort.

Health related quality of life (HRQL) is gaining worldwide acceptance as patient centric approach of any healthcare intervention.[1] HRQL could be defined as physical psychological and social dimensions of health that are influenced by a person's experiences, beliefs, expectations and perceptions.[2] The idea of HRQL measurement is to convert the subjective feeling of physical and mental health of an individual into an objective numerical score by using properly structured questionnaires. Physical function, emotional status, pain, social function and general perception about health are some of the important components of HRQL measurements.[3]

Patients are the best evaluators for estimating their own HRQL. Perspective of close family members such as a spouse may be considered, for example if there are problems like sexual difficulties or serious behavioural symptoms affecting the patient.[1] By simply asking "Please rate your quality of life or overall health on a scale from 1 to 10," leaves "quality of life" and "overall health" ambiguously defined.[3] Therefore, HRQL instruments are carefully developed by taking help from clinimetrics and psychometrics analysis.[3]

HRQL instruments could be sub classified into two major subtypes depending on their usage. The instruments which are used across various medical conditions known as generic instruments, prominent examples being SF-36, SF-12, WHO-QOL BREF and EQ-5D. These HRQL scales are important to make comparison across intervention and conditions. They may not cover the disease of interest adequately in sufficient detail and their validation may be inappropriate.[1] Specific instruments are those which focus only on a particular disease of interest and the questions reflect only physical and mental health related to the disease concern. Examples of specific questionnaires include Asthma Impact Survey (AIS-6), Headache Impact Test (HIT-6), Hepatitis Quality of Life Questionnaire (HQLQv2), etc. See http://www.qualitymetric.com/WhatWeDo/DiseasespecificHealthSurveys/tabid/189/Default.aspx

The questionnaires are basically stratified into number of questions which then add up to form a number of domains or dimensions. Mostly equal importance is given on each item considering their values to be equal.[4]

SF-12, one of the most widely used generic questionnaire for quality of life assessment consists of 12 items which assess eight domains: (1) physical functioning;

(2) role-physical; (3) bodily pain; (4) general health; (5) vitality; (6) social functioning; (7) role-emotional; and (8) mental health.[5] The first four domains comprise of physical component summary measure (PCS-12) and mental component summary measure (MCS-12) includes the last four domains.

Physical and mental component summaries are scored from 0 to 100, with 100 representing the best health for scale. If a questionnaire is intended to be used outside the country in which it was developed it is important to translate into local regional language keeping in mind the cultural acceptability and conceptual equivalence.[4]

It is important to establish the validity and accuracy of an instrument before its use in a particular study. The most important property of an instrument used as an outcome measure is responsiveness, the ability to detect changes that occur as the result of an intervention.[3] Cost effective analysis, cost benefit analysis and cross sectional study are some of the important study designs to evaluate HRQL.[3] A HRQL instrument should ideally be administered at the beginning of treatment and subsequently at 3 months or 6 months interval.

The growing importance of HRQL estimation is recognized by clinicians, healthcare policymakers, drug regulatory agencies and pharmaceutical companies all over the world in choosing optimum treatment choice for patients, policy framing, new drug approval and deciding pharmaceutical marketing policies. Physicians are increasing using HRQOL to measure the effects of chronic illness in their patients to understand how an illness interferes with a person's day-to-day life.

HRQL study is also used by public health professional to identify subgroups with poor physical or mental health for better equitable distribution of health care resources. Drug regulatory agencies all over the world giving more emphasis on quality of life data from clinical trials in order give faster approval to a new drug. Pharmaceutical companies also claim superiority of their product and decide marketing price based on quality of life data generated from trials.

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THE NEW ZEALAND MEDICAL JOURNAL
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Salt reduction in New Zealand: are we keeping up with Australia?

Australia recently announced its first salt reduction targets for breads and breakfast cereals in its campaign to reduce population salt intakes.[1] Salt reduction is part of their government's preventative health strategy, and complements the Australian division of World Action on Salt and Health's 5-year campaign to reduce salt in manufactured and pre-prepared food by one-quarter. With Australia, and other countries around the world, gaining momentum in salt reduction, it raises the question of what is happening here in New Zealand (NZ)?

As three-quarters of salt consumed is from manufactured and pre-prepared foods,[2] widespread reformulation of mainstream high-volume products has the greatest potential to reduce salt intakes. Some food companies in NZ have already embarked on salt reduction programmes. As an example, Sanitarium and Kelloggs have reduced salt in cornflakes by 30–40% over the last few decades. Recently, major bread companies, in collaboration with the Heart Foundation, successfully reduced salt in white bread by up to 18%, removing up to 150 tonnes of salt from the food supply annually.[3] A similar collaborative approach with a wider focus is now being taken with Project HeartSAFE.

Project HeartSAFE creates a platform for industry-led cross-category salt reduction in NZ, with representation from major food sector players (initially focused on processed meats and breakfast cereals), industry bodies and government. This cross-sector approach allows food companies to learn from each other and for simultaneous salt reduction. The project is facilitated by the Heart Foundation and Network PR, under a contract with the Ministry of Health. This initiative will be complemented by the NZ Food Safety Authority's focus on the science to support salt reduction.

Salt reduction is vitally important to population health, with consumption estimated at 150% of the recommended upper level of intake.[4] There is strong evidence that too much salt raises blood pressure (BP) and increases risk of cardiovascular disease.[5,6]

Globally, high BP is the leading risk factor for mortality, ranking second only to tobacco use in high-income countries.[7] In NZ, one in seven adults report taking medication for high BP.[8] Furthermore, a 25% reduction of salt in manufactured food is predicted to result in 2745 fewer heart attacks and 2064 fewer strokes each year (an 18% reduction in incidence of both), saving 930 lives/year by 2018.[9]

To reduce salt intakes to even the recommended upper level of intake requires a one-third reduction in salt from manufactured and pre-prepared foods, and in salt added to food by consumers. This level of reduction presents challenges as salt is an inexpensive ingredient playing an important role in food texture, preservation, and taste. Thus, there are foods where a one-third reduction may be difficult to achieve. However, there are undoubtedly foods where salt is added in excess of what is needed for food safety and functionality, or where changes in production methods or ingredients could facilitate lower salt levels.

If salt reduction is conducted in a gradual, stepwise manner, consumers are unlikely to detect changes and taste buds will gradually adapt to lower salt levels, until their taste threshold is reached. Such an approach will ensure that foods still meet consumer expectations whilst reducing salt intakes.

Apart from benefits to consumers, Project HeartSAFE has strategic importance to the food sector. It fits with the voluntary and self-regulatory approach which they favour. Failure to reduce salt will put the food sector out of step with other countries.

The commitment by Australia has trans-Tasman implications, as many companies operate in both markets. The United Kingdom has undertaken a successful across-the-board salt reduction programme led by the Food Standards Agency, and salt reduction campaigns are underway in European countries, Canada and the United States (US), amongst others.

The IOM has recently released its recommendations on a salt reduction strategy for the US. The focus on salt in other countries is likely to lead to increased consumer awareness of the negative effects of excess salt consumption, potentially increasing demand for less salt in products marketed in NZ. Mintel in the US has predicted that salt reduction will be "... the next major health movement".[10]

What can be done to support the food sector in salt reduction? Unlike nutrients such as fat, there is currently little consumer demand for food companies to lower salt in their products. Greater consumer demand would provide more incentive and support for salt reduction by food manufacturers. While opportunities definitely exist to raise consumer awareness of salt at a population level (which is successfully happening in the United Kingdom), health professionals can play their part at an individual level. This can be achieved through reminding consumers about the adverse effect of salt on health, the difference between salt and sodium, how to choose lower salt/sodium foods, and gradually reducing salt added to food.

In summary, initiatives to reduce salt in the NZ food supply are happening. A coordinated population approach to salt reduction in high-volume low-cost foods has potential to generate enormous health gains for NZ. Change is needed at multiple levels, including the food supply and consumer choice, in order to reach population salt reduction goals.

Note: Further information on Project HeartSAFE will be available from www.nhf.org.nz under 'Healthy Eating'.

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THE NEW ZEALAND MEDICAL JOURNAL
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Health Practitioners Disciplinary Tribunal: Professional Misconduct – Not Established (Med08/107D)

Charge

The Director of Proceedings charged that Dr Enrique Jose Tomeu (the Doctor) was guilty of professional misconduct.

The particulars of the charge were:

1. The Doctor, as the consultant obstetrician on call, on being advised by the registrar that ventouse delivery had been unsuccessful, attempted a further ventouse delivery.
2. The Doctor failed to give the Patient adequate information upon which she could consent to a further attempt at ventouse delivery. In particular he did not tell her that:
    - Her labour was obstructed; and/or
    - A further attempt at ventouse was not appropriate; and/or
    - The appropriate option was to proceed to delivery by caesarean section.
3. In the course of attempting the delivery, the Doctor treated the Patient disrespectfully, raising his voice and telling her to shut her mouth and push.
4. Having delivered the baby's head by ventouse delivery, the Doctor handed the delivery over to the Midwife.
5. When the Midwife discovered a nuchal cord and while she was preparing the clamp and scissors, before she could cut the cord the Doctor manually moved the cord over the baby's head and/or used excessive force in doing so.

Finding

The Tribunal found the Doctor not guilty of professional misconduct.

Background

The Doctor was an obstetrician and gynaecologist at Southland DHB from August 2005 until September 2006.

The Patient was 29 years old and had had an uneventful pregnancy. Her estimated due date was 2 June 2006. On 7 June 2006 her Midwife visited her at home. The Patient was experiencing considerable hip pain. Induction was discussed because of the pain and so a referral was made for an assessment by an obstetrician at Southland Hospital.

The Patient was seen on 9 June 2006 and an induction of labour was scheduled to take place the next day.

On 10 June 2006 the Midwife induced labour at 0920 hours with 1mg of prostaglandin E2. A CTG was taken for an hour, and it was normal before and after the prostaglandin was inserted.

The Patient was told she could return home. She and her partner returned to Southland Hospital at about 1500 hours. A further dose of 2 mg of prostaglandin E2 was given at 1515 hours. A CTG recording at that time showed that the Patient was contracting 5-6 times each 10 minutes.

The Patient said she was in constant pain. At 17.30 hours the Patient was given pethidine and maxalon. The Tribunal found that the Patient's pain continued unabated.

The Tribunal considered that there should not have been any provision of a second prostaglandin. The Tribunal accepted this was a precipitous labour as it was over stimulated by the administration of the second prostaglandin. The situation was exacerbated with the absence of pain relief.

The Tribunal found the Patient was obviously in significant pain and discomfort and she was encouraged to push without pain relief.

At 1825 hours, the senior house officer (SHO) was called. Upon arrival the SHO encouraged the Patient to bear down; she noted the baby's head was coming down, but still remained at station plus two. She informed the Patient she would try and help her deliver the baby using a vacuum cup (ventouse). The baby was not delivered during the ventouse attempts by the SHO.

The SHO left the room to call the Doctor so he could assess the Patient for a caesarean section (CS). She said that she told the Patient, prior to the ventouse attempts, that if the baby did not deliver easily, then it might be necessary to resort to a CS. The Patient agreed.

The SHO explained to the Doctor on the telephone that the Patient had been fully dilated for one hour, that she had attempted delivery by ventouse but had failed to deliver the baby, and that she wanted him to assess the Patient. He told her immediately to prepare for a CS. The Doctor anticipated an obstructed labour.

After reading the notes at the nurses' station, the Doctor entered the delivery room. He was then told by the SHO that the Midwife was not happy with the prospect of a CS.

While the Doctor was being telephoned, the Patient left the bed, and continued to push from a standing position. When the Doctor arrived and examined the Patient, the fetal head was distending the introitus, and moved down when he applied fundal pressure.

The Doctor then undertook a pelvic examination and found the head was at the level of the introitus, in the left occipito anterior position, and that the cervix was fully dilated. The head was already oedematous from previous attempts to deliver by venthouse prior to his arrival. Although he had originally considered that delivery by

CS would be necessary, he now considered in light of the examination that a further attempt at vacuum extraction should be undertaken.

The Patient was making noise with each contraction. The Doctor gave her an instruction which was the subject of differing recollections. The Patient's recollection of the words used was "you've got to stop using your words and use your energy to push the baby out". The Doctor denied that he told the Patient to "shut her mouth and push".

There was also an issue as to the extent of discussion of options between the Doctor and the Patient at this point. The Doctor says he did discuss the alternatives of CS and a further attempt at a vacuum extraction. He said he could recall explaining that the baby's head was already oedematous from the previous attempts to vacuum prior to his arrival, and there was a danger of injuring the baby by using instruments again; but there was also a risk of injuring either or both of them while performing a caesarean with the baby deep in the maternal pelvis. The Patient said there was no discussion as to the possibility of her having a CS, when he came into the room. Had she been made aware of that option she would have consented. She would not have placed her baby at risk, and would have taken the option of a CS had those things been explained.

The Doctor then applied the vacuum extractor, and pulled with one contraction, easily delivering the fetal head. Following delivery of the head, the Doctor invited the Midwife to complete the delivery.

The Midwife discovered the umbilical cord was positioned loosely around the back of the baby's neck, and that it ran down either side of her body. In order to deliver the baby in that position, she said she needed to remove the cord from where it was. She said when she tried to move the cord she discovered she could not lift it over the baby's head; and that she then put her hand out so the Doctor could pass her the required instruments.

The Doctor's recollection was that there were no clamps or scissors immediately available. He moved in and put his hand on the baby's head but as he touched it the Patient pushed, so that the baby was delivered and the cord avulsed.

Following the baby's delivery, it became clear that the attachment of the umbilical cord to her abdomen had been torn, and that there was bleeding from the torn area. This was clamped and sutured in order that the bleeding could be controlled. The Patient suffered a large vaginal tear which the Doctor repaired in theatre under general anaesthetic.

The delivery of the baby was completed about 10 minutes after the Doctor's arrival at the hospital. The baby was in fair condition with apgar scores of six at one minute, and seven at 5 minutes. She weighed 3480grams.

Approximately 30 minutes after birth, the baby stopped breathing. She was intubated and ventilated. At about 2100 hours the possibility of a subgaleal hematoma was raised by paediatric staff. The baby's condition subsequently deteriorated despite blood transfusion. She was transferred to Dunedin by helicopter at about 0500 hours on 11 June 2006. The baby died on 12 June 2006.

Reason for Finding

The Tribunal accepted that there were three possible modes of delivery which needed consideration, at the time the Doctor undertook his clinical assessment of the Patient. These were:

- An instrumental delivery, whether by vacuum extractor cup or the use of forceps.
- Caesarean section—a normal step after a failed attempt at a vaginal delivery.
- To allow the labour to continue naturally without further intervention, if need be on a wait and see basis.

The Tribunal found, given the highly charged atmosphere the Doctor found, and the need to effect a prompt delivery, it was appropriate for him to act as he did. The Tribunal does not consider that the Doctor's clinical judgment, which he exercised appropriately, was affected by the difficulties in professional relationships which existed between himself and the Midwife. Accordingly, the first particular was not established.

In the joint note which was prepared by the Doctor and the Midwife after the delivery, it was stated that informed consent had been obtained. The obtaining of informed consent would have been difficult, given the administration of pethidine an hour and a quarter prior to the Doctor's involvement. There was also significant maternal distress. The Patient was not in a good position to give consent.

Particular 2 was not established in any respect. The Tribunal was of the view that the labour was not obstructed. Consequently the first subparticular was not established. The Tribunal reached the conclusion that a further attempt at ventouse was appropriate and therefore the second subparticular was not established. The Tribunal did not accept that it was appropriate to proceed to delivery by caesarean section, and therefore the third subparticular was not established.

The Doctor stated that he could not recall telling the Patient to "shut her mouth", and that he would not use terminology of that type in such a situation. He agreed with what the Patient had said in her evidence, that he had told her she had to stop using her words and instead use her energy to push the baby out.

The Tribunal concluded:

- The words used were as recalled by the Patient ("you've got to stop using your words and use your energy to push the baby out"), who was unshaken in her account of them.
- The words contained in the particular were not used, that the Doctor was not intending to be disrespectful to the Patient, and that particular 3 was not established.

It was established that the Doctor did "hand the delivery over" to the Midwife—although it was also noted that he remained close by, and was able to be involved in subsequent events. The Tribunal concluded that to "hand delivery over" to the Midwife was a common and acceptable practice.

The Midwife was examining for the cord, and found it was positioned loosely around the back of the baby's neck, and that it ran down either side of her body. In order to deliver the baby in that position she needed to remove the cord from where it was. When she tried to remove the cord she discovered she could not lift it over the baby's head. She put her hand out, so the Doctor could pass her the instruments required as she could not access them.

The Doctor thought the equipment that was needed was unavailable, so he stepped in, because the baby was in the course of delivery. The Tribunal did not consider his actions unreasonable. The delivery was progressing very rapidly, and action was required.

The first limb of particular 5 alleged that the Doctor manually moved the cord over the baby's head. There was no evidence that this occurred.

The Tribunal accepted the Doctor's evidence that at the moment he touched the cord, there was a sudden push with the cord then avulsing, this providing a plausible explanation for the "snapping" of the cord. There was a plausible natural explanation for what occurred, albeit an unusual occurrence. Therefore, the assertion raised by the second limb of particular 5, relating to the use of excessive force, was not established.

Conclusion

As none of the particulars were established, the charge was dismissed.

The full decisions relating to the case can be found on the Tribunal web site at www.hpdt.org.nz
Reference No: Med08/107D.

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Robin Frances Fancourt (nee Allen)

1946–2009; CNZM 2003; MBChB (Otago) 1969; MRCP (London) 1973; FRACP (1981)

Robin's death in October 2009 brought to an end a long battle with cancer which began when her brain tumour was first diagnosed in 1987.

Robin was born in Dunedin the daughter of Dr Denis Allen (Pathologist) and his wife Doris (nee Francis). Robin was 4 when the family moved to New Plymouth where Denis her father took up a post as a Pathologist at Taranaki Base Hospital and where there were already strong family links with two of Robin's uncles Chalmers and Peter Allen who were working as Radiologists—and an aunt, Barbara Allen, working as a General Practitioner.

Robin grew up in New Plymouth with her two younger siblings Mathew (now a local General Practitioner) and sister Charlotte. She returned to Dunedin in 1963 to Medical School where she met and married fellow medical student Mr Michael Fancourt in 1968 before they both graduated in 1969.

Her first house surgeon posts were in Christchurch in 1970. Then in 1971 she and Michael travelled to the United Kingdom via a medical house surgeon job in the West Indies. Paediatric posts followed in London particularly at the Hammersmith and Queen Charlotte's Hospitals and it was here that Robin first became acutely aware of the effects of abuse on children—an area of paediatric practice that was to dominate her later career.

It was also during this time that the first of her three children Tineke was born. Robin then spent 12 months as a senior paediatric registrar at Buragwanath Hospital in South Africa. She returned to New Zealand with Michael and Tineke in 1977.

Her first consultant post was in Blenheim where Sam and Nicholas were born. The family returned to New Plymouth in 1985.

At this time her interest in the effects of child abuse and its prevention increasingly dominated her practice, and in 1995 she moved out of public health system and poured all her considerable energies into developing services for children who had suffered physical, sexual and emotional abuse—becoming a leader in this field in New Zealand.

Robin was a true pioneer at a time when the long-term damaging effects on children of such abuse was poorly understood and there was little resource committed to research, diagnosis, treatment and intervention. Robin was heavily influenced by the work of Dr Bruce Perry with whom she spent some time working in America and continued to collaborate with over the next several years. He has described her as "a selfless paediatrician who transformed an entire country by her efforts."

During the 1990s she established The Children's Agenda, a multidisciplinary child advocacy group which she chaired until 1998 when she cofounded the Brainwave Charitable Trust along with former Children's Commissioner Dr Ian Hassall among others. Robin was one of the first Presidents of Doctors for Sexual Abuse Care (DSAC) an organisation aiming to educate professionals caring for abused children. She was also an executive member of the International Society for the Prevention of Child Abuse and Neglect (ISPCAN) and CEO when the society successfully held its 12th international meeting in Auckland in 1998.

In 2000 Robin published *Brainy Babies* (Penguin) bringing together her understanding of infant development and the importance of a loving, nurturing environment in programming that development.

In 2001 the Paediatric Society of New Zealand presented Robin with the Medal of Honour for her work and her outstanding service to the children of New Zealand was publically recognised in 2003 with the award of Companion of the New Zealand Order of Merit (CNZM).

Robin's colleagues and friends will always remember her as an elegant vivacious determined doctor who had the courage to fight her own health battle while leading the advocacy for children but who first and foremost demonstrated in her own life how important caring and nurturing your own family is.

Robin is survived by her husband Michael (General Surgeon); their three children Tineke (Pathology Registrar), Sam (Studying Ancient History), and Nicholas (Paediatric Registrar); and her two grandchildren Elise and Anya.

Dr John Doran (Chief Medical Officer, Taranaki District Health Board) wrote this obituary.