THE NEW ZEALAND MEDICAL JOURNAL
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Change of Editor in the New Zealand Medical Journal

Frank A Frizelle, Editor.

The editorship of the New Zealand Medical Journal is about to change. Gary Nicholls and his team have performed a superb job over the last three years. I am sure Gary will be glad to return to his research and clinical work. The Journal has published many world class articles in the last three years and the editorial board has been innovative, proactive and provocative in expanding the medical-political dimension of the Journal, and making many of us think more about the larger world.

The end of Gary's term as editor coincides with the Journal going web based with the eNZMJ. While I have reservations about the Journal going totally electronic, it is not my decision but that of the management committee. The decision to go totally electronic has not been taken lightly by the management committee. The decision is due to financial restraint. I am told the Journal has been losing $300 000 per annum. This sort of loss is unsustainable for the NZMA.

In the ideal world we would have both an e-journal and a paper journal. No doubt the totally electronic format will mean that we will lose some readers (this I am very disappointed about and sorry); however the only other alternative is that the Journal would disappear. An exclusively electronic journal may discourage some authors publishing in the Journal, however I hope this is not the case. A review of the last twelve months publications in the Journal suggests that much of what is published is essentially about New Zealand health issues and as such it is the best medium to disperse the information.

The Journal will not be free to all on the Internet but will only be available to members of the NZMA and subscribers. The Journal is seen as an important member benefit by the NZMA.

I assume responsibility as editor of The New Zealand Medical Journal on the 19th of July 2002. The change of editorship will be associated with structural changes to the Editorial Board which will have a more diverse national membership. Members of the Editorial Board are: Professor Tim Buckenham (Christchurch), Associate Professor Roger Mulder (Christchurch), Professor Murray Tilyard (Dunedin), Professor Richard Beasley (Wellington), and Professor Rod Jackson (Auckland). There will be an advisory body of 12-15 to assist the Editorial Board. The editorial office will be in the Department of Surgery, Christchurch Hospital. There will be an almost full time editorial assistant (Ms Sarah Webb).

I am keen for papers to be submitted electronically. I hope to speed up the review process by performing it electronically. We intend to publish some comments from reviewers or experts in that field at the end of some papers so as to put an article in perspective for readers. It is also planned to have more than one editorial in each edition mostly relating to published articles in the Journal, but also maintaining an active interest in the larger picture of medical and health related issues. At present the Editorial Board have published under the title of "The Editors", which is a style used

by some well known journals however the new Editorial Board will publish under their individual names.

From January 2003 there will be one edition a month as opposed to the present twice monthly except December and January, when monthly. We intend to publish on the first Friday of the month. We hope to be able to include the table of contents in other medical publications and we would like to distribute the table of contents by e-mail flyers.

We intend to develop new sections within the Journal, including hopefully a regular section on anaesthesia and pain, sections on medical imaging, the Journal 100 years ago and a selection of case reports. Many journals are heading away from case reports. With the advent of evidence based medicine they are no longer seen as politically correct and usually don't help a journal's impact factor. I believe, however, that as most of us treat patients, we find good case reports fun and relevant to read. We will publish case reports that are clear, brief, well written and that have a relevant take home message. Case reports are an important avenue for younger doctors developing their writing skills and learning how to get published.

The Journal has come a long way from its first edition in 1887. There have no doubt been many difficulties in the past and the Journal will have overcome many hurdles to reach its current position. If the Journal is to survive we have to make the transition to the electronic medium. While this change will be a struggle for some, it allows us to develop and removes many of the restrictions of the printed version.

I am looking forward to the next three years editing the Journal, and working with the new Editorial Board and editorial advisory group. I feel that if we grasp the opportunity this could prove to be a very exciting time and be a significant step forward for the Journal.

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Welcome to the eNZMJ

John Adams, Chairman, New Zealand Medical Association

First published in 1887, the New Zealand Medical Journal is still going strong 115 years later.

The new eNZMJ will continue to provide the medical profession in New Zealand with its own peer-reviewed scientific journal. For contributors, the move to an electronic system will streamline the process of publication. For readers, the archive and search facility will make it easier to find and access articles.

The paper version will be missed, but new reading habits have their advantages, with contents alerts sent by email, instant access from our desktops, and the ability to save and print out articles of interest. I know that some members remain uncomfortable with, or do not have access to, computers. However, to save the NZMJ for everybody, this decision to go electronic had to be made. I hope that people not used to computers at this point will find this the added impetus to join the ease of the electronic age. They may need some help from those that are reading this.

The change to an electronic-only journal was made for financial reasons. The Board would have continued with the paper version if it was at all possible, but the transition to electronic publishing ended up being the only responsible and viable option after much review and debate.

It is therefore disappointing to see comments from some members like “Money should not come into it”.[1] Unfortunately, money comes into everything, and there is no getting around this. Someone had to front up with the approximately $300 000 annual deficit for the print NZMJ. The Journal used to break even but, with substantial decreases in advertising revenue, the cost to members has risen and risen, leading to a financial haemorrhage that had to be stopped. The NZMA Board needed to act to protect members’ funds, which support all of the other activities of the NZMA.

With more members this might have been avoided. Perhaps in the future as membership increases, a print version may again become a viable option. Encourage people to join!

Some NZMA members have made comparisons between how the NZMJ and journals like the BMJ and The Lancet are published. While it is flattering to be considered in the same light as these prestigious international journals, the reality is that the NZMJ is different. The BMJ and the Lancet, for instance, have huge resources in staff and money that the NZMJ can only dream about. Their subscriber bases are many, many times larger than that of the NZMJ. They can afford to publish both paper and electronic versions. We cannot.

The future success of the eNZMJ lies with the medical community. The NZMA will continue to publish and foster the Journal, but “ownership” by the medical profession

is vital. The NZMJ needs researchers to continue to submit journal items, and readers to visit the website to read the Journal. The Journal and the Editor need your support.

Access to most of the Journal will be by password, at least to begin with. As a member, you have paid your subscription and get the password as an NZMA member benefit. Please protect it! For institutions, initially access will be by password as well. Access will be monitored and it is likely that another system, probably based on IP addresses, will be introduced for next year. For the future of the Journal, it is vital that our membership and subscriber bases are maintained.

The Editor for the last three years, Professor Gary Nicholls, has done a great job, along with his editorial team. I know that Professor Frank Frizelle, who takes over later this month, will continue the excellent work and maintain the academic rigour and high standard.

While some are nostalgic for the "good old days" of the Journal, technology has moved on and it is essential for the NZMA to be financially responsible. We believe that we have done just this, while continuing to provide an excellent, cost-effective journal for the profession. The NZMA is confident that we will be providing a great product for our members, as well as responsibly using their subscription money.

Welcome to the eNZMJ - here’s to the next 115 years!

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Reference:

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HRT, VTE and surgery: what is best practice?

Claire McLintock

The results of the survey of orthopaedic surgeons and peri-operative management of women taking hormone replacement therapy (HRT)[1] highlight concerns about advice in the recently published "Best Practice Evidence-Based Guideline -Appropriate Prescribing of Hormone Replacement Therapy" regarding the risk of venous thromboembolism (VTE) in women on HRT who require surgery[2]. Surgeons are concerned at the advice to "*stop hormone replacement therapy HRT at least 30 days before [elective] surgery and not to restart it until at least 90 days"*.

This advice was derived using data taken from the HERS study, a placebo-controlled randomised study of the effect of HRT in 2763 women with known cardiovascular disease[3]. The effect of HRT on VTE was a specified secondary outcome of the trial, which reported a 3.1-fold (95%CI 0.8-11.3) relative risk of developing idiopathic VTE and 2.5-fold (95%CI 1.2-5.3) relative risk of non-idiopathic VTE in women assigned to HRT. These figures are in keeping with the 2-4-fold rate reported in several retrospective cohort studies of women presenting with idiopathic VTE[4]. Independent of HRT use, the authors also considered the contribution of other well-recognised risk factors for development of VTE reporting an increased relative risk of VTE in women who, within a 90 day period, had either a hip fracture [(RR 5.6 (95%CI 0.7-43.8)] or other lower limb fracture [RR 18.1 (95%CI 1.6-60.4)], any in-patient surgery [RR 4.9 (95% CI 2.4-9.8)] or had been hospitalised for a non-surgical reason [RR 4.9 (95%CI 2.4-9.8)][3]. It is important to recognise that the 90-day period was not an observed period of increased risk but rather a statistical tool used by the authors based on an assumption that the risk of venous thrombosis due to such events would manifest within 90 days. The study was insufficiently powered to determine by sub-group analysis if HRT contributed further thromboembolic risk in addition these temporary risk factors. The authors attempted to determine how long the thromboembolic risk remained after stopping HRT by looking at events occurring one week, one month and three months after stopping hormonal treatment. There was a suggestion that the risk may persist up to one month (relative hazard, 2.5 [95%CI 0.6-9.7]) but there were too few events to detect a significantly increased risk[3]. Although a substantial proportion of patients do not present with symptoms of VTE until after hospital discharge the majority of patients develop symptoms in the first post-operative month. In a series of over 40 000 patients undergoing elective surgery[5] symptomatic post-operative VTE was not diagnosed until after hospital discharge in over three-quarters of patients with hip arthroplasty and half of the patients with knee arthroplasty with a mean time to diagnosis of 17 and 7 days, respectively.

There are no trial data to suggest that routine cessation of HRT either pre- or post-operatively would be of benefit in preventing venous thrombosis. The general recommendation is that thromboprophylaxis should be given to women taking HRT who require surgery[6]. The use of prophylaxis to reduce an individual's risk of thromboembolism following surgery must be balanced with any potential side effects

of such treatment. For different individuals this risk/benefit ratio will vary depending on surgical factors such as the type of operation or the choice of anaesthesia, on patient factors such as immobility, obesity, a personal or family history of VTE, the presence of a thrombophilia, and other potential risk factors including, in women, whether they are taking HRT or the combined oral contraceptive pill. Consideration of these factors should form the basis of a pre-operative risk assessment to determine the risk of operative complications including thromboembolism and haemorrhage in all patients who are to undergo major surgery. A decision can then be taken as to whether the risk: benefit ratio is in favour of pharmacological thromboprophylaxis.

The most recent consensus conference on antithrombotic therapy[7] recommends that any patient undergoing elective hip or knee arthroplasty should be given thromboprophylaxis with either low-molecular weight heparin (LMWH) or adjusted-dose warfarin as these have been shown to be most effective at reducing the rate of post-operative VTE. Despite these recommendations, there is considerable variation in the use of peri-operative thromboprophylaxis among surgeons in New Zealand and other countries. A previous survey of New Zealand orthopaedic surgeons in 1994 reported that less than 25% routinely used pharmacological thromboprophylaxis in patients undergoing elective hip surgery[8] compared to routine use by 85% of orthopaedic surgeons in the UK[9] and 97% of orthopaedic surgeons in Canada.[10]

Why should there be such variation in clinical practice? There are two major issues that polarize opinion. Firstly, what defines a clinically important venous thrombosis – one seen on routine venography or one that presents symptomatically? Secondly, although LMWH and adjusted-dose warfarin have been shown to be the most effective methods of pharmacological thromboprophylaxis, compared to placebo they are associated with an increased incidence of bleeding[7] that surgeons find unacceptable.

The majority of clinical trials comparing the efficacy of different methods of thromboprophylaxis use objective testing methods such as ascending venography to determine response to treatment. A meta-analysis[11] of 56 trials comparing methods of preventing VTE following hip arthroplasty reported that in the absence of thromboprophylaxis, the rate of DVT was 47% for all DVT and 23% for proximal DVT. Aspirin was the only method of thromboprophylaxis that failed to show a significant reduction in the rate of VTE whereas LMWH reduced the DVT rate to 17% and 6%, respectively and adjusted-dose warfarin reduced the rate to 24% and 5%, respectively.[11] Symptomatic post-operative DVT occurs much less frequently. In a cohort of 1162 patients[12] who underwent hip arthroplasty with no anticoagulant prophylaxis the rate of symptomatic DVT was only 1.9% and the rate of confirmed clinical pulmonary embolism (PE) 1.2% with an overall mortality rate due to PE of 0.3%.

That VTE is a clinical problem following major orthopaedic surgery does not seem to be under debate. The moot point is whether the inherent bleeding risks associated with prophylactic anticoagulation are acceptable given the magnitude of the clinical problem of post-operative VTE.

Although effective at preventing VTE, warfarin and in particular LMWH increase the risk of surgical-site and systemic bleeding. In a meta-analysis of thromboprophylaxis following hip arthroplasty, there was an increased rate of clinically significant

bleeding in those patients given LMWH (1.8%) compared to patients given warfarin (1.3%).[11]

The weight of evidence clearly indicates that there is a two to four fold increased risk of VTE in women taking HRT.[4] This should be sufficient to tip the risk: benefit balance in favour of pharmacological thromboprophylaxis when these women require major orthopaedic surgery. To avoid placing surgeons at risk of a medico-legal challenge, the advice regarding peri-operative management of women taking HRT contained in the New Zealand guidelines should be revised acknowledging that there is insufficient evidence to suggest that stopping HRT before or after surgery is necessary to prevent post-operative VTE. Now that the issue of surgical thromboprophylaxis has been raised, we should use this as an opportunity to review the literature and develop a set of consensus guidelines that will be acceptable to and practiced by surgeons, anaesthetists and physicians in New Zealand and Australia.

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Impact of safety alerts upon prescribing of cisapride to children in New Zealand

Marilize de la Porte, David Reith, Murray Tilyard.

Abstract

Aims To assess the volume of cisapride prescribed in New Zealand to children age 0-17 years and establish whether safety announcements on cisapride had an effect on prescription volumes.

Methods The Pharm warehouse database, which includes prescribing data from the New Zealand Health Information Service, was searched for all prescriptions for cisapride, ranitidine and omeprazole to children age 0-5 and 6-17 years inclusive, from January 1993 to October 2001. The amount of cisapride prescribed, and subsequently dispensed, was tabulated by month, using ranitidine and omeprazole as comparison groups. The time-course of prescribing patterns were compared with the timing of Medsafe alerts regarding cisapride.

Results There were a total of 27169 prescriptions for cisapride over the time-period studied. For both age groups cisapride prescription numbers increased through the mid 1990's to reach a peak prior to 1998. The prescription volumes declined following the Medsafe alerts, with the peak in prescribing by paediatricians occurring twelve months prior to that for general practitioners. Ranitidine and omeprazole prescriptions continued to rise in the younger age group throughout the study.

Conclusion The volume of cisapride prescribed in children has decreased dramatically since 1998 following the Medsafe alerts but the trends indicated delay in the response to safety announcements.

Cisapride, a gastrointestinal prokinetic agent, has been used to treat infants with gastro-oesophageal reflux (GORD), a common and usually self-limiting condition in that age group[1]. The drug is generally well tolerated but has been associated with QT prolongation and cardiac arrhythmias[2-6]. Cisapride has been prescribed to over 36 million children world-wide[7], including 19% of pre-term newborns in Canadian neonatal units. In 1999 a consensus statement by the European Society of Paediatric Gastroenterology, Hepatology and Nutrition recommended cisapride as the drug of first choice for GORD of infancy.[6]

However, since 1993, there have been reports of at least 341 cases of cardiac arrhythmias, including 80 deaths, associated with cisapride.[8] At least two deaths have occurred in children.[9] These adverse events lead to the withdrawal of cisapride from the UK and USA markets in July 2001.[8,10,11]

In New Zealand cisapride is licensed for marketing for paediatric indications and there is a paediatric oral suspension with dosing pipette available. The available data, including epidemiological studies and case reports, have been reviewed by the Medicines Adverse Reaction Committee and only one episode of (non-fatal) arrhythmia with cisapride, in New Zealand, was reported up to the year 2001.[12] In

November 2000, a warning was issued to health professionals in New Zealand cautioning against the use of cisapride and there was a notification of indication changes for cisapride to "*use should be restricted to children with severe gastro-oesophageal reflux, where the diagnosis has been made or confirmed by a specialist physician or surgeon*".[12]

Considering the profile of cisapride and its safety announcements, our aim in the present study was to assess the volume of cisapride prescribed in New Zealand to children from January 1993 to October 2001. We also endeavoured to establish whether safety announcements on cisapride had an effect on prescription volumes.

Methods

A search was performed on the Pharm warehouse database for all prescriptions to children age 0-17 years inclusive, for cisapride, ranitidine and omeprazole for the period January 1993 to October 2001. The Pharm warehouse is a subset of a large automated database, the New Zealand Health Information Service (NZHIS), which contains records of all domestic pharmacy claims. Pharmacists are reimbursed for prescriptions dispensed under the national subsidised scheme. Each claim record includes patient identification number, age category, social status, prescriber number, date of dispensing, dose, formulation of drug and demographic data. Claims are submitted electronically to the NZHIS database, and thus an electronic record exists for all prescriptions dispensed under the scheme. Data are loaded onto the NZHIS database monthly, which is made available for research and administration purposes.

The amounts of cisapride, ranitidine and omeprazole prescribed were tabulated by month, using ranitidine and omeprazole as control groups. To overcome limitations of expressing consumption in terms of units prescribed or sold, each drug was tabulated as a Defined Daily Dose (DDD).[13] This is the unit used by the Nordic Council on Medicines and has now been recommended as a unit of measurement for comparative drug consumption statistics. The DDD corresponds to what is assumed to be the average dose per day for the drug when used in its main indication. The DDD for cisapride, ranitidine and omeprazole was 30 mg, 300 mg and 20 mg respectively. Data for drug prescriptions were also tabulated in relation to age of patients, 0-5 years and 6-17 years inclusive, as well as prescriber type, namely general practitioners and paediatricians. The archive of health warnings was accessed from the Medsafe website.

Table 1. Prescriptions by drug and age category, January 1993 to October 2001.

Drug	0 to 5 years	6 to 17 years	Total
Cisapride	21197	5972	27169
Raniditine	10640	16074	26714
Omeprazole	4183	7421	11604
Total	36020	29467	65487

Results

The total number of prescriptions given for cisapride, ranitidine and omeprazole in the period studied are presented in Table 1. Results show that 78% of the total amount of cisapride prescribed was to the younger group, age 0-5 years, compared with ranitidine and omeprazole which was predominantly prescribed to the older group,

age 6-17 years. Prescription numbers are presented by formulation and age category in Table 2. Around 25% of the omeprazole prescriptions for the 0-5 year age group were for the 20 mg formulation.

Table 2. Usage (prescriptions) by formulation and age, January 1993 to October 2001.

Formulation	0 to 5 years	6 to 17 years
Cisapride Oral liquid (1 mg/mL)	20735	3300
Cisapride 5mg tablets	368	1835
Cisapride 10 mg tablets	94	837
Ranitidine Oral liquid (150 mg/10mL)	8850	794
Ranitidine 150 mg tablets	1449	12915
Ranitidine 300 mg	340	2364
Ranitidine 25 mg injectable	1	1
Omeprazole 10 mg capsules	3131	1330
Omeprazole 20 mg capsules	1035	3300
Omeprazole 40 mg capsules	17	193
Omeprazole 40 mg injectable	0	2
Total	36020	29467

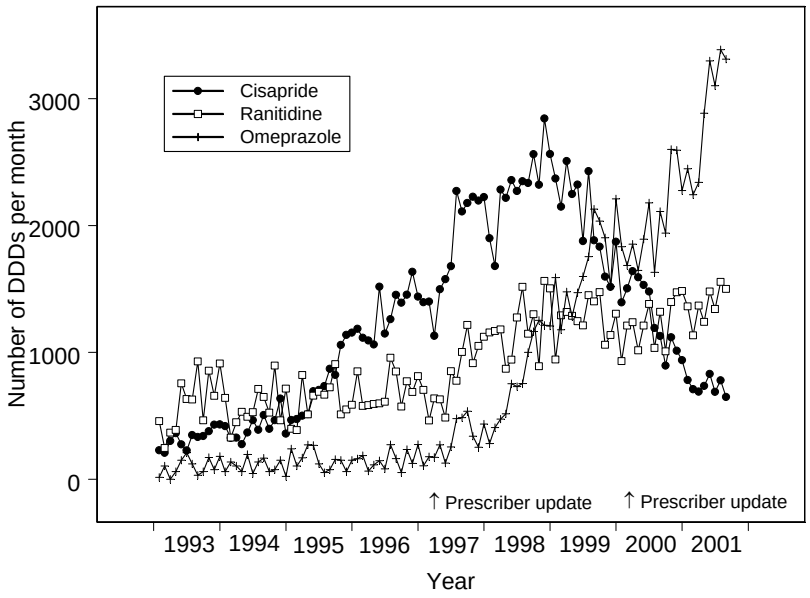
The volumes of cisapride, ranitidine and omeprazole expressed in DDD are displayed by age category in Figure 1. For the 0-5 year age group, the volume of cisapride that was dispensed increased through the mid-1990's to reach a peak in late 1998 before rapidly falling. The volume of ranitidine dispensed had increased slowly, but steadily over the time-period of the study. The volume of omeprazole dispensed had increased rapidly from 1997 and continued to increase at the same rate in 2001. The 6-17 year age group followed a similar pattern except that a relatively smaller volume of cisapride was dispensed for that age group.

The volumes of cisapride liquid formulation prescribed, and subsequently dispensed, by paediatricians and general practitioners demonstrated different patterns over the time-course of the study (Figure 2). Initially, more cisapride liquid was prescribed by paediatricians but by late 1996 a greater volume was being prescribed by general practitioners, and this relationship continued up to the end of the study. The peak in paediatricians prescribing of cisapride liquid occurred in late 1997, more than six months after the first Prescriber Update. The peak in general practitioner prescribing of cisapride liquid occurred in late 1998, twelve months after that of the paediatricians, and more than eighteen months after the first Prescriber Update. The total volume of cisapride dispensed mirrored the pattern of general practitioner prescribing.

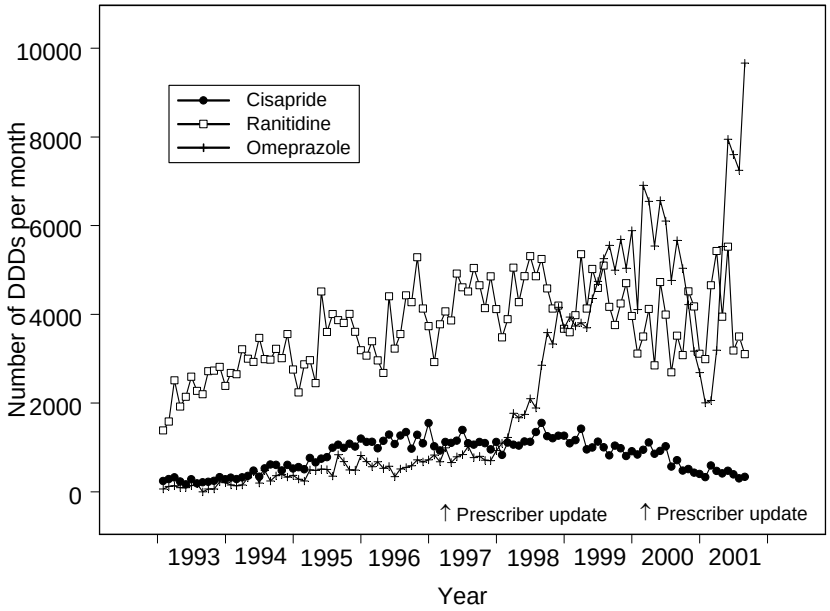
The volumes of omeprazole prescribed, and subsequently dispensed, by paediatricians and general practitioners is displayed by age group in Figure 3. The use of omeprazole in the children appears to be increasing at a rapid rate. Prescribing by general practitioners was greater than that for paediatricians from 1998, when omeprazole was made more generally available. This increase in omeprazole

dispensing to children, and a similar but less marked increase in ranitidine, appears to be occurring as the usage of cisapride declines.

Figure 1. Dispensing of cisapride, ranitidine and omeprazole by DDD.



Amount prescribed per month in DDD: Age 0 to 5 years.

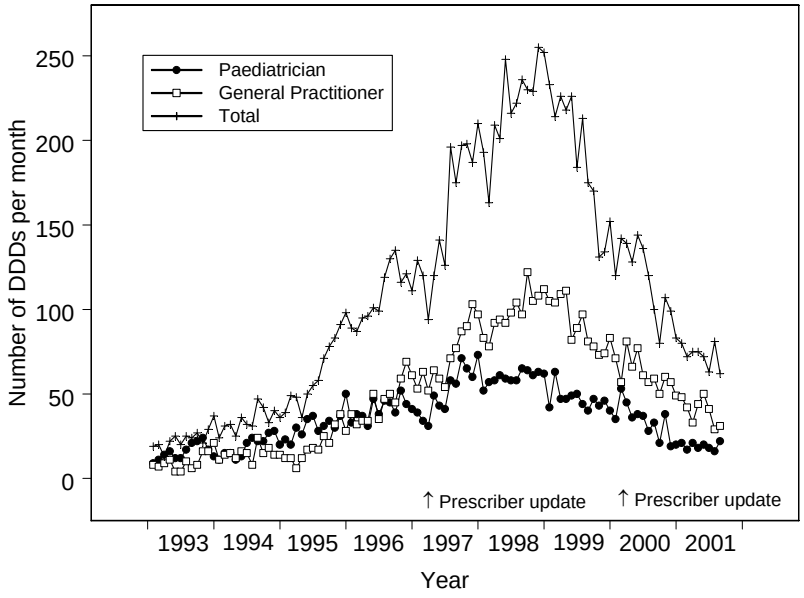


Amount prescribed per month in DDD: Age 6 to 17 years.

Discussion

The use of automated databases in pharmacoepidemiological studies of drug use is well established.[14-16] The primary advantages of such studies are that the data are reliable and that the studies are extremely efficient. A major restriction in the conduct of most case-control and cohort studies is the time, energy and expense necessary to assemble the case series or the series of exposed patients. In comparing the different medicines we used the DDD, and this may not be a good indicator of paediatric drug use given that the DDD is calculated for adults. In addition, the dose of omeprazole used in children compared to the adult dose is relatively larger than that for either cisapride or ranitidine; hence we cannot conclude that the changes in utilisation of these drugs are inter-related. The advantage of using the DDD was that it enabled some comparison to be made of the volume of the medicines used given their wide disparity in milligram dosage and the differences in pack sizes.

Figure 2. Prescriptions of cisapride liquid formulation.



It is clear that the utilisation of cisapride, mainly in the younger age group, has decreased substantially in the last couple of years but the present study indicated delay in the paediatricians' response to the Prescriber Updates and to a greater extent the general practitioners' response. A similar study examining the effect of "Dear Doctor" letters on the co-prescribing of cisapride with contraindicated medications found that letters with surrounding publicity had a greater impact on prescribers than isolated letters.[17] The delay between the response of paediatricians and general practitioners suggests an 'opinion leaders' effect that required the paediatricians to respond before the general practitioners. The influence of 'opinion leaders' is well described and focusing campaigns, to improve prescribing, upon them is a recognised strategy.[18,19] Therefore, future attempts to alter the prescribing of medicines in

children would be enhanced by the targeting of paediatricians initially, and by broadening the campaign beyond letters and Prescriber Updates.

The appropriateness of prescribing of cisapride in children is complicated by lack of convincing evidence of efficacy and an inability to adequately quantify the risks associated with the drug.[20] Currently, the use of cisapride in New Zealand is restricted to children with severe GORD, where the diagnosis has been made or confirmed by a specialist physician or surgeon and it is funded only on a specialist endorsement.[12] In practice its use has been extended to children with lesser degrees of reflux and with gastrointestinal dysmotility. A systematic review of randomised controlled trials with the aim to determine the effectiveness of cisapride compared with placebo, or other non-surgical therapies for the treatment of symptoms of GORD in children**,** found no evidence of a significant effect of cisapride.[1,21] These findings contradicted widely held opinions of a beneficial effect of cisapride. In addition, some surrogate endpoints of GORD have been demonstrated to improve with cisapride.[22,23] It has been argued that the efficacy and safety profile of cisapride is far better documented than for any other prokinetic, and that cisapride remains the prokinetic of choice.[23] Patients may be denied the benefit of cisapride simply because of the need for closer monitoring and extra time spent for parent education. Where pro-kinetic therapy is indicated in children, cisapride dosing should be limited to 0.8 mg/kg/day divided into three or four doses in a 24-hour period, based on a consensus recommendation of the Cisapride Committee of the North American Society of Pediatric Gastroenterology and Nutrition, and should not exceed the recommended adult dose.[24] Clinical studies recommend cisapride 0.15-0.3 mg/kg 3 to 4 times daily in neonates and infants.[25-27]

The present study indicates a volume of ranitidine and omeprazole being prescribed for young children that is beyond what would be expected for the indications of these drugs, given that severe oesophagitis is relatively uncommon in infants and young children. Acid suppressant therapy is recommended in severe eosophagitis, but does not rectify primary disordered motility, a major pathophysiologic mechanism underlying GORD in children. Evidence of efficacy for ranitidine in childhood GORD is limited and its use has not been evaluated in published randomised controlled trials.[28] For the treatment of GORD and erosive oesophagitis, the recommended dosage is 5 to 10 mg/kg/day given in two divided doses (Prod Info Zantac ®, 2000).

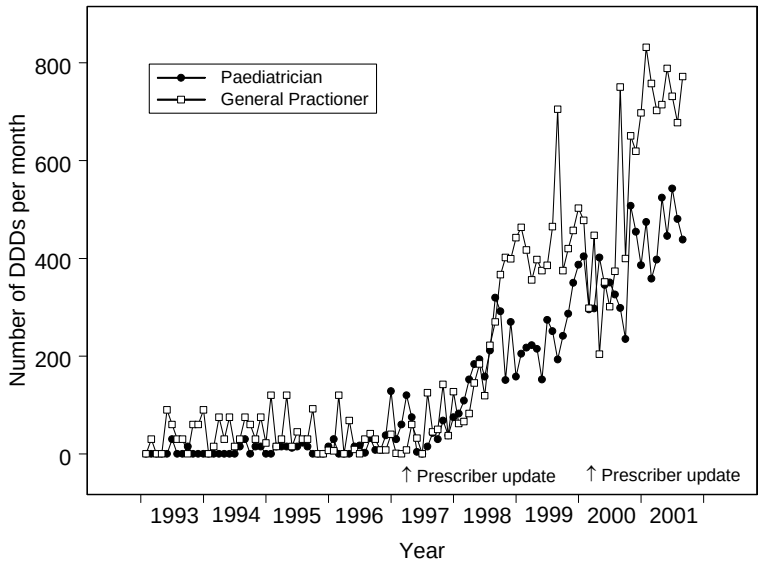
The recommended oral dose for ranitidine for children between 2 to 18 years old is 1.25 to 2 mg/kg/dose every twelve hours.[29] The adverse effects of ranitidine include tachyphylaxis and heart rhythm effects.

The use of the higher dose formulations of omeprazole in one quarter of the prescriptions may indicate that the patients are being treated for severe oesophageal erosions rather than just GORD. Proton pump inhibitors (PPI) are very effective in the healing of severe oesophagitis associated with GORD in adults but, although the use of PPI in severe oesophagitis due to GORD in children has been reported, their role has not been validated or appropriate dosage determined. The manufacturer does not provide omeprazole dosing guidelines for children as its safety and efficacy in children has not been established (Prod Info Prilosec ®, 2000). In an efficacy trial of omeprazole in erosive oesophagitis the effective dosage for children (n=15, mean age, 1.8 years) with GORD was in the range of 0.7 to 3.3 mg/kg/day. Omeprazole was well tolerated with no major side effects noted during that trial.[30] As omeprazole is

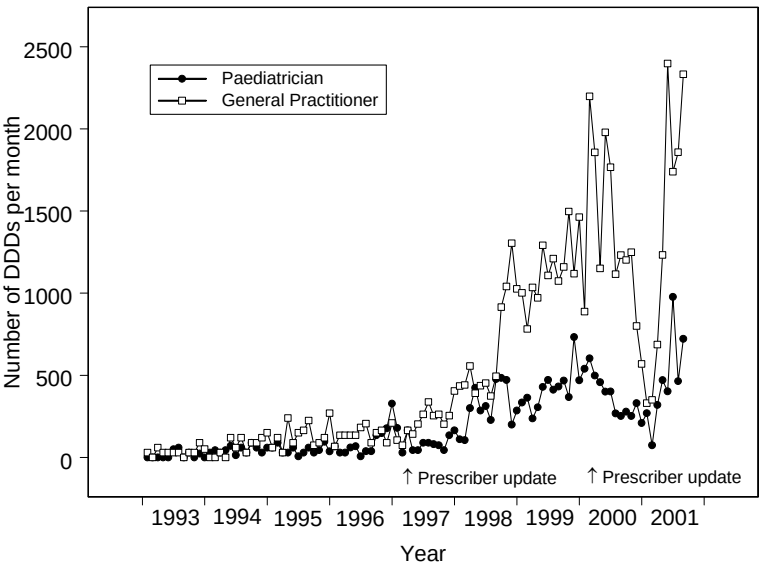
available only as 10, 20 or 40 mg capsules the dose should be rounded up to 10, 20 or 40 mg.

In conclusion, there was delay in the response of prescribing of cisapride to safety announcements. A higher than expected amount of ranitidine and omeprazole is being prescribed for the paediatric age group.

Figure 3. Omeprazole prescribing by DDD.



Omeprazole 0 to 5 years.



Omeprazole 5 to 17 years.

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Normal glycated haemoglobin in a patient with poorly controlled diabetes mellitus and haemoglobin D Punjab: implications for assessment of control

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A 52-year-old male patient was being monitored for control of type I diabetes mellitus with regular checks of his glycated haemoglobin (HbA_{1c}). The values obtained were unexpectedly low and in practise would only be obtainable at the expense of frequent hypoglycaemia. Moreover, they appeared inconsistent with the plasma glucose values (Table 1).

In September 1998, a new high performance liquid chromatography (HPLC) (BioRad Variant) analyser revealed a double haemoglobin A (HbAo) peak not previously recognised by an older HPLC method. This prompted further studies. Haemoglobin was purified by ion exchange chromatography and further analysed by electrospray ionization mass spectrometry (ESI-MS). This revealed normal alpha chains (molecular weight 15126 Da) but abnormal beta chains (15866 Da), a decrease of 1 Da. Examination of tryptic digests of purified abnormal globin by ESI-MS showed that the observed 1 Da mass difference was in the peptide β-13, and could be accounted for by a substitution of glutamine for glutamate at amino acid 121. This occurred in about half of the beta chains, indicating heterozygosity for a recognised amino acid substitution, haemoglobin D Punjab.[1]

Further specimens were analysed in tandem by HPLC as well as by an immunological method (DCA 2000 – Bayer) which is not affected by variant haemoglobins. As expected, the DCA 2000 results were higher (though still showing reasonable control), reflecting the prevailing glucose levels (Table 1).

Table 1. Glucose and HbA_{1c} values by different methods in a patient with diabetes mellitus and Hb D Punjab. *Target range <7% for both methods.

Sample	Glucose (mmol/L)	HbA_{1c} by HPLC method (%)*	HbA_{1c} by DCA 2000 (%)*
1	15.9	4.3	-
2	11.2	4.0	-
3	13.0	4.6	-
4	15.0	4.5	6.7
5	15.0	4.5	7.2

Discussion

The Variant HbA_{1c} method uses cation exchange HPLC to separate various haemoglobin fractions. A buffer gradient of increasing ionic strength elutes any haemoglobin fractions adhering to the cation exchange particles in order of increasing net positive charge on the haemoglobin molecules. The addition of glucose to the N-terminal of the beta chains in HbA_{1c} reduces net positive charge by 1 so that HbA_{1c} elutes from the cation exchange column ahead of HbAo.

In Hb D Punjab, the replacement of glutamate by glutamine at position β-121 increases the molecular charge by one so that any glycated HbD co-elutes with HbAo. This therefore reduces the apparent value for total glycated haemoglobin. In contrast, the immunoassay for HbA_{1c} uses a monoclonal antibody which recognizes the glycated N-terminal four amino acids of the beta chain and is unaffected by the substitution at position β-121.

HbD Punjab is in itself an otherwise benign variant, common in India especially the Punjab. There are over 700 known haemoglobin variants, many of which alter the charge on the haemoglobin molecule and give misleading results, both higher and lower than the true level.[2] Other causes of misleading results, depending on the analytical method used, include haemolytic anaemia (by shortening red cell survival), uraemia, lead poisoning, alcoholism, high dose salicylates and hereditary persistence of foetal haemoglobin.[3]

With the increased incidence of haemoglobin variants as a consequence of in-migration, doctors need to be aware that misleading HbA_{1c} levels will become more frequent. As with other laboratory tests, it would be appropriate to communicate with the laboratory service when results are not in keeping with the clinical picture.

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Peri-operative use of oestrogen containing medications and deep vein thrombosis - a national survey

David W Ardern, Denis R Atkinson, Anna J Fenton.

Abstract

Aim To determine the practice of New Zealand orthopaedic surgeons when women taking hormone replacement therapy (HRT) or a combined oral contraceptive pill (COC) present for major surgery. Current practice is compared with recently produced guidelines and manufacturers advice.

Methods A postal survey was sent to all New Zealand orthopaedic surgeons.

Results The response rate was 80% (118/148). There was wide variation in beliefs surrounding the peri-operative use of both of these medications. 44% of surgeons indicated that they would routinely advise discontinuing the COC pill peri-operatively for major surgery. 24% indicated that they would routinely advise discontinuing HRT peri-operatively. Recently released guidelines recommend that HRT should be stopped for at least 30 days prior to elective surgery and withheld for 90 days following surgery. Less than 3% of surgeons appeared to be routinely following this recommendation. Most manufacturers of COC pills recommend stopping the medication for at least four weeks prior to elective surgery. Only 25% of surgeons routinely practice in accordance with these recommendations.

Conclusions This survey clearly demonstrates substantial differences between current clinical practice, recently revised HRT guidelines and oral contraceptive manufacturers advice. These differences need to be brought to the attention of surgeons and guideline producers. Particular medico-legal caution in this area is advised.

Hormone replacement therapy (HRT) and combined oral contraceptives (COCs) are believed to increase the risk of developing deep vein thrombosis (DVT) and pulmonary embolism among users. Public advice given by the New Zealand Ministry of Health states that the odds of having a blood clot increase by 3 - 4 times for those on second generation pills and 6 - 8 times for those on third generation pills.[1] For women taking hormone replacement therapy there is now good evidence to suggest that the risk of developing venous thromboembolism (VTE) is increased by 2 - 4 times.[2-6]

Surgery is associated with factors which promote DVT. It would be reasonable to expect, therefore, that the combination of an oestrogen containing medication and surgery could lead to significantly increased risk and avoidable post-operative complications. Evidence to support this assumption, however, is lacking and the risks associated with discontinuing medication are uncertain. The advice given by pharmaceutical companies is generally to discontinue a COC four weeks prior to surgery.[7] Some also suggest withholding the medication for two weeks post-operatively. The advice given by manufacturers for HRT is to consider temporary

discontinuation peri-operatively.[7] In May 2001, the New Zealand Guidelines Group released recommendations to discontinue HRT for at least 30 days prior to elective surgery and for 90 days following surgery.[8]

Major orthopaedic surgery is known to be associated with a relatively high incidence of DVT. Studies using surveillance methods have reported that in the absence of prophylaxis the incidence of DVT following major hip or knee surgery is approximately 50%.[9-11] A recent survey showed the prevalence of HRT use in New Zealand women aged between 45 - 64 years to be 20%.[12] Almost half of the women surveyed had started it to prevent osteoporosis. Last year there were over 400 000 prescriptions written for COC pills within New Zealand. The presence of guidelines for their use peri-operatively is therefore of importance in orthopaedic surgery. This is especially so given the high level of media and public interest in this general area and the potential medico-legal implications. This is a survey of orthopaedic surgeons but the issue is relevant to all clinicians who may advise women about the use of medications in the peri-operative period.

Methods

A postal questionnaire was sent to all practicing orthopaedic surgeons within New Zealand. A follow-up letter was sent to non-responders after six weeks. Those surveyed were asked to indicate if they would stop such medications peri-operatively for major orthopaedic surgery either routinely, only in patients considered to be high risk, or would not discontinue. Neither the specific surgical procedures classified as "major orthopaedic surgery", nor the specific risk factors that would create a "high risk patient" were listed in the questionnaire. These were left up to the interpretation of the individual responding to the survey. Such specific lists are not found in the relevant guidelines for clinical practice in this area. Surgeons were then asked to record how long prior to, and following surgery they would discontinue the medication.

Results

Response. There were 118 responses suitable for analysis out of the 148 surveyed (80%). Not all surgeons answered every question.

Discontinuing HRT peri-operatively (Table 1). 24% of the responding surgeons indicated that they would routinely advise discontinuing HRT peri-operatively. 25% would only do so in patients whom they considered to be at high risk, and 51% would not advise discontinuing HRT.

Table 1. When would medication be stopped prior to major orthopaedic surgery?

	HRT (n=118)		COCs (n=117)	
	(No.)	(%*)	(No.)	(%*)
Routinely	28	24	51	44
Only in high risk patients†	30	25	27	23
Not stopped	60	51	39	33

*Proportion of surgeons. †High risk patients as perceived by the surgeon.

Discontinuing the COC pill peri-operatively (Table 1). 44% of surgeons would routinely advise women to discontinue their contraceptive pill peri-operatively. A further 23% would only advise this in patients who they considered to be at high risk, and 33% would not advise discontinuing the pill.

Clinical practice compared with guidelines (Tables 2, 3). Less than 3% (3/113) of responding surgeons indicated that they would advise withholding HRT for at least 30 days prior to surgery and for 90 days following surgery as suggested by the New Zealand Guidelines Group. 25% (28/113) would advise women to discontinue their contraceptive pill for at least 30 days prior to surgery as suggested by most pharmaceutical companies.

Table 2. Peri-operative use of hormone replacement therapy in relation to guidelines*.

No. days stopped pre-op.	**No. surgeons**	**% surgeons**
Not stopped	60	53
<30	35	31
30	11	10
>30	7	6
No. days re-started post-op.	**No. surgeons**	**% surgeons**
Not stopped	60	53
<90	50	44
90	3	3

*NZGG recommendations are to discontinue HRT for 30 days prior to surgery and 90 days following surgery.

Table 3. Peri-operative use of oral contraceptives in relation to guidelines*.

No. days stopped pre-op.	**No. surgeons**	**% surgeons**
Not stopped	38	34
<30	46	41
30	22	19
>30	7	6
No. days re-started post-op.	**No. surgeons**	**% surgeons**
Not stopped	38	34
<14	16	14
14	13	11
>14	46	41

*Most manufacturers advise discontinuing COC's for at least 30 days prior to surgery +/- withholding for 14 days following surgery.

Discussion

As 80% of practising orthopaedic surgeons within New Zealand completed the questionnaire the results are likely to reflect current practice.

This survey has demonstrated widespread variability of practice and significant differences from the relevant guidelines. This is especially so for the peri-operative use of HRT where only 3% of orthopaedic surgeons appear to be practicing in accordance with recently released guidelines. It would seem that surgeons are largely unaware of the new HRT guidelines released by the New Zealand Guidelines Group (NZGG).[8] It is also noted that these guidelines differ substantially from recommendations made by the pharmaceutical companies and authorities elsewhere (Table 4). Evidence for such recommendations is generally lacking and they tend to be based upon knowledge of the theoretical risks and resulting opinion. The recently published HERS study [6] has been cited as the only significant study to date to assess the effect of surgery on risk of VTE.[8] This randomised controlled trial was designed to provide information on the outcome on subsequent cardiac events in

postmenopausal women. It included older women with a mean age of 67 years, and all had established coronary artery disease (CAD). The findings suggest significantly increased risk of VTE among HRT users following lower-extremity fractures and for 90 days following surgery. Trial investigators thus recommended that participants discontinue HRT during periods of high risk such as surgery, immobilisation or severe illness and restart their medication when they return to normal mobility.[13] The increased risk in this group has however been extrapolated to include all women in the recommendations to stop HRT for 30 days prior and for 90 days following surgery made by the NZGG.[8]

Table 4. Recommendations for peri-operative use of oestrogen containing medications.

Hormone Replacement Therapy	
BNF	may be prudent to review the need for HRT
ACOG	benefit of stopping HRT has not yet been established
RCOG	no evidence at present to support a policy of routinely stopping HRT prior to surgery provided that appropriate thromboprophylaxis is employed
ICS	In the absence of other risk factors, there is insufficient evidence to support a policy of routinely stopping HRT; heparin thromboprophylaxis advisable where not discontinued
Combined Oral Contraceptives	
BNF	preferably stop 4 weeks pre-op. & re-commence at the first menses occurring at least 2 weeks after full mobilization
ACOG	no studies to confirm the clinical benefits of stopping OC's pre-operatively; balance the risks
RCOG	insufficient evidence to support a policy of routinely stopping OC's prior to major surgery in the absence of other risk factors; prophylaxis may be warranted if additional risk factors are present
ICS	consider discontinuing 4 – 6 weeks before surgery but this should be balanced against risks of unwanted pregnancy; thromboprophylaxis advisable when not discontinued and other risk factors are present

BNF=British National formulary[22], ACOG=American College of Obstetricians and Gynaecologists,[23] RCOG=Royal College of Obstetricians and Gynaecologists,[21,20] ICS=International Consensus Statement.[19]

The most obvious effects of discontinuing HRT for a period of time peri-operatively are likely to be a recurrence of unpleasant menopausal symptoms. The risks of precipitating more serious harm however, remain unknown. The authors of the HERS study concluded that although starting HRT for secondary prevention of CAD was not recommended given the favourable pattern of CAD events after several years of therapy, it could be appropriate to continue treatment in women already taking HRT.[14] In view of this it would be wise to seek advice from the patient's cardiologist before necessarily discontinuing HRT. Furthermore, it has been observed that the elevated risks of VTE appear to be greatest in the first year or two of HRT use.[3,5,6] These observations might be due to a selective effect of HRT on women with a pre-existing risk for thrombosis.[6] As yet, however, there is no certainty about this and the risks of temporarily discontinuing HRT for a substantial period of time before re-starting it are not clearly defined.

We believe that the apparent lack of adherence to the new HRT guidelines is likely to be contributed to by both a lack of awareness of their existence and a lack of confidence in their validity. The feasibility of being able to advise patients to

discontinue their medication for a full month prior to surgery under presently-used hospital booking arrangements is also questionable.

Most pharmaceutical companies recommend stopping the oral contraceptive pill for four weeks prior to surgery, but this is not universally advocated by specialist groups (Table 4). This survey demonstrates that although 44% of orthopaedic surgeons routinely advised women to stop the pill prior to major surgery, only 25% advised women in accordance with the recommendations made by pharmaceutical companies. One reason for this variance is likely to be the perceived risks of unwanted pregnancy compared with the potentially small increased risks of not stopping the pill prior to major surgery. A policy of routinely stopping the contraceptive pill prior to surgery could well result in unwanted pregnancy.[15] Pregnancy carries a much greater risk of VTE than does oral contraceptive use. In addition, the possibility of subsequent termination, with its associated physical and psychological risks, needs to be considered.

As with HRT there are relatively few data to quantify the increased risk posed by the use of oestrogen containing oral contraceptives around the time of major surgery. One large prospective study suggested that the risk of post-operative VTE was around two times but this was not statistically significant.[16] Pro-thrombotic changes in haematological variables observed with oestrogen administration tend to return to baseline within one to two menstrual cycles after stopping treatment.[17,18] Such observations have been used in the formation of recommendations by oral contraceptive manufacturers.

The use of anticoagulants has been advocated in women who have additional risk factors present and do not stop their contraceptive pill[19,20], or hormone replacement therapy.[19,21] In practice this is likely to include most patients taking HRT.[19,21] Anticoagulant use in preference to withdrawing medication may also help explain the findings of this survey. This was not specifically enquired about in the survey.

Clearly the scientific data are confusing. Despite this we feel it is important for surgeons to make patients aware of the risks of using oestrogen-containing drugs. This is particularly so for patients undergoing elective surgery in the lower limbs. This should form part of the normal consent process and it should involve the prescriber and the patient. We also draw attention to the potential that guidelines have for creating unnecessary medico-legal risk in an increasingly hostile environment.

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VEGF-D expression is associated with lymph node status in primary human breast carcinomas and regulated by estrogen in breast carcinoma cell lines.

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Angiogenesis, the formation of new blood vessels from existing vasculature, is essential for tumour growth and metastasis. Vascular Endothelial Growth Factor-D (VEGF-D), a recently identified VEGF family member, is a potent angiogenic factor *in vivo* and stimulates endothelial cell proliferation and migration *in vitro*. Although overexpression of VEGF-D has been shown to promote tumour cell metastases in animal studies, its contribution to tumour neovascularization and metastasis in human breast tumours is unknown. We therefore measured the level of VEGF-D mRNA by relative RT-PCR in 10 normal and 53 invasive breast cancers and correlated their level of expression with standard clinicopathological parameters. Tumours expressed more VEGF-D than normal breast tissue, and VEGF-D gene expression was significantly associated with tumour size ($p=0.05$), nodal status ($p=0.008$), and the number of involved nodes ($p=0.0053$), but not with patient age, estrogen receptor (ER)($p=0.209$), progesterone receptor ($p=0.193$), tumour histology ($p=0.136$), grade ($p=0.796$), vascular invasion ($p=0.645$), or expression of VEGF-D receptors KDR ($p=0.935$) and flt-4 ($p=0.589$). Since VEGF family members have been shown to be estrogen regulated we assessed the effect of 17β-estradiol on VEGF-D mRNA expression in a panel of ER positive (MCF-7, T47D) and ER negative (MDA231, MDA453, MDA435, MDA468, BT20, SkBR3) breast carcinoma cell lines. We observed that physiological amounts of estrogen (1nM) significantly upregulated VEGF-D in T47D cells at 18 hours ($p<0.01$). These data suggest that VEGF-D expression may provide a surrogate marker of nodal metastasis that may be used to stratify patients for adjuvant chemotherapy, and give additional support for targeting VEGF receptors as an anti-cancer therapy.

Alcohol use and misuse among older people in the community: hidden problem.

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To determine patterns of alcohol use and misuse among community-dwelling people aged 65 years and over in Christchurch and to assess how often this comes to medical attention, a cross-sectional survey of alcohol use and misuse was conducted followed by a self-administered postal survey among non- respondents. GPs of the respondents completed a self-administered questionnaire on patients' alcohol use and misuse. The response rate was 58% (141/243). The prevalence of hazardous alcohol consumption in the past 12 months (AUDIT cut-off score 8 or more) was 9.9% (95% CI = 4.9-14.9) and the prevalence of lifetime alcohol dependence using DSM-IV diagnostic criteria was 24.8% (95% CI = 17.6-32.0). Men were more likely than women to report lifetime dependency and current hazardous patterns. The response rate among GPs was 77.7% (108/139). None of the GPs who responded identified or diagnosed any alcohol problems in the past 12 months among this group and reported a history of alcohol problems in only 4 (4.0%) patients. Those with current hazardous patterns of alcohol use were twice as likely to be admitted to hospital (RR=2.4; 95% CI 1.2-5.1) but significantly less likely to visit their GPs in the previous 12 months (RR=0.55; 95% CI 0.7-1.1). A significant proportion of community-dwelling elderly people reported patterns of alcohol consumption that put them at risk of future damage to physical or mental health. Hazardous drinkers were less likely to visit their GPs and only in a few cases, were GPs aware of such potential problems.

Gene expression of VEGF-A, VEGF-B, VEGF-C and their tyrosine kinase receptors in human colorectal cancer. **V Hanrahan[1], M J Currie[1], S P Gunningham[1], H R Morrin[1], P A E Scott[2], B A Robinson[2], S B Fox[3].**
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The contribution of vascular endothelial growth factor (VEGF) family members to neovascularisation and metastasis in human colorectal carcinoma (CRC) is unclear. We therefore measured the mRNA levels of VEGF-A isoforms (VEGF-A_{189}, VEGF-A_{165}, VEGF-A_{121}), VEGF-B, VEGF-C, and their tyrosine kinase receptors VEGFR1 (Flt-1), VEGFR2 (KDR), and VEGFR3 (Flt-4) in normal colon (n=20), adenoma (n=10), and invasive colorectal carcinoma (n=71) samples by RNase protection assay (RPA), and correlated expression levels with standard clinicopathological variables. VEGF-A and VEGF-C mRNA levels were positively correlated with tumour grade and tumour size ($p<0.05$), but not patient age, sex, presence of infiltrative margin, lymphocytic response, vascular invasion, Duke's stage, or node involvement ($p>0.05$). VEGF-B mRNA abundance showed a positive association with the presence of an infiltrative margin ($p=0.044$). Gene expression studies demonstrated differential regulation of VEGF ligands during adenoma-carcinoma progression. VEGF-A mRNA abundance was greater in adenoma and carcinoma samples compared with normal tissue ($p<0.05$), and VEGF-B mRNA levels were highest in adenoma samples ($p=0.012$). In contrast, VEGF-C mRNA abundance was higher in carcinoma than normal or adenoma tissue ($p=0.003$), with expression levels highest in invasive adenocarcinomas with lymph node metastases (Duke's Stage C). Flt-1 and KDR receptor mRNA levels were higher in adenoma and carcinoma compared to normal tissue ($p\leq0.001$), whereas Flt-4 mRNA levels appeared lower in carcinoma

samples. These data support the hypothesis that VEGF ligands undergo an angiogenic switch at different stages during progression from normal colon to invasive CRC: VEGF-A and VEGF-B initiate and sustain angiogenic responses, whereas VEGF-C promotes invasive tumour growth and lymph node metastasis.

Patterns of alcohol use and misuse among elderly rest home residents in Christchurch, New Zealand. N Khan[1], T J Wilkinson[1], D J Sellman[2], P Graham[3]. [1]Health Care of the Elderly, Department of Medicine; [2]Department of Psychological Medicine; [3]Department of Public Health and General Practice, Christchurch School of Medicine and Health Sciences, University of Otago, Christchurch.

To determine the prevalence of alcohol use and misuse among elderly rest home residents in Christchurch, a cross-sectional prevalence survey was conducted among 175 residents aged 65 and over, randomly selected from 30 rest homes in Christchurch in 1998. Hazardous patterns of alcohol consumption in the past 12 months were determined by the Alcohol Use Disorders Identification Test (AUDIT) questionnaire and alcohol dependence in the past 12-months and lifetime was determined by a structured clinical interview using DSM-IV criteria. Of 246 eligible participants, 175 (71.1%) residents were interviewed, 115 women and 60 men. The mean age of participating residents was 82.6 years (SD=7.8) compared with 83.2 years (SD=6.3) for non-participants in the study. The prevalence of hazardous patterns of alcohol consumption in the past 12 months by the AUDIT (cut-off score 8) was 5.1% (95% CI=1.8-8.4). According to DSM-IV criteria, the prevalence of lifetime alcohol dependence was 20.5% (95% CI = 13.5-27.6). The prevalence of alcohol dependence in the past 12 months was 0.5% (95% CI = 0-1.7). The prevalence of lifetime alcohol dependence was significantly higher in men 36.7% (95%CI = 23.2-50.1) than women 12.2% (95% CI = 5.6-18.8) (p=0.0001). In spite of advanced age, a small proportion of elderly rest home residents consumed quantities of alcohol that puts them at risk of future damage to physical or mental health. Lifetime prevalence of alcohol dependence was comparable to the general population estimates and was higher in men than women.

Pressure controlled ventilation compared with volume controlled ventilation in anaesthetised adult patients. RA French. Department of Anaesthesia, Christchurch Hospital, Christchurch.

Ventilators for use in the Intensive Care Unit have been able to offer a variety of ventilatory modes for some years. The introduction of anaesthesia “work-stations” now allows the anaesthetist a choice of ventilatory mode, principally volume vs. pressure control ventilation. No comparative study of these modes of ventilation appears to have been performed in the anaesthetic setting.

This study examined patients undergoing general anaesthesia with the use of intermittent positive pressure ventilation. Ethics committee approval was gained and twelve patients studied. Pressure control (PCV) and volume control (VCV) modes (Datex Anaesthesia Delivery Unit) were used within the same patients in situations of stable respiratory mechanics. VCV and PCV modes were used sequentially and

pressure, flow and volume waveforms, as recorded by sidestream spirometry (Datex AS/3), were captured using an analogue to digital converter and a computer.

Pressure control ventilation and volume controlled ventilation delivered a clinically equivalent tidal volume and peak airway pressure in all patients studied. In the majority of patients (11 of 12), PCV delivered a slightly greater tidal volume per cmH_20 applied peak pressure. The mean difference was 2.2 ml per cm H_20 applied ($p<0.001$, 95% CI 1.1 to 3.3 ml/cm H_20).

Pressure control ventilation offers a satisfactory mode of providing intermittent positive pressure ventilation in anaesthetised adults. It possesses a small advantage over volume control ventilation when considering the tidal volume delivered per unit of peak pressure. This may be of benefit when attempting to limit peak airway pressures whilst maximising tidal volume.

Oxidation of β_2-agonists by peroxidases and its relevance to asthma control. S J Hoskin, A J Kettle. Free Radical Research Group, Department of Pathology, Christchurch School of Medicine and Health Sciences, Christchurch.

β_2-agonists are useful for dilating airways in acute episodes of asthma but regular use may worsen asthma and cause tolerance. The aim of this study was to investigate a biochemical mechanism that could explain such findings. Using absorbance spectroscopy, we investigated whether β_2-agonists act as substrates for peroxidases – the enzymes released by eosinophils and neutrophils during inflammatory processes like asthma. Fenoterol, isoproterenol, terbutaline, salbutamol and formoterol, were all capable of reacting with myeloperoxidase (MPO) and eosinophil peroxidase (EPO.) Fenoterol and isoproterenol showed highest affinity whereas salbutamol was a very poor peroxidase substrate. Oxidised terbutaline formed several new products which we detected using high performance liquid chromatography (HPLC.) Some products were fluorescent and showed an absorbance spectrum characteristic of phenol dimers. Oxidation of terbutaline also produced a terbutaline peroxide, measured using the ferrous oxidation of xylenol (FOX) assay. Isolated neutrophils and eosinophils oxidised terbutaline to form the same range of products as isolated enzyme. In conclusion, β_2-agonists are oxidised by peroxidases in the presence of hydrogen peroxide. Drug affinity for peroxidase roughly correlates with adverse effects. Closer investigation of terbutaline revealed that oxidation occurs via a free radical pathway to produce multiple products including phenol dimers and peroxide. β_2-agonist administration into the inflammatory environment of an asthmatic airway could result in products capable of increasing inflammatory damage in the lung. The β_2-agonist could also be inactivated. Our investigations confirm that inflammatory cells are capable of oxidising terbutaline. Further studies are needed to identify whether β_2-agonist oxidation occurs *in vivo.*

Patient agitation and heart rate variability. Z H Lam[1], S Hunt[1], J G Chase[1], G Shaw[2]. [1]University of Canterbury, Department of Mechanical Engineering; [2]Departmment of Intensive Care Medicine, Christchurch Hospital, Christchurch.

The dynamics of agitated patients are not understood and the resulting over-sedation has a high social cost and risk to the patient. This research aims to develop sensor arrays and signal processing systems to quantify the agitation response of sedated and ambulatory patients. Data from continuously monitored electrocardiographs ECG's were taken from a lightly sedated, mildly agitated critically ill patient, and from two normal ambulatory subjects. The normal subjects also underwent a cold compress test in order to simulate physiological effects of agitation. The signal 'noise' of the ECG was reduced with the use of a moving average filter before determining the RR-intervals. The RR-intervals were then analysed for heart rate variability (HRV). Our results show that although the overall heart rate does not increase significantly with agitation, the RR-intervals have higher power content in the 0.4-0.5Hz high frequency range. During the cold pressor test spectral power around the low frequency (0.05Hz) band reduces approximately 5dB transferring to peaks over 10dB greater in the high frequency (0.4-0.5Hz) band. These results show the potential for determining the state of agitation employing Fourier analysis and autoregressive modelling of the RR-interval. It is hoped this research will enable better patient care, create commercial opportunity in medical devices and systems and provide a quantifiable technology platform for assessing the efficacy of a wide range of sedation therapeutics.

Sialic acid content of fibrinogen in pregnant women and in individuals on fibrate therapy. G Maghzal, S Brennan, P George. Molecular Pathology, Canterbury Health Laboratory, Christchurch.

Fibrinogen is a plasma glycoprotein, which plays a pivotal role in blood coagulation, and has been associated with a higher risk of cardiovascular disease and thrombosis. A distinct correlation has been made between the sialic acid content of fibrinogen and the thrombin clotting time (TCT) of plasma. For example, acquired dysfibrinogenemias caused by liver disease have an increased sialic acid content of fibrinogen and a significant delay in TCT. We have studied the sialic acid content of fibrinogen in two populations: 1) pregnant women, who reportedly have increased fibrinogen and sialic acid levels and an increased risk of thrombosis; and 2) individuals on fibrates, which are used to control dyslipidaemia and have been shown to decrease the functional level of fibrinogen. Using electrospray ionisation mass spectrometry, we found a 5.4% increase in the sialic acid content of fibrinogen ($p < 0.01$) in the fibrate population (n=12) compared to normal controls (n=6). While in the pregnant women who were in the third trimester (n=11), there was a 5.5% decrease in the sialic acid content of fibrinogen ($p < 0.05$). Pregnant women also had significantly higher fibrinogen levels and lower TCT. We also measured the thrombin-catalysed polymerisation rate of these fibrinogens and found that the fibrates group had a significantly lower rate (V_{max}) compared to the controls (5.6×10^{-4} vs 6.6×10^{-4} s^{-1}) while this rate was increased in the pregnant women. These findings strongly suggest that the sialic acid content of fibrinogen affects its clotting and may contribute to the increased risk of thrombosis in pregnant women and the decrease of functional fibrinogen during fibrate therapy.

C-type natriuretic peptide (CNP) and amino terminal pro C-type natriuretic peptide (NT-proCNP) in a sheep model of mild sepsis. T C R Prickett[1], T G

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CNP is a peptide hormone synthesised in the brain, vascular endothelium and bone, where it functions as a neurotransmitter, vasorelaxant and stimulator of long bone growth respectively. We have identified a circulating peptide from the amino terminal end of the precursor proCNP in human and sheep plasma. This peptide has an apparent molecular weight of 5 kDa, similar to that expected for NT-proCNP(1-50) – a potential fragment released during processing of proCNP. However the relation between the two forms, and the source of the immunoreactive forms found in plasma is unknown. In health, plasma levels of CNP are close to detection limits and only in the setting of sepsis has elevation of CNP been observed *in vivo*. Since endothelial cells stimulated by lipopolysaccharide (LPS) release CNP *in vitro* we aimed to see if CNP levels were raised in an animal model of mild sepsis and whether plasma concentrations correlated with NT-proCNP. Sixteen sheep received an i.v. bolus of LPS (800ng/kg live weight) or vehicle. Changes in rectal temperature at 4 h were –0.2 $\pm$ 0.1 ^{0}C (mean $\pm$ sem) for control sheep, and +1.1 $\pm$ 0.2 ^{0}C for LPS treated sheep. LPS induced a rise in plasma CNP at 2 h (P<0.005), and NT-proCNP at 3 h compared with control sheep. CNP and NT-proCNP plasma concentrations were significantly correlated (R=0.44, P<0.0001). These results support the hypothesis that CNP and NT-proCNP are released from the same source during the processing of proCNP. Plasma measurements of the novel peptide NT-proCNP, which circulate at higher levels than CNP, opens the possibility of studying factors regulating CNP *in vivo.*

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Effect of a rapid assessment clinic on the waiting time to be seen by a doctor and the time spent in the department, for patients presenting to an urban emergency department: a controlled prospective trial

MW Ardagh, J Elisabeth Wells, Katherine Cooper, Rosa Lyons, Rosemary Patterson, Paul O'Donovan.

Abstract

Aims To test the hypothesis that triaging certain emergency department (ED) patients through a rapid assessment clinic (RAC) improves the waiting times, and times in the department, for all patients presenting to the emergency department.

Methods For ten weeks an additional nurse and doctor were rostered. On the odd weeks, these two staff ran a RAC and on even weeks, they did not, but simply joined the other medical and nursing staff, managing patients in the traditional way. Patients suitable for triage to the RAC were those for whom disposal was readily apparent, interventions required were quickly undertaken, and lengthy investigations or assessment were not required. After the ten-week period data from the five weeks of the RAC and the five weeks with no RAC, but the same staffing level, were analysed and compared.

Results During the five weeks of the RAC clinic a total of 2263 patients attended the ED, and 361 of these were referred to the RAC clinic. During the five control weeks a total of 2204 patients attended the ED. There was no significant difference in the distribution across triage categories between the RAC and non-RAC periods. The waiting times to be seen by a doctor show no difference at Triage 2 and 3 and a difference of several minutes for Triage 4 and 5 categories. The times patients spent in the ED also show no difference for Triage 2 and 3 and about 20 to 25 minutes advantage for RAC-week patients in Triage categories 4 and 5.

Conclusions The rapid management of patients with problems which do not require prolonged assessment or decision making, is beneficial not only to those patients, but also to other patients sharing the same, limited resources.

The setting for this study was the Emergency Department (ED) of Christchurch Hospital, Christchurch. It is the only ED in the city, servicing a population of approximately 400 000 people and attending to more than 65 000 patient presentations per annum. It sees patients across the whole breadth of emergency medicine and the medical staff consist of a mix of fellows of the Australasian College for Emergency Medicine, registrars and senior house officers. It is staffed by approximately 65 full time equivalent emergency nurses. All patients are triaged at point of arrival by an emergency nurse trained in triage and according to the triage scale of the Australasian College for Emergency Medicine.[1] One of the key performance indicators of the ED is the waiting time for patients of each triage category to be seen by a member of the medical staff.

The efficient functioning of a busy ED relies on the ability to maintain patient flow, so that patients are moved on to the next phase of their care in a timely fashion and consequently new patients can take their place in the treatment area. Two barriers to efficient patient flow are at point of entry to, and point of exit from, the ED.

At point of entry, patients undergo triage primarily to determine urgency for care. Those triaged as most urgent will be seen by a doctor before those triaged as less urgent. The waiting time to see a doctor will be determined by a number of factors, but particularly the medical resource available, the nursing resource, and the physical space available to accommodate the patient for medical assessment, as well as the number of patients waiting and their mix of urgency as determined by the triage process.

Once seen by a doctor, the barrier to moving to the next phase of care is also contributed to by a variety of factors, including difficulty accessing a hospital bed, but also difficulties in decision making manifest by ongoing investigations and assessment of the patient.

The authors recognised that a proportion of patients presenting to an ED required little or no decision making, as their needs were readily apparent. However these patients are not identified by the triage process, which purely identifies urgency for care, rather than a capacity to be managed quickly. Indeed these patients would frequently wait for medical attention in a treatment area, thereby denying the treatment area for patients waiting in the waiting rooms or in corridors.

The aim of this study was to introduce another dimension to triage, the rapid assessment clinic (RAC), to determine if this would reduce the waiting times and times in the department for all patients.

Methods

For ten weeks from 28th February 2000, an additional nurse and an additional ED registrar were rostered a 0900 to 1700hr shift Monday to Friday. On the odd weeks, these two staff ran a RAC and on even weeks, they did not run a RAC, but simply joined the other medical and nursing staff, managing patients in the traditional way. A total of two nurses and five emergency medicine registrars were rostered to RAC duties. The RAC was held in the same two adjacent cubicles for the duration of the study.

From 0900 to 1700hr Monday to Friday during the odd weeks, the triage nurse would identify patients who could be managed in the RAC. During the even weeks, patients would be triaged in the usual way, without identifying those suitable for rapid assessment. Patients suitable for the RAC were those for whom disposal was readily apparent, interventions required were quickly undertaken, and lengthy investigations or assessment were not required. Suitability for the RAC was independent of triage category and although it tended to include a disproportionate number of lower triage category patients, no triage category was exempt. A list of patients suitable for the RAC was provided to the triage nurses (Table 1).

After the ten-week period the five weeks of the RAC and the five weeks with no RAC, but the same staffing level, were analysed and compared, using the week as the unit of analysis, which is a conservative analytic strategy.

The RAC weeks and the control weeks were compared for total patient presentations to the ED, the waiting time to be seen by a doctor and the length of time in the department. Data for those who went through the RAC clinic were not specifically analysed, but instead data were analysed for all patients in the department. The reason for this was that it would be easy to show that those patients put through a RAC are seen rapidly and dispatched promptly, but it was the purpose of this study to determine if the RAC improved patient flow for the department overall. In addition, prospectively identifying ‘rapid assessment type’ patients during the control weeks would have altered the way they were managed by ‘flagging’ them as quick patients.

Table 1. Patients suitable for the rapid assessment clinic.

- Minor orthopaedic patients who could be referred quickly to the Orthopaedic Fracture Clinic.
- Patients with deformed limbs after trauma who need prompt intravenous access and analgesia prior to referral to the fracture clinic.
- Partial thickness burns of less than 10% body surface area, (ie minor burns)
- ?Deep venous thrombosis for ultrasound
- ?Neutropenic oncology patient – for quick intravenous access, antibiotics, bloods to laboratory and referral to Oncology.
- Fractured nose without wound.
- Possible facial fracture for x-ray
- Possible ingested foreign body in children
- Possible pneumothorax in a well young adult
- Medical triage of patients accepted already by inpatient services
- Likely torsion of testicle
- Paediatric ingestions of poisons in a well child
- GP referrals to the Paediatric Assessment area, who need medical review prior to transfer
- Follow up of eye problems for slit lamp examination
- Children with fever or asthma, who are triage categories 3, 4 or 5.
- Minor wounds requiring only minor interventions such as steri-strips and dressings.
- Follow up dressings for wounds managed in the Emergency Department previously.
- Any others for whom disposal is apparent and Emergency Department interventions are likely to be brief.

NB: Any patients, after medical assessment, who needed more thorough ED assessment or treatment would be referred to another part of the ED for management by doctors and nurses who are not running the rapid assessment clinic.

For each week the mean times were calculated, thus producing five replicates for the RAC period and five for the non-RAC period. There was a considerable amount of missing data for the time to see a doctor and this was mostly due to a number of patients who left the department without seeing a doctor (nurse initiated referrals to Orthopaedic Outpatients or the Children's Acute Assessment Area, or patients who did not wait to be seen). There were no missing values in the length of time in the department but there were a number of extreme outliers which were thought to result from staff recording disposal subsequent to the event. Because of the skew in both time variables and because of the outliers the median was also calculated for each week which produced a very similar pattern of results to that obtained from the weekly means.

The raw data were extracted from the ED module of PMS, the Patient Management System used at Christchurch Hospital. Analysis was carried out in SAS using PROC FREQ and PROC TTEST[2].

Results

During the five weeks of the RAC clinic (0900 to 1700hr Monday to Friday) a total of 2263 patients attended the ED, and 361 of these were referred to the RAC clinic. Of the 361 patients managed in the RAC there were 235 males and 126 female patients and their age distribution and presentation by weeks of the trial are given in Table 2. A list of their presenting problems is given in Table 3.

Table 2. Age range and number of patients seen in the rapid assessment clinic.

	Week					
Age Range	Week 1	Week 3	Week 5	Week 7	Week 9	Total (%)
0-4 Years	6	5	9	6	3	29 (8)
5 to 9 Years	7	2	4	4	3	20 (6)
10 to 14 Years	6	1	6	4	1	18 (5)
15 to 19 Years	8	3	8	5	2	26 (7)
20 to 39 Years	22	26	34	27	16	125 (35)
40 to 59 Years	15	10	26	18	6	75 (21)
60 to 69 Years	2	11	4	3	1	21 (6)
70 to 79 Years	5	9	2	6	5	27 (7)
80 years and over	4	7	3	3	3	20 (6)
Total	75	74	96	76	40	361

Table 3. Presenting problems and the number of patients who presented to the rapid assessment clinic.

Limb injury	86
Deep venous thrombosis	43
Wound	37
Eye problem	28
Finger injury	24
Specialty admission, requiring brief ED assessment	19
Wound infection	17
Facial injury	15
Ingestion of medication by children	8
Ingestion of foreign body by children	7
Minor chest injury	7
Back pain	4
Abdominal pain, ?cause	3
Renal colic	3
Spontaneous pneumothorax	3
Follow up of wound care	4
Minor burn	3
Febrile child	3
Irritable hip	3
Croup	3
Immunisations	4
Pilonidal sinus	4
Head injury	5
Testicular torsion	3
Bursitis / arthritis	4
Foreign bodies in ear	3
?fractured neck of femur	2
Post ictal patients	2
Other	14

During the five control weeks (0900 to 1700hr Monday to Friday) a total of 2204 patients attended the ED, and a retrospective review of presenting complaints undertaken by the authors identified 349 patients who would most likely have been triaged to the RAC, had it been running.

Table 4. Triage category breakdown for all patients presenting during the RAC (study) and non–RAC (control) periods and comparison with RAC–only patients.

Triage Category	RAC periods (%)	Non-RAC periods (%)	RAC-only patients (%)
1	19 (1)	19 (1)	0 (0)
2	196 (9)	206 (9)	10 (3)
3	910 (40)	837 (38)	80 (22)
4	969 (43)	986 (45)	210 (58)
5	168 (7)	156 (7)	61 (17)
Total	2262*	2204	361

* One patient coded as Triage=0. (RAC-only patients are those managed in the RAC). RAC = rapid assessment clinic.

A comparison of the triage category breakdown for all patients presenting during the RAC periods and during the non-RAC (control) periods, and for patients managed in the RAC is given in Table 4. Combining over weeks, there was no significant difference in the distribution across triage categories between the RAC and non-RAC periods (χ^2=3.1, df=4, p=0.53).

Table 5. A comparison of average waiting time (in minutes) to see a doctor, by triage category, for RAC and non-RAC periods (sd across weeks given in brackets).

Triage	Measure	RAC period	Non-RAC period	Difference (95% ci)	P value
2	Mean	8.2 (1.9)	7.7 (1.4)	0.5 (-2.0,3.0)	0.65
	N over 5 weeks	169	177		
	Missing*	27	29		
3	Mean	29.7 (4.4)	28.4 (1.5)	1.3 (-3.4,6.1)	0.54
	N over 5 weeks	822	765		
	Missing*	88	72		
4	Mean	34.5 (3.4)	42.7 (3.0)	-8.3 (-12.9,-3.6)	0.004
	N over 5 weeks	862	875		
	Missing*	107	111		
5	Mean	34.3 (4.7)	45.4 (6.7)	-11.2 (-19.6,-2.8)	0.02
	N over 5 weeks	148	133		
	Missing*	20	23		

*See Methods. RAC = rapid assessment clinic.

The waiting times to be seen by a doctor are outlined in Table 5, which compares the RAC and the non-RAC (control) periods within each triage category. Each summary measure has been averaged over the five relevant weeks. The pattern of results is for no difference at Triage 2 and 3 categories and a difference of several minutes for Triage 4 and 5 categories. These results cannot be attributed to different amounts of missing data as 10.8% of times were missing in both the RAC and non-RAC periods.

The times patients spent in the ED are shown in Table 6 for RAC and non-RAC periods. Note that time in the department includes time undertaking imaging in the

Department of Radiology. The pattern of results is similar to that for time to be seen by a doctor, with no difference for Triage 2 and 3 and about 20 to 25 minutes advantage for RAC-week patients in Triage categories 4 and 5. However because of the extreme variability in length of time in the department these differences are not precisely estimated, especially for Triage category 5 which had only a sixth as many patients as Triage category 4.

Table 6. Average time in department (in minutes) by triage category, for all patients presenting during RAC and non-RAC periods (sd across weeks given in brackets).

Triage	Measure	RAC period	Non-RAC period	Difference (95% ci)	p value
2	Mean	172 (20)	193 (36)	-22 (-64,21)	0.28
	N over 5 weeks*	196	206		
3	Mean	190 (21)	191 (8)	-1 (-24,23)	0.95
	N over 5 weeks*	910	837		
4	Mean	131 (4)	158 (23)	-27 (-51,-3)	0.03
	N over 5 weeks*	969	986		
5	Mean	65 (12)	85 (16)	-19 (-40,1)	0.06
	N over 5 weeks*	168	156		

*No missing data – see Methods

Discussion

The purpose of this study was to determine the value of a RAC in improving patient flow in an ED. The five RAC periods and the five control periods showed a similar number and triage profile of patients presenting, although it was also noted that average waiting times were not long. This is a reflection of the fact that the trial was undertaken at the department's least busy time. A previous study of patient presentations to Christchurch Hospital ED showed that winter and evenings had a consistently higher workload than summer and daytime, and that the weekends attracted a greater proportion of patients suitable for RAC management than weekdays[3]. Given the small proportion of patients going through the RAC and the paucity of barriers to patient flow during the quiet time of the study, this study will struggle to show a benefit to the department for a RAC. However despite this, the RAC did bring a reduction in waiting time to see a doctor, and time in department for the lower triage categories.

These findings confirm that the rapid management of patients with problems which do not require prolonged assessment or decision making, is not only beneficial to those patients, but also to other patients sharing the same, limited resources. The value of a RAC is likely to be much greater in the evenings, weekends and wintertime and this will be the subject of further study.

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Factors influencing alcohol consumption during pregnancy and after giving birth

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Abstract

Aims This study explored the demographic profile of women consuming alcohol during pregnancy and after giving birth, as part of a larger cohort study of smoking during pregnancy.

Methods This was a prospective study of a cohort of 665 women registered with a maternity care provider organisation for antenatal care in Wellington. Data were collected from postal questionnaires sent at intervals during gestation and the postnatal period. The questionnaires elicited information about smoking, alcohol consumption and demographic data.

Results At 24 weeks gestation, 74% of women reported not consuming any alcohol in the preceding seven days. Women who were pregnant for the first time, women who experienced nausea, women who were socio-economically deprived and women who smoked were less likely to report having consumed alcohol. At six weeks after giving birth the number of women reporting not consuming any alcohol in the preceding seven days decreased to 46%. Socio-economic deprivation was associated with abstention and tertiary education with alcohol consumption.

Conclusions Approximately a quarter of women continue to drink alcohol during pregnancy. Health education aiming to reduce alcohol consumption in pregnancy needs to take into account the profile of women who drink during pregnancy.

In first world countries such as New Zealand, there has been increasing concern about alcohol consumption during pregnancy because of its damaging and long-term effects on the foetus. A substantial body of evidence points to the dangers of heavy drinking and there is increasing evidence that even light consumption may give rise to long-term problems.[1-3]

Two recent New Zealand studies show that approximately a quarter of all pregnant women continue to drink after pregnancy recognition with a significant number drinking at intoxicating and damaging levels.[4,5] The general directions for limiting the harm caused by alcohol have been set by the National Alcohol Strategy 2000-2001,[6] and a number of initiatives directed specifically towards reducing the consumption of alcohol by pregnant women are currently underway.[7]

The effectiveness of policies and initiatives aimed at reducing alcohol consumption during pregnancy will be enhanced if the social characteristics and health beliefs of those who drink at this time are well understood. Data on alcohol consumption collected prospectively from a cohort of Wellington women as part of a study of smoking behaviour are reported in this paper.

Methods

Study population. The study population consisted of all pregnant women who registered with the maternity care provider, 'Matpro' for their antenatal care by the time they were 24 weeks pregnant. 'Matpro' is an organisation of midwives, general practitioners and specialists contracted to provide primary maternity care. In New Zealand primary maternity care is usual care and Matpro providers deliver 95% of all primary maternity care in the Wellington City, Porirua and Kapiti area of New Zealand, the locality in which the study took place.

Data collection. All 1047 women registering with 'Matpro' for their antenatal care by the time they were 24 weeks pregnant with last menstrual period (LMP) dates over a six month period were eligible for inclusion. 75 women became ineligible for inclusion as a result of miscarriage, termination of pregnancy or moving from the locality. All eligible women were sent a questionnaire when they were 20-24 weeks pregnant. 665 (68.4%) consented to take part in a longitudinal study. Further questionnaires were sent at 36 weeks gestation and at 6-10 weeks postpartum. Dates for mailing follow-up questionnaires were based on the expected delivery date. Questionnaires were mailed in monthly batches. A reply paid and addressed envelope was included for replies. Non-responders were sent one reminder letter and a further copy of the questionnaire. Data on alcohol consumption were collected at 20-24 weeks gestation, 36-40 weeks and at 6-10 weeks postpartum. Alcohol consumption data were collected by asking women "on how many days in the last seven days would you say you drank any type of alcohol?" The following pre-coded responses were available: every day, 5-6 days, 3-4 days, 1-2 days, no days, don't know.

Ethics approval for the study was granted by the Wellington Ethics Committee, accredited by the Health Research Council of New Zealand.

Analysis. Data were entered into a Microsoft Access database. Ten percent of data entered were manually checked against questionnaires. Data were transferred to SAS and odds ratios and 95% confidence intervals (CI) calculated. Selection of variables to find the model that best predicted the outcome of interest was performed using stepwise regression. Variables included in the model were ethnicity, tertiary education (defined as any post secondary school diploma, degree or other qualification), Community Service Card (CSC) status (a subsidy available for health care for low income earners), whether the pregnancy was planned, whether nausea had been experienced during the pregnancy and smoking status. Ethnicity data were collected using the ethnicity question from the 1996 New Zealand Census which asked people to tick as many boxes as necessary to show which ethnic group(s) they belonged to. In the analysis Maori were defined as women identifying either as sole Maori or Maori plus another ethnic group.

For a sample of 600 with α_2=0.05 and power of 80%, a difference of 10-13% could be detected between the two groups defined by a particular predictor variable, with the difference depending on whether the sample was split 50/50 or 70/30 on that variable, and if one of the groups had 30% of women reporting drinking.

Results

Response rate. The first questionnaire at 20-24 weeks gestation was sent to 1117 women: 665 (68.4%) responded. The second questionnaire was sent to 639 women and responses were received from 559 (87.5%). The third was sent to 634 women and responses received from 548 (86.4%).

Was the cohort representative? Grouped demographic data from a subset of women who did not respond to the 20-24 week questionnaire were available from the Wellington Hospital Perinatal Information Monitoring System (PIMS). When compared to responders, non-responders included a higher proportion of women who were not married or in a defacto relationship (11% vs 24%; χ^2= 17.8, p=0.001), women who smoked (14% vs 26%; χ^2= 18.9, p=0.001), had no tertiary education (35% vs 49%; χ^2= 10.8, p=0.001) or were receiving a benefit (8% vs 19%; χ^2= 14.9,p=0.001). The mean age of non-responding women (29.9 years) was slightly lower than responding women (31.9 years) (χ^2= 18.6; p=0.001). It is possible that some of these differences reflect the characteristics of the subgroup of women

delivering at Wellington Hospital for whom PIMS data were available. Data were not available for women delivering at other hospitals in the region and these hospitals, although smaller, served localities with a higher proportion of socio-economically deprived women. There was no difference between responders and non-responders in alcohol consumption data recorded on PIMS, weeks gestation, parity, gravida, baby's birthweight or Apgar score.

Antenatal alcohol consumption. At 20-24 weeks 487 women (73.8%) responding to the question had not consumed any alcohol in the preceding seven days and 26 women (3.9%) had consumed alcohol on three or more days. At 36-40 weeks rates of alcohol consumption were similar. At 20-24 weeks abstention was associated with socio-economic deprivation as measured by CSC status (OR 0.34) and by receipt of income support (OR 0.48), current smoking (OR 0.55), first pregnancy (0.58) and experiencing nausea or vomiting (OR 0.66) (Table 1).

Table 1. Women who had consumed any alcohol during the last seven days, at 20-24 weeks gestation.

		Number in cohort	Women who consumed alcohol		Univariate analysis (OR)	95% CI
		N	n	%		
Employed	Yes	401	111	27.7	1.30	0.89-1.89
	No	233	53	22.8		
CSC holder*	Yes	122	15	12.3	**0.34**	**0.19-0.61**
	No	520	151	29.0		
Receives income support	Yes	114	18	15.8	**0.48**	**0.28-0.82**
	No	516	145	28.1		
Maori	Yes	66	13	19.7	0.69	0.37-1.30
	No	588	154	26.2		
Has tertiary education	Yes	363	95	26.2	1.05	0.73-1.52
	No	258	65	25.2		
First pregnancy	Yes	256	50	19.5	**0.58**	**0.40-0.85**
	No	398	117	29.4		
Planned pregnancy	Yes	471	123	26.1	1.22	0.81-1.83
	No	178	40	22.5		
Smoker at 20-24 weeks	Yes	100	17	17.0	**0.55**	**0.32-0.96**
	No	552	150	27.2		
Experienced nausea	Yes	489	115	23.5	**0.66**	**0.45-0.98**
	No	161	51	31.7		

*Community Services Card (CSC) held or applied for (Income level for a couple with 1 child <$32000 pa).

A forward stepwise regression model yielded three significant predictors of lower alcohol consumption: CSC status (OR 0.31; 95% CI 0.17-0.58), first pregnancy (OR 0.47, 95% CI 0.31-0.71) and nausea (OR 0.60, 95%CI 0.39-0.91) (each odds ratio is controlled for the other variables in the model).

Alcohol consumption after giving birth. At 6-10 weeks postpartum, 247 women (45.7%) responding to the question had not consumed any alcohol in the preceding seven days and 89 women (16.4%) had consumed alcohol on three or more days. Alcohol consumption was associated with tertiary education (OR 1.46) (Table 2). Abstention was associated with socio-economic deprivation as measured by CSC status (OR 0.44). A forward stepwise regression model yielded one predictor of lower

alcohol consumption: CSC status (OR 0.40, 95% CI 0.23-0.69). Current smokers were more likely to have consumed alcohol (OR 2.00 95% CI 1.09-3.58).

Table 2. Women who had consumed any alcohol during the last seven days, at 6-10 weeks postpartum.

		Number in cohort	Women who consumed alcohol		Univariate analysis (OR)	95% CI
		N	n	%		
Employed	Yes	343	197	57.4	1.32	0.92-1.90
	No	178	90	50.6		
CSC holder*	Yes	77	29	37.7	**0.44**	**0.27-0.73**
	No	259	259	57.7		
Receives income support	Yes	79	39	49.4	0.77	0.48-1.24
	No	440	246	55.9		
Maori	Yes	47	22	46.8	0.73	0.40-1.33
	No	490	268	54.7		
Has tertiary education	Yes	307	177	57.7	**1.46**	**1.02-2.08**
	No	203	98	48.3		
First pregnancy	Yes	210	118	56.2	1.16	0.82-1.64
	No	325	171	52.6		
Planned pregnancy	Yes	400	225	56.3	1.48	0.99-2.19
	No	131	61	46.6		
Smoker at 20-24 weeks	Yes	67	40	59.7	1.30	0.78-2.19
	No	470	250	53.2		
Experienced nausea	Yes	403	213	52.9	0.86	0.58-1.28
	No	129	73	56.6		

*Community Services Card (CSC) held or applied for (Income level for a couple with 1 child <$32000 pa).

An increase in the number of days in the last seven on which alcohol was consumed between 20-24 weeks gestation and six weeks after giving birth was associated with tertiary education (OR 1.52). No increase was associated with socio-economic deprivation as measured by CSC status (OR 0.58) (Table 3). A forward stepwise regression model yielded only one predictor for increased alcohol consumption: tertiary education (OR 1.52, 95% CI 1.05-2.20).

Discussion

This prospective cohort study provides some information about the profile of New Zealand women consuming alcohol during pregnancy and after giving birth. The cohort studied was broadly representative of urban New Zealand as a whole. However, socio-economically deprived women were likely to be under represented in the responding group, probably due to the choice of postal questionnaire as the method of data collection.

The number of women in the cohort who reported consuming alcohol increased after giving birth compared to that reported during pregnancy. This postpartum increase implies that a reduction in consumption occurred related to the pregnancy, suggesting many New Zealand women are aware of at least some of the risks of alcohol consumption during pregnancy. A reduction in the quantity of alcohol consumed and the frequency of consumption after recognition of pregnancy has also been identified in other New Zealand studies.[4,8]

Table 3. Women who had increased their alcohol consumption by 6-10 weeks post partum.

		Number in cohort	Women who increased alcohol†		Univariate analysis (OR)	95% CI
		N	n	%		
Employed	Yes	346	145	41.9	1.16	0.80-1.68
	No	180	69	38.3		
CSC holder*	Yes	77	23	29.9	**0.58**	**0.34-0.98**
	No	453	192	42.4		
Receives income support	Yes	79	31	39.2	0.93	0.57-1.52
	No	444	182	41.0		
Maori	Yes	48	15	31.3	0.66	0.35-1.24
	No	492	201	40.9		
Has tertiary education	Yes	311	136	43.7	**1.52**	**1.05-2.19**
	No	204	69	33.8		
First pregnancy	Yes	213	93	43.7	1.29	0.91-1.83
	No	327	123	37.6		
Planned pregnancy	Yes	402	168	41.8	1.33	0.89-2.00
	No	134	47	35.1		
Smoker at 20-24 weeks	Yes	67	31	46.3	1.33	0.80-2.23
	No	471	185	39.3		
Experienced nausea	Yes	406	163	40.2	1.05	0.70-1.58
	No	131	51	38.9		

*Community Services Card (CSC) held or applied for (Income level for a couple with 1 child <$32000 pa). †Includes women who continued to drink every day.

Approximately a quarter of women in the cohort studied continued to drink to some extent during their pregnancy. Rates of 19% at full-term were reported in a study of women attending a Dunedin hospital in 1989.[9] In a more recent study of nutrition during pregnancy in a sample of North Island women, 29% of those surveyed continued to drink to at least some extent during pregnancy.[4] In the current study women who continued to drink were more likely to be European, to have planned their pregnancy and to be in the middle and higher socio-economic groups.

The current study did not provide information about the amount of alcohol consumed by women continuing to drink. However, Watson and McDonald found women who binged and drank heavily during pregnancy were disproportionately Maori or Pacific women, women under 25 years and those in a lower socio-economic group.[4]

In discussing alcohol consumption with pregnant women, health professionals need to be aware that while women from higher socio-economic groups are more likely to continue to drink during pregnancy, heavy or binge drinking is more likely to be undertaken by younger women, socio-economically deprived women and Maori women.

The health professional's role in providing advice about alcohol consumption during pregnancy is complicated by the fact that it is not clear whether the effect of alcohol consumption is linear, implying that there is no safe level of alcohol consumption during pregnancy or whether there is a threshold, implying a safe level of drinking.[2] Research on animals suggests that the relationship between alcohol consumption and central nervous system development may have a threshold but the relationship with physical growth may be linear.[2] However, there is strong evidence that heavy drinking[1] and binge drinking[2,10,11] adversely affect foetal outcomes. Current advice to health providers is conflicting. Curtis[12] in her advice to New Zealand health

professionals promotes total abstinence during pregnancy as do more recent New Zealand publications and resources directed at health professionals.[13] In contrast the Royal College of Obstetricians and Gynaecologists (UK) recommends limiting alcohol consumption to no more than one standard drink per day.[14] A 1999 survey of midwives, in reporting that the majority indicated a need for further training to facilitate communicating information about alcohol to their clients,[5] highlighted the problems facing health professionals in deciding which advice to follow when advising patients. More information is needed to enable the development of clear, evidence-based recommendations for health professionals regarding the advice they can give to pregnant women about safe levels of alcohol consumption.

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House dust mite allergen levels in University student accommodation in Dunedin

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Abstract

Aim To quantify the levels of *Dermatophagoides pteronyssinus* (*Der p1*) in different university student accommodation in Dunedin, and to assess relationships with housing characteristics and housekeeping practices.

Methods Dwellings (n=178) were randomly selected from a database of first year university students in Dunedin. Dust samples were collected from both bed and the bedroom floor by standardised procedures. *Der p1* levels were quantified by monoclonal antibody ELISA techniques. Details of housing characteristics, occupancy and housekeeping practices were obtained by questionnaire.

Results Geometric mean (95% confidence intervals) *Der p1* allergen levels from bedroom floors were: family homes (n=61) 5.58 (3.73-8.36) μg/g; student flats (n=43) 3.89 (2.49-6.07) μg/g; halls of residence (n=74) 0.26 (0.16-0.43) μg/g. *Der p1* allergen levels from beds were: family homes 15.85 (9.78-26.57) μg/g; student flats 10.5 (6.41-17.19) μg/g; halls of residence 3.25 (2.33-4.54) μg/g. In all accommodation lower levels of *Der p1* were found on the floor compared to the bed ($p<0.005$). Halls of residence had significantly lower *Der p1* levels in both bed and floor ($p<0.0005$). Higher levels of *Der p1* were associated with longer duration of occupancy, a history of condensation or mold in the accommodation, failure to use a hot wash for sheets, mattress age greater than one year and infrequent vacuuming of the bedroom floor.

Conclusions Wide variations in *Der p1* levels were observed between different forms of student accommodation. Higher levels of *Der p1* are found in family homes than in student flats or halls of residence.

House dust mite allergen, *Dermatophagoides pteronyssinus (Der p1)* exposure is a major risk factor for the development and maintenance of asthma in genetically susceptible individuals. Around one third of the population sufficiently exposed to house dust mite will become sensitised, particularly families with a history of atopy.[1] The suggested threshold for sensitisation to *Der p1* is 2 μg/g house dust, with the threshold for exacerbation of symptoms being 10 μg/g.[2]

The temperate New Zealand climate with high year round outdoor humidity has been found to be highly conducive to house dust mite growth and proliferation. As a result, New Zealanders are exposed to higher levels of *Der p1* in their domestic environments than individuals in other countries.[3,4] Relatively low levels of *Der p1* have been documented in Canada,[5] Denmark[6] and Sweden,[7] with relatively higher levels in the United Kingdom[8] and the Netherlands.[9] However the highest *Der p1* allergen levels have been measured in coastal Australia (mattress levels 22.5 μg/g,

bedroom floor levels 21.6 μg/g in Sydney)[10] and in New Zealand (mattress levels 46.6 μg/g, bedroom floor levels 26.4 μg/g in Wellington).[3]

Otago university students make up a relatively large and unique subsection of the Dunedin population. Many live in low cost, poorly maintained rental accommodation. Others live in newer-style but often underventilated flats. Furnishings, curtains and carpets are generally old and/or dusty in these flats. Students living in the close confines of the halls of residence have no choice in the types of bedding or flooring used or the frequency of bed linen changes, and may not have access to a vacuum cleaner. Previous studies have identified such environments as promoting house dust mite proliferation.[9,11-13] Assessment of the *Der p1* levels in the various forms of accommodation may give us some insight into risk factors for asthma morbidity in the university student population.

This study aimed to quantify the levels of *Der p1* in different university student accommodations in Dunedin, and to assess the relationship between allergen levels, housing characteristics and housekeeping practices. Levels of *Der p1* had not previously been measured in the city. Whereas the New Zealand environment differs from other countries, the Dunedin climate is not comparable to other New Zealand cities hence data on *Der p1* levels from earlier studies could not easily be extrapolated.

Methods

Subjects. A database of 1730 Otago University first year students was established from a short questionnaire administered at the commencement of the 1998 academic year. Student dwellings (n=178) were randomly selected from this database, following grouping according to the type of accommodation. All students were in their first year of University study in Dunedin and had lived in their accommodation for at least six weeks prior to the study. A history of asthma or allergy was not required.

Design. The study was cross-sectional, involving the assessment and measurement of *Der p1* levels in three different forms of student accommodation: family homes (including boarding arrangements), student flats and halls of residence.

Visits took place between May-September 1998. In each dwelling, reservoir dust samples were collected from two different sites, the bedroom floor and the bed. Floor samples were taken from the area adjacent to the bed. Samples were collected from $1m^2$ area of carpeted floor or $2m^2$ of uncarpeted floor. Rugs and other removable floor coverings were removed prior to sampling. Bed samples were taken from $1m^2$ area of the top of the mattress.

Sampling was performed using an Hitachi CV-2500, 1100 watt vacuum cleaner, with a small furniture head attachment. A 15 cm length collection sock, made of 25μm pore-sized nylon mesh (nytel HP25), was attached to the furniture head. Each area was vacuumed for one minute using firm pressure. The floor sample was obtained before the bed sample and a new vacuum cleaner head was used for the collection of each sample. The sock containing the sample was tied then frozen at –20 °C until further preparation in the form of sieving and weighing of the sample was carried out. Weighed fine-sifted (425 μm) dust samples were extracted in phosphate-buffered saline at room temperature for 30 minutes, and *Der p1* levels in the centrifuged extracts were estimated by double-monoclonal antibody ELISA.[14]

At the time of dust sampling, details of housing characteristics, occupancy and housekeeping practices were obtained by questionnaire.

Analysis. Floor and bed samples of *Der p1* were analysed separately. *Der p1* levels were log-transformed and compared by site and between dwelling groups by one-way analysis of variance. Multivariate analyses were done by linear regression of the log-transformed *Der p1* levels.

The study was approved by the Otago Regional Health Authority Ethics Committee.

Results

Bedroom dust samples and questionnaire data were obtained from all 178 students enrolled in the study. Accommodations were grouped into family homes (n=61), student flats (n=43) and halls of residence (n=74).

Der p1 concentrations were significantly higher in dust from beds than from bedroom floors in the three forms of student accommodation (Table 1). There were significantly lower levels of *Der p1* in halls of residence compared with family homes and student flats.

Table 1. Geometric mean (95% confidence intervals) Der p1 allergen levels according to type of accommodation.

Type of accommodation	n	Bedroom floor μg/g	Bed μg/g	p value
Family home	61	5.58 (3.73-8.36)	15.85 (9.78-26.57)	<0.001
Student flat	43	3.89 (2.49-6.07)	10.50 (6.41-17.19)	<0.003
Halls of residence	74	0.26 (0.16-0.43)	3.25 (2.33-4.54)	<0.0005
p value		<0.0005	<0.0005	

Univariate analysis showed significantly higher floor levels of *Der p1* associated with the type of accommodation (p=0.0005), fewer than fifteen people sharing the accommodation (p=0.0005), occupancy of their current accommodation for longer than two years (p=0.0005), the presence of a washing machine or clothes drier inside the accommodation (p=0.0005), pets inside the accommodation (p=0.0005), the use of electric or central heating (p=0.0005), infrequent vacuuming of the bedroom floor (p=0.0005), failure to use a hot wash for sheets (p=0.0005), a history of condensation or mold inside the accommodation (p=0.005), the sharing of the accommodation with a smoker (p=0.004) and failure to vacuum the mattress (p=0.03).

Univariate analysis showed significantly higher bed levels of *Der p1* associated with a mattress greater than one year of age (p=0.0007), the type of accommodation (p=0.0005), fewer than fifteen people sharing the accommodation (p=0.0005), occupancy of their current accommodation for longer than two years (p=0.0005), the presence of a washing machine or clothes drier inside the accommodation (p=0.0005), pets inside the accommodation (p=0.0005), the use of electric or central heating (p=0.0005), infrequent vacuuming of the bedroom floor (p=0.0003), failure to use a hot wash for sheets (p=0.0001), a history of condensation or mold inside the accommodation (p=0.005), a history of asthma in the occupying student (p=0.026) and the sharing of the accommodation with a smoker (p=0.01). There was no association between bed *Der p1* levels and vacuuming of the mattress.

The type of accommodation that the student was living in had a major influence on the measured allergen levels. When the type of accommodation was adjusted for by multivariate regression analysis, higher floor levels of *Der p1* were associated with fewer people sharing the accommodation (p=0.035), the presence of a washing machine inside (p=0.02), the presence of a clothes drier inside (p=0.01) and an electric heater being used as the primary form of heating (p=0.006).

When the type of accommodation was adjusted for by multivariate regression analysis, higher bed levels of *Der p1* were associated with a longer duration of residence in Dunedin (p=0.0005), a longer duration (>2 years) of occupancy of the

current accommodation (p=0.004), a mattress greater than one year of age (p=0.0005) and an electric heater being used as the primary form of heating (p=0.03).

No association was demonstrated between *Der p1* levels and the sex of the student, use of a mattress cover, type of mattress on the bed, the washing of bedding, age of carpet in the bedroom, the presence of carpet or rugs on the bedroom floor, a lack of heating in the accommodation or the frequency of clothes drier and washing machine usage.

Detailed tables of results are available from the authors on request.

Discussion

Dunedin is a city where, during the university term, approximately 10% of the population is composed of University of Otago students. This study was designed to quantify levels of *Der p1* in university student accommodation and determine factors that might influence the levels.

We found that *Der p1* levels varied widely between the three different forms of student accommodation. Students were exposed to higher levels of the allergen living in family homes, boarding environments and in student flats when compared with halls of residence. Similar low levels of *Der p 1* have been demonstrated in University Colleges compared with nearby homes in Sydney, Australia.[15]

A number of possible explanations exist for this difference. Rooms in halls of residences are cleaned and sheets laundered on a regular basis. These rooms tended to have low pile, commercial grade carpet and be well heated and ventilated. Halls of residences are typically vacant for a three month period over summer, possibly resulting in a fall in house dust mite levels from the ensuing reduction in food sources and humidity.

Other studies have shown that significant differences exist between *Der p1* levels in public buildings when compared to domestic dwellings.[16,17] Our results suggest that the level of *Der p1* students are exposed to in halls of residence is more in keeping with that of a public building. The geometric mean floor level of *Der p1* in halls of residence was 0.26μg/g, compared with 0.58μg/g measured in public buildings in two New Zealand cities.[16] The geometric mean bed level of *Der p1* in the halls of residence was 3.25μg/g, very similar to the 3.57μg/g measured in hotel beds in the same study.[16]

In all forms of accommodation the *Der p1* concentrations were significantly higher in dust collected from beds than from bedroom floors, consistent with results from both earlier New Zealand studies as well as overseas research. Indeed the *Der p1* levels measured in mattress dust in student flats and family homes were above the recognised threshold for the exacerbation of allergy symptoms, and bedroom floor levels exceeded the sensitisation threshold.[2]

Our results suggest that bed and floor *Der p1* levels may be influenced by different environmental factors. Higher bed levels were associated with factors relating to a longer duration of residence in the studied dwelling. Our finding of higher levels of *Der p1* allergen in mattresses greater than one year of age is in keeping with an earlier study by Custovic et al,[18] where it was demonstrated that mattresses can become a

significant source of exposure to mite allergens after as little as four months, with allergen levels generally stabilising after one year.

We found that higher floor levels of the allergen were associated with the presence of a washing machine and clothes drier inside. Although both factors may contribute to increased indoor relative humidity, there is uncertainity as to the importance of this in terms of *Der p1* levels. The design of our study did not allow for the actual measurement of relative humidity in the dwellings. Earlier studies[16,19,20] however have found that the measurements of relative humidity did not consistently correlate with the *Der p1* levels. Possibly the measure is an inadequate indicator of the more humid mite microclimate in beds and carpets or alternatively mite growth occurs independently of humidity once minimum conditions for mite breeding are satisfied.[19]

We were unable to demonstrate in our study a relationship between the *Der p1* levels and the use of a mattress cover or vacuuming of the mattress. This was most likely to be due to the low number of students practicing these measures, which are generally perceived as being for sufferers of asthma and allergy. Barrier covers have been advocated to trap house dust mites and their allergen inside the mattress. Although some studies have demonstrated a significant reduction in allergen levels with their use,[21,22] other studies have failed to show benefit.[23]

It is difficult to explain why, even after adjusting for the type of accommodation, higher floor levels of Der p1 were associated with fewer people sharing that accommodation. Although this negative correlation was also reported by Kuehr et al,[24] most studies have shown an association between increased occupancy and higher mites levels.[5,9,16] Our finding would suggest that in our accommodation environments, food supply may not be the most important factor in limiting mite population growth.

In conclusion, this study has demonstrated that significant variations in the levels of *Der p1* allergen can be found in different forms of university student accommodation. Students are exposed to lower levels of allergen living in halls of residence than in other types of accommodation. Further research needs to be carried out in order to determine the relative impact of differing allergen levels results on asthma and allergy symptoms in this population.

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Visitation of God

'Scrutator' (NZ Med J 202; 115: 266) should not have been surprised at seeing death ascribed to the 'Visitation of God'. It was very common in the middle of the nineteenth century to attribute sudden unexplained deaths to this cause. It had no direct association with insanity. Visitation was invariably spelt with a capital V in due homage to the Almighty.

I have seen the death certificates of two medical practitioners in New Zealand where death was blamed on this cause. The first victim was Dr John Dorset, Wellington provincial surgeon, who died suddenly a visit to Nelson. The local coroner, Dr J F Wilson, gave the cause of death as 'rupture of a blood vessel'. Another certificate was issued in Dorset's home town of Wellington and that gave the cause as 'Visitation of God'. Perhaps that may give us some clue to the actual cause. The other case occurred in Lyttelton in 1859. Dr James Vaux died suddenly and the coroner, Dr William Donald, stated the cause as 'Visitation of God'. Having doctors as coroners was very common until the Coroners Act 1885 ruled it out for doctors in practice.

As knowledge of pathology improved, many doctors came to dislike deaths being ascribed to 'Visitation of God', believing that it was unfair to blame God for deaths which were the result of pathological changes. There was some active correspondence in the British Medical Journal of 1874, the doctors condemning the traditional verdict and coroners defending it.

Dr R E Wright-St Clair
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A seasonal variation in breast cancer

Heather McIntyre, Jackie Blue, John Harman.

Abstract

Aim To demonstrate a seasonal variation in the detection of breast cancer in women diagnosed at St Marks Breast Centre, Auckland.

Method Data on women diagnosed with breast cancer at St Marks Breast Centre from January 1992 till December 2001 were obtained from the computerised database.

Results A total of 1760 women were diagnosed with breast cancer; 1584 were referred by their general practitioner and 176 self referred. The peak incidence of seasonal diagnosis was in spring (September, October, November) with 521 cases. The lowest incidence was in summer (December, January, February) with 375 cases. These findings were consistent annually from 1992 to 2001.

Conclusions There is a seasonal variation in the incidence of breast cancer similar to that noted in other studies. Our findings suggest that temporal factors and possible behavioural patterns may have a role in this seasonal variation.

A seasonal variation in the month of detection of breast cancer, with an increased incidence in the late spring/early summer, has been observed.[1-7] This variation has been related to both biological and behavioural factors.[1-3] Biological influence has been attributed to daylight-related hormonal factors while female health behaviour and the availability of health services are thought to account for behavioural factors. Some studies suggest that the month of diagnosis is a significant independent prognostic factor in breast cancer survival.[4] The aim of this study was to determine if there was a similar seasonal variation in women diagnosed at St Marks Breast Centre from 1992-2001.

Methods

The number of women presenting to the breast centre with a diagnosis of breast cancer was obtained from the breast cancer database. A monthly figure was obtained for each year from the opening of the breast centre in January 1992 up to December 2001. These figures were collated as both totals and percentages and compared for both the month and the season. In the southern hemisphere the summer months are December, January and February; the autumn months are March, April and May; the winter months are June, July and August; the spring months are September, October and November.

Results

The total number of women diagnosed with breast cancer at the breast centre from January 1992 to December 2001 was 1760; 1584 were referred by their general practitioner and 176 self- referred. The peak incidence of seasonal diagnosis was in spring (September, October, November) with a total of 521 cases. The lowest incidence was in summer months (December, January, February) with a total of 375 cases (Figures 1 and 2). November had the highest average number of cases per month (average = 21.6) and April the lowest (average = 10.7) – Figure 1. These findings were consistent for each year.

Figure 1. Average number of women diagnosed per month with breast cancer (1992-2001)

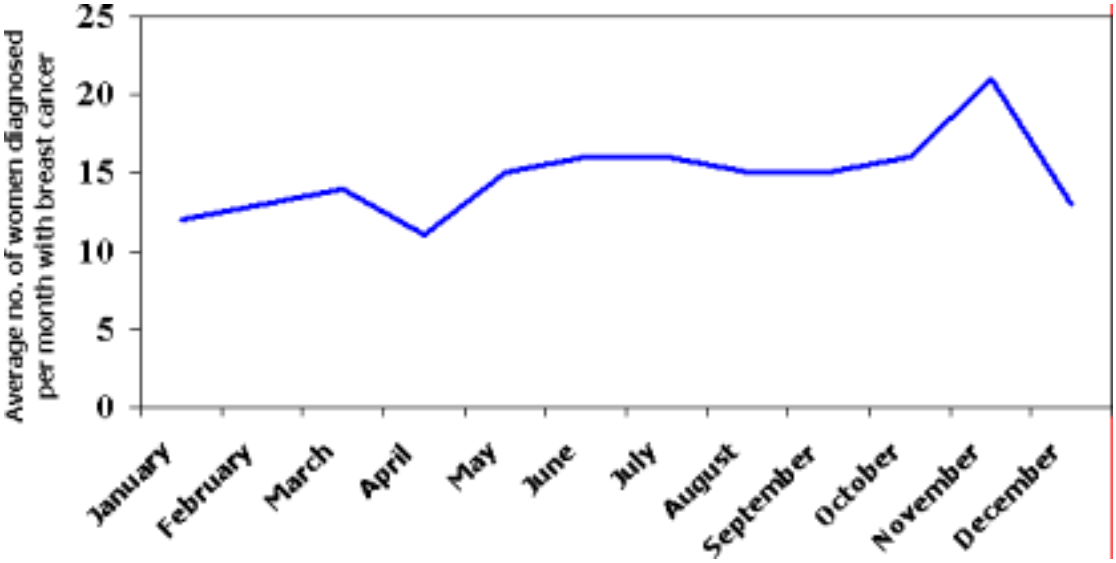
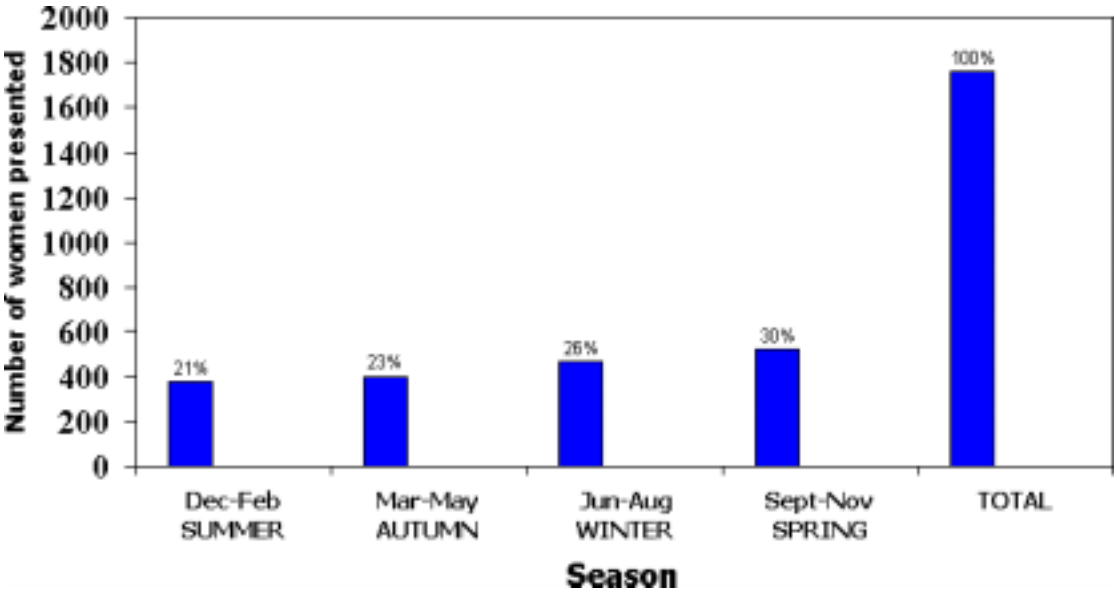


Figure 2. Seasonal variation in diagnosis of breast cancer in women presenting to St Marks Breast Centre, January 1992-December 2001



Discussion

The results of this study suggest there is a seasonal variation in the incidence of breast cancer in Auckland. There are no comparable figures available from the Auckland Breast Cancer Registry at the present time.

Our findings are in agreement with other studies that have demonstrated a seasonal variation in the incidence of breast cancer. However the data from this study show the peak incidence occurs in late winter-early spring, while other studies from both Northern and Southern hemispheres have found a peak incidence in late spring-early summer.

Some studies have attributed this seasonal variation to a biological factor involving the light responsive hormone melatonin and its cyclic secretion. It has been proposed that an excess exposure to environmental light may contribute to breast cancer risk via impaired pineal secretion of melatonin and its influence on ovarian function.

Seasonal changes in the levels of the steroid hormones oestrogen and progesterone have also been studied and are conflicting. Holdaway[3] showed a peak level of progesterone in spring that coincided with the peak incidence in breast cancer detection and that the detection of breast cancer may in part reflect the hormonal responsiveness of tumour tissue. Other studies that have shown a seasonal variation in the incidence of breast cancer have related the findings to behavioural factors.

A review of our data suggests that temporal factors such as holiday and work patterns along with possible behavioural patterns may also influence the seasonal incidence of breast cancer although, clearly, additional information is needed. The peak presentation occurred in November, which follows the national Breast Cancer Awareness month in October and this has been a consistent finding annually.

The number of women presenting to the breast centre declines in December and January in contrast to the findings of other studies. This decline following the peak presentation in November could reflect the Christmas and New Year holidays taken by both the women and health professionals. The study did not, however, show a 'catch up' period following this decline in presentation over the holiday period.

The low number of women diagnosed with breast cancer in April has been consistent annually and may be due to two behavioural factors. The financial year in New Zealand is at the end of March and might present a financial constraint that delays presentation. In addition, Easter and school holidays coincide with this time and it has been observed at this centre that women delay presentation over school holiday periods. Other factors, which may contribute to these findings, have not been addressed in this study.

In conclusion, our observations support a seasonal variation in the detection of breast cancer that may be influenced by behavioural factors.

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Cardiomyopathy in an Obese Man

A 70 year old Maori man was admitted to hospital after a two day history of severe breathlessness. He was massive, weighing 142 kg, and was almost moribund with cardiogenic shock. He was obtunded and unresponsive. Systolic blood pressure 70 mm Hg, and pulse rate 134 beats/min. Atrial fibrillation was present. Chest x-ray showed cardiomegaly and pulmonary congestion. Direct current cardioversion failed. Intravenous dobutamine, amiodarone, and frusemide had no effect. Electrocardiography showed no signs of acute myocardial infarction, and three troponin T tests over 6 hours were normal. Blood glucose was 7.6 mmol/L. He died after 6 hours.

He had been obese all his adult life. His parents and sibs were likewise obese. He did not smoke, and drank little alcohol. There were no cardiac deaths in the family. Three years before, his body weight was 136 kg and body mass index 45 kg/m^2. Blood pressure at that time ranged from 120/80 to 146/90 mm Hg. Random blood glucose 7.6 mmol/L. One year later he complained of shortness of breath and had signs of cardiac failure which was treated with cilazipril 0.5 mg daily and frusemide 40 mg daily.

At necropsy the heart weighted 836 g, left ventricular thickness was 23 mm, and right ventricular thickness 9 mm. There was no evidence of acute myocardial infarction, and the coronary arteries were patent with no atheroma. Heart valves were normal with no vegetations. Histology of the heart muscle was normal. There was no pulmonary embolus. He was considered to have cardiomyopathy of uncertain origin.

Patients presenting in cardiac failure of uncertain aetiology have been investigated, and cardiomyopathy has been distinguished into “ischaemic” and “non-ischaemic” groups. 50% of patients with “non-ischaemic” cardiomyopathy have no identifying aetiologic features, and are labelled ‘idiopathic’.[1] This patient could have fallen into this category. However, in the context of longstanding progressive obesity, the patient may have had cardiomyopathy of obesity.[2,3] Reported necropsy findings were identical with the present case.[4]

Weight reduction through diet is accompanied by regression of cardiac size to normal in cardiomyopathy of obesity.[5] Echocardiographic regression of cardiac dimensions can occur with cardiomegaly associated with obesity when the patient has undergone gastric restriction surgery[6,7], suggesting a treatment option in those patients who cannot otherwise lose weight. Treatment of patients with cardiomyopathy of obesity consists of *effective* weight reduction, however achieved, plus standard cardiac failure therapy of angiotensin converting enzyme inhibitors, loop diuretics, spironolactone, and beta-blockers.[8]

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Public support of tobacco taxation

A recent article in the Journal provided some valuable information about the support for key tobacco control measures by the New Zealand public.[1] Bans on tobacco advertising were supported by 70% of respondents, sponsorship bans by 60%, enforcement of the law prohibiting the sale of tobacco to minors by 89%, and support for government funded smoking cessation programmes by 72%. In contrast, only 40% considered that higher tobacco taxes would help people to quit smoking and only 38% considered that higher taxes would prevent children from becoming smokers. These attitudes on tobacco taxes contrast markedly with the strong scientific evidence that indicates that higher tobacco prices reduce consumption, increase quit rates and prevent children from becoming smokers.[2,3] More specifically, there is New Zealand evidence that tobacco taxation increases have consistently resulted in reduced supermarket cigarette sales[4]. Given that tobacco taxation is probably the most important single component of New Zealand's tobacco control programme, there is obviously a need for the government to change elements of its policy.

We suggest that public support for tobacco taxation would be much higher if a substantial proportion of the revenue was invested in prevention and smoking cessation services. This policy change *could* be achieved without tying the revenue to such investment, but would be much more likely to occur if a set or increasing proportion of the revenue was dedicated. The public perception of the link between the tax and the tobacco control work would also be much stronger.

The objections to tied taxes centre on their erosion of Government's decision-making ability. However, it is precisely because that decision-making has resulted in the Government's tobacco control investment being less than 3% of the tobacco tax revenue gathered,[5] that a tied tax is necessary. Furthermore, the revenue from tobacco taxation is unique in the degree to which it stems from the use of a highly addictive and dangerous substance. We consider that there are ethical issues raised where the Government taxes tobacco and then does not adequately use the revenue to reduce the level of nicotine dependency in the community. It appears to us to be both unethical and iniquitous for the Government to use tobacco tax revenue for general funding purposes.

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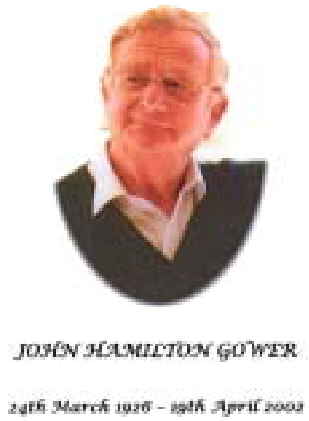
John Hamilton Gower

Dr John Hamilton Gower, born in the Superintendent's House at Waikato Hospital, 26th March 1926, the second child and only son of George and Elsie Gower, died 19th April 2002.



He spent his early years at the hospital until his parents built their home on the edge of Hamilton Lake. From an early age Dr Gower was surrounded by medicine and its institutions. His early schooling was at Hamilton West School until 1939 when he went to board at Wanganui Collegiate. Leaving Wanganui Collegiate towards the end of the war he spent a year at Auckland University completing Medical Intermediate. He found, however, that places at Medical School were preferred for returning soldiers so his solution to this was to travel to Ireland and attend The Royal College of Surgeons in Dublin. He arrived in Dublin in 1947. He had no family nearby and post-war Ireland was pretty dull and dreary, though being neutral throughout the war was not subject to rationing. His class was international and he made friendships, which have endured to this day.

Graduating from The College of Surgeons in 1952, Dr Gower worked his passage back to New Zealand on the Wellington Star as the Ship's Surgeon. He then began working as an Orthopaedic Registrar at Waikato and assisted his father in his private surgical practice. He met his future wife, Sue Fowler, who was a theatre sister at Waikato Hospital. They were married in 1956 but not before the Waikato vs Springbok match occasioned a change in wedding date.

John moved to Te Awamutu where he purchased a practice and settled into a successful family practice. In 1971 he was one of six GPs who amalgamated and were instrumental in designing and building a large family practice clinic (Gresham Clinic), completed in 1972. After 30 years this clinic still continues to reflect John's vision of patient centred family practice where GPs could share knowledge and experience, take in younger practitioners and create good conditions of work and rostered time off. He was manager during some of the development time and guided the team with his typical honest, caring attitude, always with high ethical standards, and emphasising that the most important person in the organisation was the patient.

He served on many medical and other advisory panels, as well as other public community boards.

From 1972 until 1991 he was the visiting GP to Matariki Hospital and he was the Waikato representative on the Waikato/Bay of Plenty Divisional Disciplinary Committee since 1987. He was a foundation member and president of the Waikato Division of Arthritis Foundation, and a past member of the Medical Advisory Panel to the Waikato Cancer Society. He was Branch President of the Waikato Division

NZMA in 1987. He was also a voluntary officer in the Territorial Force in First Field Ambulance, examiner of Army Boards, and served on the Boards of Governors of Te Awamutu College and St Paul's Collegiate.

Dr Gower was a Lion for 39 years, serving as president in 1967, and was elected to life membership of the Lloyd Morgan Trust in 2000. He was a visiting Medical Officer at Waikeria Prison until 1998. He retired from general practice in 1992. His patients missed his loyal advocacy on their behalf and his calm experienced, cradle to grave care. The staff and partners remember John for his forthright, caring and good-humoured approach to life, and a thoroughly professional attitude to his work.

Once John retired he kept up a very active life with golf, tramping and bridge, as well as time out with his family at the beach.

John is survived by his wife Sue, their children, Roger, Rachel, Campbell, Kaye and David, and ten grandchildren to whom we offer our condolences.

We are grateful to Dr Russ J Falconer for this obituary notice.

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Kevin Francis Greene

Born Ballyjamesduff, Co Cavan, Ireland, 21st October 1926.

Died Rotorua, New Zealand, 2nd May 2002.

Rotorua has lost one of its true health professionals with the death early on May 2nd of Dr Kevin Greene, the last person to hold at the same time the post of Medical Superintendent of Rotorua Hospital and Queen Elizabeth Hospital.

Dr Greene was appointed as Medical Superintendent of Rotorua Hospital in 1979, stepping into the senior medical role after practising for fourteen years as one of just two specialist obstetrician/gynaecologists operating in the Rotorua region. In 1983 Dr Greene was also appointed to the role of Medical Superintendent of Queen Elizabeth Hospital and he successfully held both positions through until his retirement in 1991. Through this time, the combined hospitals were the largest employer in the city, and through his role as Medical Superintendent, Dr Greene was involved to some degree with all branches of community care and health initiatives in the region. He was a foundation member of the Board of Trustees of the Rotorua Community Hospice and a member of the Board of Trustees of the Rotorua Continuing Care Trust.

The system of accreditation of hospital services and facilities which was refined at Rotorua Hospital under Dr Greene's stewardship opened another venue for service for the health professional. Over the six years following his retirement from the role of Medical Superintendent, he led or participated in the quality surveys of more than 130 hospital and rest home facilities in New Zealand.

Further service to the Rotorua community came in Dr Greene's capacity as the Chairman of the Board of Governors of John Paul College for six years, while Dr Greene's service ethos and community involvement was also evident in his leisure. A racing enthusiast, Dr Greene served on the Committee of the Rotorua Racing Club for twelve years, three of these years as the club's President. His battle with cancer curtailed his growing interest in the sport of bowls at his favourite Arawa greens.

Dr Greene was born in Ballyjamesduff, Co Cavan, Ireland, the youngest of five sons born to his schoolteacher parents, Thomas and Rose Greene. He graduated from University College in Dublin in 1949, practising first in England where he met and married his wife of the last fifty years, Belfast-born Elizabeth Stewart. The couple immigrated to New Zealand shortly after their marriage in 1952, Dr Greene practising as a general practitioner in the Hokianga, Auckland and Hamilton before gaining his specialist MRCOG qualifications in England in 1965 from where he returned to establish his practice in Rotorua. In 1979 Dr Greene was admitted as a Fellow to the Royal College of Obstetrics and Gynaecology.

At one point in his career as a GP in Hamilton, Dr Greene was delivering up to 200 babies a year, this interest ultimately steering him towards his speciality in obstetrics and gynaecology. Through his lifetime, Dr Greene estimated he had delivered somewhere between 2000 and 3000 babies through the Waikato and Bay of Plenty.

Known and regarded equally for his knowledge and generosity of his time as much as for his humility and general manner, Dr Greene is survived by his wife Elizabeth, his daughter Mary and three sons, Patrick, Timothy and Johnny, along with eight grandchildren.

We are grateful to Tim Greene for this obituary notice.