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Paediatric inflammatory bowel disease in New Zealand
Jason Yap, Alison Wesley, Stephen Mouat, Simon Chin

The incidence of paediatric inflammatory bowel disease in New Zealand is comparable to North America and Europe, but at the lower end. Crohn’s disease is more common than ulcerative colitis. Only a minority of patients with Crohn’s disease have the classic triad of symptoms of abdominal pain, weight loss, and diarrhoea at presentation. Drug therapy is used much more commonly than nutritional therapy. It is rare that New Zealand Polynesian children develop inflammatory bowel disease.

Partying on? Life after BZP-based party pills
James A Green

This study considered whether the banning of benzylpiperazine (BZP)-based party pills was likely to increase illegal drug use. Around half of those participants who had intentions of using BZP in the future thought they would be more likely to use illegal drugs after BZP was withdrawn from the market, with Ecstasy the most likely substitute. Although BZP has now been replaced by new legal 'party pills', any further restriction of such legal alternatives may increase illegal drug use.

High prevalence of gout in patients with Type 2 diabetes: male sex, renal impairment, and diuretic use are major risk factors
Ravi Suppiah, Ajith Dissanayake, Nicola Dalbeth

Gout is a form of arthritis that causes severe joint pain and damage. This study has shown that gout affects one in five people with Type 2 diabetes attending diabetes clinics at Counties Manukau District Health Board. Male sex, kidney problems, and diuretic medications are important risk factors for developing gout in these patients. Rates of gout were highest (41%) in men with Type 2 diabetes over the age of 65 years. Almost half of the patients with gout and diabetes were not receiving recommended preventive treatment for gout. Improved recognition of the impact and treatment of gout is needed to ensure optimal management of these patients.
Evidence-based resource use by practice nurses in the Greater Auckland region of New Zealand
Karen J Hoare, Jane Steele, Felix S F Ram, Bruce Arroll

Practice nurses have a significant role to play in achieving the vision of the Primary Health Care Strategy. The main aim of this Strategy is to reduce inequalities in health between ethnic groups in New Zealand. Adherence to best practice and clinical guidelines is one way to address inequalities. New Zealand Guidelines and BPACNZ produce user friendly information but these resources were not widely known amongst practice nurses who were surveyed. Strategies to advertise these resources to practice nurses need developing.

When should I do rural general practice? A qualitative study of job/life satisfaction of male rural GPs of differing ages in New Zealand
Tom Noonan, Bruce Arroll, David Thomas, Ron Janes, Raina Elley

This paper explores the areas of satisfaction and dissatisfaction amongst male rural GPs from various stages of family life. Particular themes this paper looks at relate to the influences and effects of community, the environment, the GP’s family, and factors related to the GP themselves. Significant changes in the attitudes towards on-call work, depression, and burnout, visibility in a small town, and family relationships suffering are noted and discussed in more detail.

Clozapine and myocarditis: a case series from the New Zealand Intensive Medicines Monitoring Programme
Geraldine R Hill, Mira Harrison-Woolrych

The Intensive Medicines Monitoring Programme has been monitoring adverse reactions associated with the antipsychotic medicine clozapine in New Zealand. Myocarditis is a known adverse reaction associated with clozapine but the risk of developing this condition is unknown. This paper examines a series of twenty-five cases of myocarditis associated with the use of clozapine that have been reported to the IMMP, and makes comparisons with a recent, similar Australian case-series. Clozapine-associated myocarditis most commonly occurs within 1-2 months of starting clozapine, but may develop at any time while on the medicine, and can occur even at very low doses. A further study linking national morbidity and mortality datasets with the IMMP data could estimate the risk of developing clozapine-associated myocarditis.
Inflammatory bowel disease in New Zealand children—a growing problem

Richard B Gearry, Andrew S Day

The inflammatory bowel diseases (IBD), Crohn’s disease and ulcerative colitis, are no longer rare medical conditions seen only by hospital specialists.

IBD epidemiology—what’s happening in New Zealand?

Over the past 50 years there has been a dramatic rise in the incidence of IBD in New Zealand, as demonstrated by three hospital-based studies and one population-based study.1–3

A particularly striking increase in the incidence of CD has been seen in Canterbury over recent years. Indeed, the age-specific incidence of CD in Canterbury in 2004 was estimated at 16.5/100,000 which is one of the highest described incidence rates worldwide. Furthermore, this high incidence has transferred to a high prevalence of CD and for the first time, the prevalence of CD (155.2/100,000) was shown to be greater than that of UC (145.0/100,000).4 This high incidence and prevalence are likely to be seen across New Zealand.

The study by Yap et al published in this issue of the Journal also shows geographical differences between provinces, with the highest incidence rates of IBD seen in the South Island (Yap et al. Paediatric inflammatory bowel disease in New Zealand: http://www.nzma.org.nz/journal/121-1283/3287).

As stated by the authors, this regional difference is likely to relate to varying proportions of Māori and Pacific Island people across the country. IBD is less common in Māori than Caucasian people and has hardly been described in Pacific Island people.4

With IBD emerging as a health problem amongst non-Caucasian populations in Asia and the high rates of IBD seen amongst the second generation of Asian immigrants to other countries, including the UK and Canada, one might expect to see more IBD in non-Caucasian populations in New Zealand.

Paediatric IBD—a more aggressive phenotype?

While the peak age of IBD incidence is between 15 and 35 years, the study by Yap et al shows that, there is an important and growing group of paediatric patients who, while they share similarities with adult patients, also have a number of fundamental differences. Firstly, in almost all studies, CD is more common amongst males than females in a paediatric population until 16 to 18 years of age when CD becomes significantly more common amongst females.

The reason for this switch in incidence rates is not understood but hormonal changes associated with adolescence have been implicated. Secondly, the phenotype of disease is different amongst paediatric patients. Children with CD more frequently have...
inflammation of the proximal small intestine than in adults, while 39% in this study had perianal disease at presentation (compared with 182/715 [25.5%] after a mean of 6.5 years follow-up in the Canterbury IBD Study).

Recently published data from Canterbury has confirmed that early age of diagnosis, proximal small bowel disease and perianal disease are all independent predictors of stricturing and penetrating disease behaviour which, in turn, leads to increased morbidity, requirement for medication and ultimately intestinal resection with the possibility of a permanent stoma.  

BD presenting in childhood also has a huge impact upon nutrition, with weight loss common at diagnosis and impaired height acquisition a frequent concern. Thus, this paediatric IBD population not only live with IBD for longer, they also have a more aggressive phenotype, with consequent significant medical, nutritional, and psychological impacts.

**Paediatric CD—a difficult diagnosis?**

While UC almost always presents with the overt symptoms of bloody diarrhoea that usually leading to rapid medical consultation, referral for and completion of colonoscopy, the diagnosis of CD may be less obvious in all age groups.

Inflammation of the small intestine (which is more common in the paediatric age group) may lead to more non-specific symptoms such as abdominal pain, nausea and weight loss. However, Yap et al show that measurement of C-reactive protein and albumin, positive and negative inflammatory markers respectively, may be helpful in this situation.

Although blood tests can be difficult in infants and children, paediatric patients with gastrointestinal symptoms should be screened with serum inflammatory markers as well as appropriate tests to exclude other gastrointestinal conditions (e.g. tissue transglutaminase antibodies for coeliac disease). Furthermore, faecal inflammatory markers now provide a non-invasive and accurate means of identifying those with intestinal inflammation who require further investigation.

The high incidence of CD seen in this study is a reminder to primary care physicians to keep CD in mind for children presenting with gastrointestinal symptoms at any age.

**The treatment of paediatric IBD—can we do better?**

The medical treatment of IBD aims to reduce symptoms and morbidity by reducing and controlling inflammation. Standard medical therapies that are effective at inducing remission include glucocorticoids, biological agents (such as infliximab and adalimumab), and azathioprine (although the latter has a slow onset of action).

Therapies used to maintain remission include azathioprine, methotrexate, and the biological drugs. However, exclusive enteral nutrition (EEN) using a polymeric or elemental formula offers paediatric patients a unique opportunity of an effective treatment to induce and maintain remission in CD. Furthermore, EEN has positive effects on growth, bone health, the immune system, general nutrition and mucosal healing, unlike glucocorticoids that frequently lead to a plethora of serious adverse events.
Only 37% of the CD patients in the study by Yap et al were treated with EEN, which is disappointing given the high use of glucocorticoids (73%) and 5-ASA products (94%). This high use of 5-ASA drugs is surprising given that this class of drug has limited data to support its use in CD despite its importance in the management of UC. One can only assume that such low uptake of EEN as a primary therapy reflects the limited access to paediatric gastroenterologists who are experienced prescribing EEN outside of the Auckland region. In addition, 32% of the children with CD had been prescribed azathioprine in this study, which is appropriate given the compelling data in paediatric populations that early use of thiopurines leads to an improved long term outcome.¹²

There are also no data presented concerning the use of biological drugs in this population. While these drugs are not without potential serious adverse effects, the aggressive phenotype seen in this cohort would suggest that many would benefit from these agents, particularly if azathioprine was not effective.

**Conclusions**

Yap et al have shown that IBD, particularly CD, is an emerging problem amongst New Zealand children and this reflects data shown in other epidemiological studies undertaken in this country. While the magnitude of the problem has been described, primary care physicians must now work towards reducing diagnostic delay by being more aware of the diagnosis in all age groups and using laboratory investigations appropriately to screen for IBD and other gastrointestinal diseases.

Delays in access to endoscopic assessment, more so in the adult population, remain a barrier to diagnosis and timely initiation of therapy. Finally, access to appropriate treatment such as EEN in the paediatric age group, and biological agents amongst all IBD patients in New Zealand is limited by the geographic distribution of expertise and insufficient funding from government. Increased funding is desperately needed to increase the colonoscopy resource and improve access to biological drugs for New Zealanders.

**Competing interests:** None known

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Medicines safety—closing the loop

Timothy J Maling

The current catch phrase “safe use of medicines” suggests that prescription medicines can be used safely when in fact the prescription medicines we use today are inherently unsafe. So what does “safe use” really mean? In New Zealand (NZ) we have a system of regulation and monitoring to ensure that a prescription medicine is as safe as possible at the time of marketing, but in practice its safe use depends on a balance between benefit and risk, which only becomes clear with use over time. There are salutary reminders of this limitation extending over more than 4 decades from practolol to the COX-2 inhibitors—medicines risk is never fully identified prior to marketing.

Pharmacovigilance is the collective term for the systems and processes used to detect, assess, communicate, and prevent the adverse effects of medicines, so as to understand a specific medicines risk in its treatment context. In NZ, resource constraints have limited the focus to post-marketing surveillance of adverse drug reactions through two main programmes.

The spontaneous reporting of observed adverse drug reactions to the Centre for Adverse Reactions Monitoring (CARM) is voluntary, and although nationwide, it has limited efficiency as a detection system. The Intensified Medicines Monitoring Programme, which collects both drug exposure data and adverse events uses prescription event monitoring and cohort analysis. It is a powerful but relatively expensive process which limits its utility in the fiscally constrained NZ health-funding environment. The challenge is to link the outputs from the existing pharmacovigilance activity to clinical improvement and patient outcomes—post-marketing surveillance feeds into quality use of medicines.

In this issue of the Journal, Kunac et al highlight the critical importance of post-marketing surveillance of medicines and provide a timely update of the core services provided by the Dunedin-based NZ Pharmacovigilance Centre, a business unit of the University of Otago. Importantly, the authors point to the overlap between reporting of adverse drug reactions (ADR) and adverse drug events (ADE), noting that NZ lacks a coordinated national process for medicines error recognition and prevention. They suggest that we may be best served by a national medicines safety centre.

Spontaneous reporting of ADRs and ADEs is notoriously inefficient. Initiatives for effective management of medication error also vary markedly across New Zealand District Health Boards (DHBs). Centralised reporting and monitoring functions for both ADRs and ADEs, with agreed national standards for reporting and communication of data, could provide significant benefits for both patients and DHB administrations. Such a facility could promote wider data linkages, which are currently poorly defined, between different sectors of the healthcare environment.

The data linkage project funded from the research partnership between Medsafe and the Health Research Council is a clear signal of the need to gain some traction in this
area. Similarly, the World Health Organization (WHO) through the World Alliance for Patient Safety notes the risk of “valuable lessons…often trapped within the walls of hospitals…the opportunity to generalize the problem is lost and the opportunity to generate more powerful and generalisable solutions is missed”.

The Safe Medication Management Programme, launched in June this year as part of the QIC National Improvement Programme, has a real challenge ahead to pull together the different initiatives across the DHBs in the drive to reduce medication error. Its initial focus is on hospitals but medication error in the primary care sector is still to be addressed and both sectors could benefit from an ADE national database and monitoring strategy.

Non-punitive and confidential voluntary reporting programmes are better sources of information about errors and their causes than mandatory systems. Spontaneous reporting programmes should also encourage practitioners to report the “near misses” which constitute a crucial part of solutions to avoid potential disasters. Building on the existing spontaneous ADR reporting system, as Kunac et al propose is a logical step.

The essentials for a NZ pharmacovigilance strategy include timely medicines regulation, signal detection systems, accessible medicines safety information, and ADR reporting and monitoring systems. These must fit within a properly resourced national pharmacovigilance framework to ensure effective communication of medicines risk for New Zealanders, but medicines risk is about the definition of medication error just as much as it is about identification of adverse drug reactions.

The drive in the last decade for medicines error management has highlighted the philosophical differences between medicines regulators—traditionally responsible for pharmacovigilance strategies, and new international alliances, which are focused on medicines errors arising from unsafe practice with medicines. There is a view amongst some regulatory agencies that the latter should not be part of pharmacovigilance; yet there are root causes for medicines error, such as those arising from international medicines labelling practices, which are clearly the aegis of the regulators.

In 2006 the International Network for Safe Medicines Practice Centres published the Salamanca Declaration to promote safe medication practices globally. The Declaration notes:

”…medication errors are an important system-based public health issue and an integral component of the patient safety agenda” and ”each country should recognise an independent focal point (centre) for safe medication practice in a collaborative and complementary way to pharmacovigilance systems.”

For the medicines safety loop to be closed, the current focus of pharmacovigilance on post marketing surveillance strategies in NZ must be expanded to include medication error recognition and prevention. How that sits within the mindset of the Quality Improvement Committee and the frameworks of the new patient safety initiatives is unclear, but the concept offers a unique step forward in the quest for an effective NZ medicines safety strategy.

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What are the major political parties’ healthcare policies for New Zealand?

Frank A Frizelle

Healthcare policy is shaping up to be a major election issue in New Zealand in 2008. I have asked, as NZMJ Editor, for both major parties to provide us with an outline of their health policies. This week we have an editorial from Hon Tony Ryall of the National Party; the next edition (October 17) we expect to have an editorial from the Labour Party.

Both major parties have published their main points on the Internet. We know historically that whichever party wins the election they are unlikely to follow-through on a number of items, however we are left to judge them on their track-record and their promises.

Labour has shown, with its dynamic Minister of Health, the Hon David Cunliffe, that it has got the experience to deal with issues in the health sector, and has intervened as we have seldom seen before.

Labour Party Policy

Labour outlines what they consider to be the major issues on their website: http://www.labour08.co.nz/policies/Health/Health

**General practitioners (GPs) and primary health organisations**—Labour states that it will keep primary healthcare subsidies universal, so that everyone is able to get cheaper doctors visits and cheaper prescription medicines.

**Hospital and district health boards (DHBs)**—Labour states that it will continue to maintain and improve hospital buildings and campuses so they are better able to cope with high demand in the public health system. Indeed, five major hospital redevelopments have now been approved and are underway, on top of eight major refurbishments and seven new hospitals built since 1999. Labour claim that they are committed to retain the right for local communities to have their say on local health issues. Labour states that they will also ensure that DHBs work together to ensure that a consistently high standard of healthcare is available throughout the country.

**The health workforce**—Labour will increase the number of nurses and doctors; since 1999 there have been an additional 4000 nurses and 1000 doctors. They wish to retain the recent doubling in the number of GPs to be trained (up from 50 to 104 each year), and will also preserve changes to primary care services that have improved incomes for GPs and are making the area increasingly attractive to work in.

**Caring for older people**—Labour is committed to the progressive removal of asset-testing for older people in long-stay residential care, and to increasing funding for aged residential care by looking at ways to improve the funding model, and to improve quality controls in the aged-care sector.
They also state that they will also maintain the significant increases to home-based support funding, so older New Zealanders can be the ones to choose to stay in their own homes—not have the choice made for them.

**Child health**—Labour is dedicated to making sure our kids get the best start in life. They wish to roll out the new free “School Ready” check up for all children before they start school.

**Prevention and promotion**—Labour will continue to promote healthy, active lifestyles, including through *Fruit in Schools* and *Mission On*, which encourages our children to think and act in ways that keep them fit and healthy. Labour is committed to fighting against cervical cancer with the introduction of an immunisation programme which is expected to save around 30 lives a year. The human papillomavirus (HPV) immunisation programme will be offered to women aged 12–18.

**Dental/oral health**—Labour believes that good oral health is fundamental to the overall health of New Zealanders. They will keep building the oral health workforce and continue the fundamental shift towards focusing on preventive oral health. Protecting the oral health of our children is a top priority. Labour will continue to shift services for children and teenagers from the existing School Dental Service to Community Oral Health Services.

**Improved rural services**—Labour will continue to support the substantial improvement in rural health services that has occurred in recent years.

**National Party Policy**


**Reducing waiting**—More convenient care in GP surgeries, with GPs with special interests able to provide a wider range of minor surgery in their clinics. They should also be able to provide a level of specialist assessment currently provided in hospitals, including the ability to order immediate diagnostic tests. Walk-in access at general practice should be more widely available to provide choice and faster care for patients.

**Smarter use of the private sector**—The judicious use of public-private partnerships can increase the availability of elective surgery and reduce waiting-lists.

**Innovative management**—Separating acute and elective service provision can allow health professionals to concentrate on the efficient delivery of elective services without being disrupted by urgent cases.

**GPs in emergency departments**—Hospital emergency department delays can be reduced by some co-location of GP services.

**Quality use of medicines**—They can speed up our medicines approval process by recognising international medicine approvals.
Moving more services closer to home—Some hospital services should be moved to Integrated Family Health Centres (co-located multi-disciplinary teams).

Co-ordinating care—Primary care can provide a much wider range of care and support for patients.

Chronic care and social support—Specially trained nurses who are involved with chronic care patients should be engaged to act as brokers, or case managers, for non-health agencies to support at-risk families.

Devolving more care to the primary sector—More treatment and diagnostic services should be devolved to primary care.

A significant issue which will have to be dealt with by whichever party wins the election is the long-term heath issue related to economics of population demographic changes that we will see with the sudden and large expansion of the over 60 population requiring healthcare. Spending is already increasing rapidly as can be seen from the figure below.

![Graph showing health expenditure trends](http://www.moh.govt.nz/moh.nsf/indexmh/health-expenditure-trends?Open)

Source: Ministry of Health


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Solutions for New Zealand’s healthcare system

Tony Ryall; for the National Party

National is ambitious for New Zealand and its health service. We think that the health system can be so much more responsive to the future needs of New Zealanders. Kiwis could be healthier, the health workforce more secure, and your money more wisely invested.

At no other time in the past 9 years have so many New Zealanders been so concerned at the lack of Government leadership in health. The command and control health system of the past 9 years has absorbed huge increases in taxpayers’ money, but has little to show for it. While costs have gone up, the quality of the spending has not been ideal.

National believes the future lies in working together—primary and secondary, public and private—with a good lead from Government.

We outlined our vision last year in our 50-page health discussion paper called Better, Sooner, More Convenient. In it, we called for a new focus on the needs of individual patients, not just populations. We received hundreds and hundreds of submissions from patients, clinicians, and organisations that have all contributed to the policies we are currently rolling-out.

Investing in health

Despite a doubling of the health budget, New Zealanders have to be sicker to get elective surgery and, on a population basis, fewer people are getting surgery than 8 years ago.

This is a real challenge. Research by Victoria University shows surgical output needs to grow by around 51% from 2001 to 2026 just to deliver the inadequate current levels of elective surgery, and grow by 77% to address real elective surgery need.

New Zealand must strive to get more health service from existing spending by reducing waste and bureaucracy and by lifting productivity.

The link between higher living standards and better health is clear. By increasing prosperity and opportunity, a National-led Government will improve the health of New Zealanders. Labour has squandered the opportunity of good economic times, failing to make a lasting, positive impact on the wider determinants of health. As a result, many New Zealanders are suffering needlessly.

A comparison of health spending per capita between New Zealand and other OECD countries shows wealthier countries spend more on health than poorer countries. Countries we like to compare ourselves with—such as Australia—spend more on health, in part because they have higher incomes.

National is confident that our economic programme will deliver higher incomes, close the wage gap with Australia, and grow our wealth. That will not only help people
directly, but it will allow social spending to grow where needed. It will also allow us
to continue growing Government investment in health.

National will continue the growth in health spending set out in the 2008 Budget. This
includes the Government’s indicative spending allocations. Not a dollar less.

**Primary care**

All around the country patients tell us they are waiting longer for care, including
waiting longer to see their local GP. But the failure to move healthcare from
secondary to primary care in any significant way, despite its constant re-statement as a
policy objective, is one of the greatest puzzles of health policy over the past few
decades.

General practice in New Zealand has evolved over the past 15 years to be strongly
networked, with high levels of clinical competence and a wide range of innovative
services.

National believes that multidisciplinary Integrated Family Health Centres bringing
together a variety of health services in a convenient location will provide patients with
a wider range of health services.

We want to help GPs and hospital specialists to provide specialist assessments (FSAs)
in the community, in primary care. We want to see your patients access more minor
surgery, by specially trained GPs.

Not every general practice will want to become part of a large multi-practitioner
health centre, nor will there be any requirement for them to do so. Smaller practices
provide quality care and will choose to operate as they see fit.

*National will devolve further hospital-based services into primary care settings.
These changes will provide patients with faster and more services, delivered by teams
of health professionals, at more convenient locations.*

We will also be announcing initiatives in after-hours services.

**Workforce**

Staff turnover and the escalating use of locums ($100 million last year) and agency
nurses are having a detrimental impact on patient care. It is undermining continuity,
quality, and public confidence. The health workforce crisis is putting intolerable
pressure on regional hospitals to the point where even basic services are at risk.
Labour’s only solution is to order report after report; over 55 have been published so
far.

In addition, New Zealand has been losing a steady 800–1200 nurses a year to
Australia for the past 5 years so now our system relies on foreign-trained nurses to
survive. Nursing shortages are causing cancellations in surgery and closing beds,
while a shortage of ICU nurses is affecting heart patients.

National believes that New Zealand is extremely short of health professionals and will
implement a range of solutions including: engaging with health professionals in the
running of health services; increasing the number of medical students graduating
every year; and offering voluntary bonding for graduates wishing to work in hard-to-staff areas.

**Clinical leadership**

Around the world, clinical leadership is recognised as a fundamental driver for improved care. But under Labour, health professionals have an increasingly limited say on how health services are provided.

Labour’s failure to engage the people who have the expertise—the doctors and nurses who keep the public health system going—is eroding the health service’s ability to provide patients with the care they need. Doctors, nurses, and other health professionals need to be able to make the most of their skills and commitment. National will reduce red tape and empower you to do this.

Recent research by McKinsey and Company, based on 126 hospitals across the UK, has found a clear link between strong clinical leadership and hospital performance. The researchers found that best-practice operational approaches in hospitals reduced infection rates; improved productivity, readmission rates, and patient satisfaction; and gave value for money.

The key to this success was the level of involvement of clinicians in running their hospital services. Stronger and more direct involvement by doctors, nurses, and other clinicians means more service and better quality.

National will ensure that doctors, nurses, and other health professionals have more say in how health services are developed and improved. We will do this by requiring DHBs to involve health professionals in decision-making.

**Voluntary bonding**

New Zealand is desperately short of doctors, nurses, and midwives. Recently, the OECD lambasted New Zealand’s health workforce planning, especially the over-reliance on imported health professionals.

The retention of junior doctors is a serious concern for New Zealand. According to the Medical Council, almost 20% of junior doctors leave New Zealand by the end of their second year after graduation. This figure grows to almost 30% after 3 years. International medical graduates are even less likely to stay in New Zealand.

New Zealand is losing a lot of nurses overseas, and this outflow is temporarily being matched with an inflow of immigrant nurses. However, this is a far from ideal situation.

National will introduce a voluntary bonding scheme offering student-loan debt write-off to graduate doctors, nurses, and midwives agreeing to work in hard-to-staff communities or specialties. In return for working in these areas for 3 to 5 years after graduation, National will provide New Zealand graduates with student-loan write-offs up to a maximum $10,000 per year.

This means a medical graduate with an average $75,000 student loan can be debt-free within 5 years.
Training

National’s goal is to make New Zealand self-sufficient in doctor training over time. To move towards this goal, we will boost funded medical student places at universities, expand GP training, and encourage more training in rural and provincial areas.

National will boost the number of funded medical student places by 200 students over 5 years. This will increase the total number of funded medical student places from 365 students a year to 565—a boost of over 50%.

National will also expand the number of funded GP training places by 50 GP registrars. This will increase the total number of funded GP registrar training places from 104 a year to 154, a boost of nearly 50%.

Conclusion

There is no use pretending that every problem facing the health system can be fixed overnight. But if the health service is to deliver for New Zealanders, it has to focus on what matters to people.

When I asked to become Health Spokesman after the 2005 General Election I did so because I believed our health service could be doing so much better. With your support, a country like New Zealand should be able to lead the world in responsive patient care.

For more information on National party policy please see our website: www.national.org.nz

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Paediatric inflammatory bowel disease in New Zealand

Jason Yap, Alison Wesley, Stephen Mouat, Simon Chin

Aim To determine the incidence, presentation, and initial management of paediatric inflammatory bowel disease in New Zealand.

Methods A prospective study in collaboration with the New Zealand Paediatric Surveillance Unit was undertaken between 2002–2003. Paediatricians and healthcare professionals working with children were surveyed monthly for cases of paediatric inflammatory bowel disease.

Results There were 52 cases (30 males); 34 (66%) Crohn’s disease, 9 (17%) ulcerative colitis, and 9 (17%) inflammatory bowel disease type unclassified. The estimated incidence of paediatric inflammatory bowel disease, Crohn’s disease, and ulcerative colitis were 2.9, 1.9, and 0.5 per 100,000 per year respectively. Mean age at diagnosis was 11 years with a delay of 8.4 months from clinical presentation to diagnosis. 85% were European, while no Māori or Pacific Islanders had Crohn’s disease or ulcerative colitis. The most common symptoms at presentation were abdominal pain (63%), rectal bleeding (57%), diarrhoea (55%), and weight loss (43%). 39% of Crohn’s disease patients had perianal disease at presentation. Only 18% of the Crohn’s disease patients presented with the classic triad of symptoms—abdominal pain, weight loss, and diarrhoea. Haematological laboratory abnormalities were more common in Crohn’s disease. 5-aminosalicylic acid agents were the most common initial therapy followed by systemic steroids. 25% of the paediatric inflammatory bowel disease cohort received immunomodulators.

Conclusions The incidence of paediatric inflammatory bowel disease in New Zealand is comparable but at the lower end relative to North America and United Kingdom. There is more Crohn’s disease than ulcerative colitis and only a minority of Crohn’s disease patients presented with the classic triad of abdominal pain, weight loss, and diarrhoea. 5-aminosalicylic acid preparations and steroids as first line treatment of Crohn’s disease were much more common than nutritional therapy. It is rare for New Zealand Polynesian children to develop paediatric inflammatory bowel disease.

Crohn’s disease (CD) and ulcerative colitis (UC) are chronic inflammatory bowel diseases (IBD) of unknown aetiology that can manifest in childhood. The interplay of genetic susceptibility, dysregulated immune system, and environmental factors such as enteric microflora have been identified to be important in the aetiopathogenesis of inflammatory bowel disease.2–5

The disease can occur in children of all ages with increasing incidence occurring after 8 years of age.6,7 The incidence of paediatric IBD in certain Western European countries and Canada has increased dramatically during the last decades.6–11 This trend is predominantly driven by a significant increase in the incidence of CD.

Epidemiological data from Wales showed a doubling of the incidence of CD over an 11-year period, from 1.3 cases to 3.1 cases per 100,000 per year.9 The incidence of
childhood UC remained unchanged at 0.7 per 100,000 per year. This increase was validated later by the British Paediatric Surveillance Unit study of paediatric IBD, with CD having an incidence of 3.1 per 100,000 cases per year and UC of 1.4 cases per 100,000 per year in the United Kingdom and Republic of Ireland. Similar incidences have been reported from metropolitan Toronto, Canada (CD – 3.7, UC – 2.7), and Wisconsin, USA (CD – 4.6, UC – 2.4).

Conversely, the incidence of adult IBD in the Asia Pacific region is still low with quoted ranges of 1 to 2 per 100,000 for UC and 0.5 to 1 per 100,000 for CD. Little is known about the childhood incidence of IBD for New Zealand (NZ). Recent data from the New Zealand (NZ) province of Canterbury estimates a comparable incidence with other western developed countries.

We proposed a protocol to study paediatric IBD in NZ in collaboration with the New Zealand Paediatric Surveillance Unit (NZPSU) over a 2 year period, 2002–2003. Our aims were to compare the incidence, presentation and initial management of paediatric IBD in NZ with published literature.

**Methods**

The NZPSU was initially established with funding from the New Zealand Ministry of Health as part of the global certification to eradicate poliomyelitis by monitoring the incidence acute flaccid paralysis. The role of the NZPSU has expanded to facilitate national surveillance of uncommon high impact paediatric conditions, with the aim of improving the knowledge of these uncommon conditions in New Zealand.

Since its conception, the NZPSU has successfully collaborated in numerous peer reviewed publications. The NZPSU is currently administered through the Department of Women’s and Children’s Health, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand.

Every month, paediatricians, and other specialists working predominantly with children around NZ were sent a reply-paid card or an email by the NZPSU to report whether in the preceding month, they had encountered any new cases of certain diseases under surveillance. From January 2002 to December 2003, paediatric IBD was included in the surveillance list. When a case of paediatric IBD was notified, a short questionnaire was sent to the notifying healthcare professional to complete. The case’s identity remained anonymous.

New cases of children <15 years of age presenting with IBD in NZ between January 2002 to December 2003 were eligible for enrollment into the study. Each new case was classified into CD, UC, or inflammatory bowel disease, type unclassified (IBDU), based on established endoscopic, histologic, and radiologic findings (Table 1). The term IBDU was only applied to cases where there is evidence on clinical and endoscopic grounds for chronic inflammatory bowel disease affecting the colon, without small bowel involvement, and no definitive histological or other evidence to favour either CD or UC. The distribution of disease in each patient was classified as per the Montreal Classification (Table 2). The classification was performed by the investigators of the study from data submitted by the participating physician/paediatrician.
Table 1. Definition of paediatric inflammatory bowel disease

<table>
<thead>
<tr>
<th>Case Definition</th>
<th>At least one of the following 3 criteria:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Histological classification of inflammatory bowel disease, described by Morson &amp; Dawson and Donwitz with chronic inflammation and mucosal atrophy</td>
</tr>
<tr>
<td></td>
<td>• Endoscopic identification of at least moderate inflammatory activity and/or other mucosal findings such as granularity, mucosal atrophy or a pathologic vessel pattern</td>
</tr>
<tr>
<td></td>
<td>• Radiographic findings of colitis or radiographic findings in the small intestine classified as Crohn’s disease</td>
</tr>
<tr>
<td>AND infectious causes excluded with three faecal specimens cultured for significant pathogens</td>
<td></td>
</tr>
</tbody>
</table>

Crohn’s Disease (CD) At least 2 of the following 3 criteria:

|                 | • Histologic classification of CD or possible CD |
|                 | • Endoscopic classification of CD: aphthoid mucosal ulcers with only slight inflammation – or at least two of the following findings: serpiginous ulcer, cobblestone appearance or skip lesion/discontinuity |
|                 | • Radiologic change in the small intestine classified as CD |

Ulcerative Colitis (UC) Histologic classification of UC or possible UC and the presence of continuous mucosal disease involving the rectum and extending for a variable distance proximally

Inflammatory Bowel Disease, type unclassified (IBDU) Histologic and endoscopic evidence compatible with inflammatory bowel disease that could not fulfill the criteria for UC or CD

Table 2. Montreal classification for Crohn’s disease

<table>
<thead>
<tr>
<th>Age at diagnosis</th>
<th>Location</th>
<th>Behaviour</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1: below 16 yrs</td>
<td>L1: ileal</td>
<td>B1: inflammatory</td>
</tr>
<tr>
<td>A2: between 17 - 40 yrs</td>
<td>L2: colonic</td>
<td>B2: stricturening</td>
</tr>
<tr>
<td>A3: above 40 yrs</td>
<td>L3: ileocolonic</td>
<td>B3: penetrating</td>
</tr>
<tr>
<td></td>
<td>L4: isolated upper GI disease</td>
<td>p: perianal disease modifier #</td>
</tr>
</tbody>
</table>

* L4 is a modifier that can be added to L1-L3 when concomitant upper gastrointestinal disease is present
# "p" is added to B1-B3 when concomitant perianal disease is present
Duplicate notifications were recognized by a code derived from the patient’s particulars.
The data was analyzed in total as IBD cohort, and then subdivided into CD, UC, and IBDU. Data was expressed as mean with standard deviation. We used either a two-tailed student $t$-tests or one-sided ANOVA with Tukey’s test to compare continuous variables between two or more groups. The 2-way Fischer exact test was applied to dichotomous data. The Pearson correlation coefficient was used for normally distributed data, whilst Spearman was applied to non-parametric data correlation; $p<0.05$ was considered significant.

The incidences for IBD, CD, and UC were calculated for the period 1 January 2002 to 31 December 2003 using projected population data for NZ obtained from Statistics New Zealand.

**Results**

The NZPSU report card average response rate for the study period was 95% and 97% in 2002 and 2003 respectively. In 2002 and 2003, 189 and 191 clinicians respectively participated in the NZPSU surveillance system. All District Health Boards in NZ were represented in the surveillance study. A total of 65 completed paediatric IBD questionnaires were received. However, 13 questionnaires were excluded from analysis because of either duplicate notification, or diagnosis made outside the study period or withdrawn by the attending paediatrician because of an alternate diagnosis. In total, 52 cases were entered for final analysis: 21 cases in 2002 and 31 in 2003.

**Paediatric inflammatory bowel disease (total group)—**The estimated incidence of paediatric IBD for NZ for 2002–2003 was 2.9 per 100,000 per year (95% confidence interval [CI]: 1.79–4.03). The estimated incidence of paediatric IBD in the North Island and South Island of NZ respectively are 2.6 (95%CI: 1.83–3.00). The majority (85%) of the patients were of European ethnicity. The regional incidence of IBD is shown in Figure 1.

Of the 52 reported cases, 58% were males (Table 3). There were thirty four cases of CD(66%), nine cases of UC(17%) and nine cases(17%) of IBDU. The majority (85%) of the patients were of European ethnicity.

The age distribution of the cases is shown in Figure 2.

The mean age at diagnosis of IBD was 11 years, with a standard deviation of 3.5 years. The majority (73%) of cases presented after 10 years of age. The mean age at presentation to medical practitioner was 10.3 years. Therefore, there was a mean delay of 8.4 months between presentation to diagnosis of IBD; 7.2 months for CD. There was no statistically significant difference between type of IBD and delay in diagnosis; $p=0.8$. Neither was there any significant difference in age at diagnosis and type of IBD; $p=0.1$.

There was a family history of IBD in first or second-degree relatives in 10% of the cohort; three family members with UC and two with CD. The mean age of diagnosis for this IBD subgroup with a positive family history was older at 13.6 years in comparison to the cohort but not statistically significant.

The most common symptom at presentation to the medical practitioner was abdominal pain, present in 63% of the total cohort. Other symptoms that were frequently cited were rectal bleeding (57%), diarrhoea (55%), and weight loss (43%). Symptoms of anorexia, lethargy, pallor, nausea, and vomiting were less commonly noted. Only 37% of the cohort reported bloody diarrhoea. There were too few cases under 5 years of age to observe any different symptom reporting trend.
The mean weight z-score was -0.5 and mean height z-score was -0.34 for all cases of paediatric IBD (Table 4). There was no statistical correlation between length of delay and weight z-score (r=0.27; 95% Confidence Interval [CI]: -0.03–0.53) or height z-score (r=0.07; 95% CI: -0.27–0.4) for all IBD. Also, for CD, there was no significant difference between length of delay and weight z-score (r=0.3; 95% CI: -0.09–0.6) or height z-score (r=0.22; 95% CI: -0.2–0.57).
Figure 2. Inflammatory bowel disease—age distribution

Table 3. Patient demographics

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Total N=52</th>
<th>CD N=44</th>
<th>UC N=9</th>
<th>IBDU N=9</th>
<th>NZ Pediatric population 2001 N=220,226</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age presentation yrs</td>
<td>11.4 (9.1–12.9)</td>
<td>11.8 (9.7–13.4)</td>
<td>9.9 (9.0–10.7)</td>
<td>11.4 (4.5–13)</td>
<td>456,040 (51)</td>
</tr>
<tr>
<td>Age diagnosis yrs</td>
<td>12.0 (10.0–13.0)</td>
<td>12.2 (11.3–13.6)</td>
<td>9.9 (5.6–10.8)</td>
<td>13.2 (6.5–13.7)</td>
<td></td>
</tr>
<tr>
<td><strong>Ethnicity (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>44 (84)</td>
<td>33 (74)</td>
<td>7 (78)</td>
<td>5 (55)</td>
<td>652,000</td>
</tr>
<tr>
<td>Maori</td>
<td>3 (4)</td>
<td>1 (6)</td>
<td>1 (12)</td>
<td>1 (12)</td>
<td>216,100</td>
</tr>
<tr>
<td>Indigenous Asian</td>
<td>2 (4)</td>
<td>1 (3)</td>
<td>1 (11)</td>
<td>1 (11)</td>
<td>61,300</td>
</tr>
<tr>
<td>Pacific</td>
<td>1 (2)</td>
<td>1 (3)</td>
<td>1 (11)</td>
<td>1 (11)</td>
<td>109,000</td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>2 (4)</td>
<td>1 (3)</td>
<td>1 (11)</td>
<td>1 (11)</td>
<td>81,000</td>
</tr>
<tr>
<td>African</td>
<td>1 (2)</td>
<td>1 (3)</td>
<td>1 (11)</td>
<td>1 (11)</td>
<td></td>
</tr>
</tbody>
</table>

*Data includes individuals identifying >1 ethnicity.
Table 4. Z-scores for weight and height

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>CD</th>
<th>UC</th>
<th>IBDU</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>N=52</td>
<td>N=34</td>
<td>N=9</td>
</tr>
<tr>
<td>Ht z-score</td>
<td>-0.34</td>
<td>-0.30±1.1</td>
<td>-0.15±1.2</td>
<td>-0.5±0.68</td>
</tr>
<tr>
<td>Wt z-score</td>
<td>-0.5</td>
<td>-1.0±1.6</td>
<td>0.2±1.2</td>
<td>0.8±1.9</td>
</tr>
</tbody>
</table>

The laboratory parameters for the study cohort are shown in Table 5. The serum albumin was statistically lower for CD compared with UC† and IBDU‡ patients. The serum albumin was below the lower limit of normal for age in 68% (17/25) of CD patients. Furthermore, patients with CD had the highest mean and median serum CRP, with 86% (18/21) of the CD cohort having abnormal values.

Table 5. Laboratory parameters

<table>
<thead>
<tr>
<th>Median (IQR)</th>
<th>Total</th>
<th>CD</th>
<th>UC</th>
<th>IBDU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (g/dL)</td>
<td>111 (94 - 126)</td>
<td>108 (92 - 126)</td>
<td>112 (96 - 125)</td>
<td>121 (112 - 132)</td>
</tr>
<tr>
<td>Platelets (x10^9/L)</td>
<td>&lt;96 (372 - 635)</td>
<td>93 (405 - 656)</td>
<td>88 (405 - 507)</td>
<td>386 (271 - 625)</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>36 (30 - 38)</td>
<td>32 (29 - 36) †</td>
<td>37 (37 - 41) †</td>
<td>39 (37 - 41) †</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>27</td>
<td>27</td>
<td>27</td>
<td>26</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>9</td>
<td>31</td>
<td>1.5</td>
<td>5.3</td>
</tr>
</tbody>
</table>

*p <0.05 for CD versus IBDU; † p<0.05 for CD versus UC.

Histological tissue diagnosis was available in 96% of the patients prior to initiation of therapy. One questionnaire had been returned prior to scheduled gastrointestinal endoscopy. This patient’s diagnosis was made by radiologic features in the ileo-caecal region of the gastrointestinal tract in association with clinically severe growth impairment and gastrointestinal symptoms suggestive of CD. Therefore, treatment was undertaken prior to histologic confirmation.
Thirty-seven percent of IBD cases were diagnosed and managed by paediatric gastroenterologists. The remainder of the cohort was diagnosed by general paediatricians in conjunction with adult gastroenterologists, paediatric surgeons or adult general surgeons. Overall, 63% of the cases were cared for by general paediatricians. Adult gastroenterologists and paediatric surgeons were involved in the initial care of paediatric IBD patients 44% and 30% of the time respectively. For the seven cases requiring surgery, paediatric surgeons were involved in six of the surgical procedures.

Figure 3. Presenting symptoms paediatric IBD

Crohn’s disease (CD) subgroup—The estimated incidence of CD for NZ from 2002-2003 is 1.9 cases per 100 000 per year (95% CI: 0.82–3.0). There were 34 cases of CD in the study period. Approximately 94% of the CD cohort were European, whilst there were no Māori or Pacific Islanders with CD. The most common symptom at presentation was abdominal pain (74%) followed by weight loss (50%), rectal bleeding (47%) and diarrhoea (41%) (Figure 3). Of the CD cohort, 13 cases (38%) had perianal disease at presentation, with a single case having no other symptomatology besides perianal disease.
Mean weight z-score for CD was lower at -1.0 and mean height z-score was -0.36 (Table 4). Three cases had both weight and height z-scores less than -2, suggestive of severe growth failure. One of the three cases had a 2-year delay between developing symptoms and presenting to a medical practitioner. The mean weight z-score for CD was significantly different in comparison to IBDU; p<0.05, with a trend towards significance in patients with UC.

Ninety-one percent of CD cases underwent either colonoscopy and 76% underwent upper gastrointestinal tract endoscopy, with 74% undergoing both procedures for diagnosis. Barium meal with follow through or small bowel enema to investigate small intestine CD disease were performed in 68% of the patients. Histology was available in 94% of CD cases.

A significant proportion of CD cases had upper tract disease (72%). The anatomical distribution of CD is shown in Table 6. Approximately half of CD patients had pancolitis at diagnosis with 38% having ileocolonic disease. There were two patients (6%) in the cohort that presented with strictureing disease.

Table 6. Anatomical distribution of Crohn’s disease
(Montreal Classification\textsuperscript{15})

<table>
<thead>
<tr>
<th>Disease Location</th>
<th>No. Cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1 – Terminal Ileum</td>
<td>7 (6)</td>
</tr>
<tr>
<td>L2</td>
<td>15 (48)</td>
</tr>
<tr>
<td>L3 - Ileocolon</td>
<td>13 (39)</td>
</tr>
<tr>
<td>L4 – Upper GI</td>
<td>24 (73)</td>
</tr>
<tr>
<td>L1 + L4</td>
<td>1 (3)</td>
</tr>
<tr>
<td>L2 + L4</td>
<td>10 (29)</td>
</tr>
<tr>
<td>L3 + L4</td>
<td>11 (32)</td>
</tr>
<tr>
<td>Isolated L4</td>
<td>2 (6)</td>
</tr>
<tr>
<td>p – perianal disease</td>
<td>13 (39)</td>
</tr>
</tbody>
</table>

The preferred treatment for CD was drug therapy with only four cases attempting elemental nutrition therapy (Table 7). The most common initial therapy was systemic 5-ASA preparations (85%). Systemic steroids were used in 73% of CD patients. Thirty-two percent were commenced on the immunomodulator, azathioprine. The most common indications cited for immunomodulator use were steroid dependency, ongoing severe disease activity, and extensive inflammatory disease. Antibiotic use to
treat CD was uncommon with only 18% of patients treated with metronidazole because of perianal disease.

Table 7. Drug therapy

<table>
<thead>
<tr>
<th></th>
<th>CD</th>
<th>UC</th>
<th>IBDU</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=34</td>
<td>N=9</td>
<td>N=2</td>
</tr>
<tr>
<td>Antibiotics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-ASA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topical</td>
<td>3</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Systemic</td>
<td>29</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>Steroids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topical</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Systemic</td>
<td>25</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Immunosuppressants</td>
<td>11</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

The most common indication for surgery in CD cases was perianal disease. In total, seven CD cases (21%) required surgical intervention, five for perianal involvement, two for stricturing disease resulting in bowel obstruction and one for disease intractability.

Ulcerative colitis (UC) subgroup—The estimated incidence of UC in NZ is 0.5 cases per 100,000 patients per year (95% CI: 0.4–0.6). Two-thirds of the UC cohort were European and 89% of UC were from the North Island. Two-thirds of cases were above 9 years of age (Figure 2). The youngest case of UC was 2.75 years old. Growth was not significantly affected (Table 4). Bloody diarrhoea was the most common symptom at presentation (72%) (Figure 3).

Seventy-eight percent of patients had extensive disease while the remainder had left-sided colitis. All patients had colonoscopy as first choice investigation. Concurrent upper gastrointestinal endoscopy was performed in four cases and barium swallow with follow through in two cases.

The preferred induction therapy for UC was oral systemic 5-ASA treatment in all cases (Table 7). 44% of cases were also started on systemic steroids. Topical 5-ASA and topical steroids together were attempted in two cases.

Inflammatory bowel disease, type undetermined (IBDU) subgroup—There were nine cases of IBDU. The youngest case at diagnosis was 3 months. Despite a mean 1.2-year delay between presentation and diagnosis, the mean weight z-score was +0.8 (Table 4). There was insufficient data to calculate mean height z-score. Systemic
5-ASA was first-line therapy in eight cases (Table 7) while the youngest case in this IBDU cohort undertook dietary therapy. Interestingly, one patient failed both 5-ASA and steroid therapy for resistant colitis. Treatment was escalated to include azathioprine and subsequently oral cyclosporin to gain control of disease. In addition, one case was on a gluten-free diet for serology positive and biopsy proven coeliac disease prior to onset of colitic symptoms.

Discussion

This is the first prospective paediatric IBD study reporting the incidence of paediatric IBD for all of NZ. The estimated incidence of paediatric onset IBD in NZ in our study of 2.9 cases per 10^5 per year is in the lower end of the range when compared to North American and European countries which have quoted incidences of 2.3 to 7 cases per 10^5 per year.6–11 A recent report from the Canterbury IBD project with adult and paediatric data, estimated a crude incidence of 25.2 per 10^5 per year, 16.5 per 10^5 per year, and 7.6 per 10^5 per year for IBD, CD, and UC in the Canterbury health region.15 Interestingly, the incidence of IBD and CD in the Canterbury health region was 8.5-fold higher than our data which was collected within a few years of each other. In our study, the Auckland and Canterbury provinces had the largest number of paediatric IBD cases, despite Canterbury compromising only 11.9% of the New Zealand population.

The West Coast of the South Island appears to have the highest incidence of paediatric IBD in New Zealand. However, because of the small number of cases involved, the addition of one or two cases has the potential to produce a wide variation of incidence, particularly in sparsely populated areas such as the West Coast.

It is possible that ethnic factors may be in part an explanation for the higher regional incidence in the South Island of NZ. Both the West Coast and Canterbury are predominantly European Caucasian, with the Māori population compromising 8.4% and 6.5% of the regional population. The South Island of NZ has an approximate 7% Māori population, in contrast to the 16.2% of the North Island. NZ Māori have been shown to have a low frequency of NOD2/CARD15 single nucleotide polymorphism (SNP) that confers susceptibility to CD and this may possibly contribute to the low observed incidence and prevalence of CD in NZ Māori.23 While genetic susceptibility may play a part, there may also be important environmental factors contributing to the disparate incidence of IBD between the regions.

Early reports from Scotland showed a threefold rise in incidence of paediatric CD over a 16-year period (1968–1983) with a further 30% increase in prevalence since 1983.24 Regional data from South Wales, reported similar trends from 1983 to 1993.9 The experience in the Southern hemisphere is similar, with the paediatric gastroenterology service in the Australian state of Victoria describing an emerging trend in paediatric CD, with the incidence of paediatric CD rising from 0.128 to 2 per 10^5 per year over 3 decades.25

Paediatric CD is more common than UC in our study, with an approximate fourfold difference in incidence to UC. Similarly, the Canterbury IBD project estimated a CD to UC ratio of 2.2.15 Studies from Northern France,26 United Kingdom,10 United States,13 Toronto,12 and the Netherlands6 are consistent with CD being more common.
In contrast, other countries such as Norway\textsuperscript{27} and Sweden\textsuperscript{28} report the opposite with the number of UC cases outnumbering CD.

It must be recognised that reported incidence and comparisons between studies have to be interpreted with caution, as the definition of “childhood” varies between inclusion criteria and the steep rise in age specific incidence of IBD during the teenage years. For example, the Dutch paediatric IBD surveillance study\textsuperscript{6} and the Wisconsin population-based study included cases up to 18 years of age.\textsuperscript{13} A significant number of IBD cases in the study from the Netherlands were diagnosed between 15–18 years. Similarly, the Canterbury IBD project had a rapid rise in the prevalence of IBD from the age 15 years onwards.\textsuperscript{15}

The mean age of diagnosis of paediatric IBD in NZ was 11 years, with the majority of cases diagnosed after 9 years of age. IBD cases <5 years only accounted for 11% of cases. The mean age of diagnosis was comparable to the 12.7 years,\textsuperscript{12} 13.5 years,\textsuperscript{13} and 12.9 years\textsuperscript{10} reported from Toronto, Wisconsin (United States), and the United Kingdom and Ireland respectively. In these larger epidemiological studies, the incidence of paediatric onset CD was higher among males. A similar pattern of male preponderance was identified in paediatric onset CD in NZ, with 62% of the CD cohort being male; p=0.05. Conversely, the female to male preponderance is well described in adult patients with CD.\textsuperscript{29,30}

It is possible that there is a genotypic difference between childhood-onset and adult-onset IBD.

There were no Māori or Pacific Islanders with paediatric CD or UC in our study; New Zealand Caucasians were the majority in all three IBD subgroups. A previous survey of adult CD from Dunedin Hospital had no Polynesian patients,\textsuperscript{31} while Polynesians accounted for 0.4% of UC cases and no CD cases in a survey of Auckland public hospitals.\textsuperscript{32}

There was a distinct difference between presenting symptoms and type of IBD diagnosed. More than half of paediatric CD patients presented with symptoms of abdominal pain and weight loss in comparison to cases of UC/IBDU where the presenting symptoms were chiefly colitic such as rectal bleeding and diarrhoea. Only 18% of the CD cohort presented with the “classic triad” of abdominal pain, weight loss and diarrhoea. This is in comparison to the Toronto cohort where 80% of CD had the classic constellation at presentation.\textsuperscript{12} Our results however are comparable to the British study where 25% presented with the classic triad.\textsuperscript{33}

Other presenting features were perianal disease, pallor, lethargy, extra-intestinal manifestations, and anorexia. This wide range of presentation and lack of classic symptomatology emphasises the need for heightened suspicion in the diagnosis of CD.

Low serum albumin are not uncommonly seen in CD patients and reflects enteric loss of protein from inflammation as well as malnutrition. In our study, CD patients had a significantly lower albumin level compared with UC or IBDU patients. Our CD patients also had higher CRP levels.

A large proportion of the patients were diagnosed to have gastroduodenal inflammation (52%), with ileal involvement a close second (45%). These results are comparable to the United Kingdom study where 71% and 51% had ileal and
A fifth of their patients had jejunal involvement.

Twelve percent of our CD cohort had isolated small bowel disease which is comparable to the 19% in the Northern France and the 9% from the United Kingdom study. The higher incidence of small bowel disease was attributed to improved modern investigative protocols. Our data possibly support this notion, with 94% of CD having a histological diagnosis, 91% having undergone a colonoscopy and 74% having had both upper and lower gastrointestinal endoscopy. Furthermore, with the increasing use of capsule endoscopy, it is likely that the incidence of CD small bowel disease could increase. However, no patient in our study cohort had undergone capsule endoscopy for diagnosis of small bowel disease.

Alternatively, paediatric patients with CD may have a different phenotype, presenting more frequently with proximal disease. In paediatric UC, pancolitis seems to be a more frequent presentation compared with adults who present more with left sided colitis.

The preferred first-line treatment reported was drug therapy. Only five cases underwent elemental nutritional therapy: four for CD and one for IBDU where the diagnosis of food allergy could not be excluded despite histology. There are regional preferences to treatment of paediatric IBD. North American gastroenterologists favour using steroids followed by immunomodulatory therapy while Western European colleagues favour nutritional therapy or budesonide. The preferred first-line drug therapy in our study was systemic 5-ASA irrespective of IBD type. Few of the patients in our study undertook nutritional therapy.

Nutritional therapy may be useful in mild to moderate cases of IBD, and also in those cases with significant growth failure where steroids may have a negative impact on growth acceleration, particularly in those patients close to puberty. The poor uptake of nutritional therapy in New Zealand is not well understood. The efficacy of nutritional therapy for induction of remission is well documented. The possible explanations include poor acceptance of nutritional therapy by the patients, lack of understanding by paediatricians for its use as a possible steroid alternative, palatability of the enteral feed, paucity of resources to support a nutritional programme, and cost. In light of the known adverse effects of steroid therapy, nutritional therapy should be considered more often as induction therapy for paediatric CD.

Systemic steroids were often used (73%) for CD in this study. Systemic steroids are the mainstay of induction therapy for moderate to severe CD but are not effective as long term maintenance therapy for CD. This study was unable to correlate the severity of disease with the use of steroid induction therapy. While azathioprine was used in a number of cases, no CD patients received monoclonal antibody therapy such as infliximab. As infliximab is generally reserved in those cases were immunomodulatory therapy has failed, it is not surprising that none of our cases were trialled on this drug because of the short follow-up period of the study.

This study has a number of limitations. Firstly, cases of paediatric IBD were only ascertained through elective reporting through the NZPSU although it does have a very high monthly reply rate. Other methods to validate and confirm completeness of ascertainment were not employed, and so the true completeness of enrollment cannot
be determined. This could lead to an underestimation of the true incidence of paediatric IBD in New Zealand. It is also possible that some teenagers within the age group of interest were referred on directly to adult gastroenterologists and surgeons for diagnosis and management. The duration of study was short thus leading to a relatively small number of cases reported. A longer study period could have ascertained whether there was an increasing trend in paediatric IBD in NZ as in other countries. Although the data were collected prospectively, some aspects of the information like onset of symptoms relied on parental recall and therefore subject to possible recall bias.

Lastly, this study did not determine severity of IBD at diagnosis which may have helped correlate the severity of disease to the choice of therapy. The Paediatric Crohn’s Disease Activity Index (PCDAI)\textsuperscript{36} and Paediatric Ulcerative Colitis Activity Index (PUCAI)\textsuperscript{37} are validated research tools that accurately reflect disease activity in comparison to physician global assessment in a real world setting. They are therefore useful tools to establish severity of disease at diagnosis and following response to treatment.

In summary, this is the first prospective paediatric study reporting incidence of IBD in children for the whole of NZ. The estimate incidence for IBD, CD, and UC are 2.9, 1.9, and 0.5 cases per 100,000 per year.

The overall demographics, presentation, and management of paediatric IBD in NZ are comparable to other studies. However there are regional differences with Canterbury having a higher incidence of IBD. There were no Māori or Pacific Islanders with CD or UC in our study which may be a factor in these regional differences.

Overall, drug rather than nutritional therapy was preferred as first-line treatment. It would be valuable to repeat this survey in the future with tools like PCDAI\textsuperscript{36} or PUCAI\textsuperscript{37} to assess disease severity. In addition, a longer follow-up and study duration would help to determine response to treatment and whether the incidence of paediatric IBD will change with time.

**Competing interests:** None known.

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**Acknowledgment:** We thank all health professionals who participated in this New Zealand surveillance study.

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**References:**


Partying on? Life after BZP-based party pills

James A Green

**Aim** This study considered whether the banning of benzylpiperazine (BZP)-based party pills was likely to increase illegal drug use.

**Method** During July and August 2007, students were surveyed about their current recreational BZP and drug use, along with their future intentions to use substances that might be substituted for BZP once it became illegal.

**Results** 119 students were surveyed, with 41 indicating that they might use BZP in the future. Of those who indicated that they might use BZP in the future, around half indicated that they would be more likely to use illegal drugs (in particular, ecstasy) after the ban. Around half were also considering stockpiling party pills before the ban took effect, and a similar proportion would consider taking new legal party pills if they became available.

**Conclusions** The withdrawal of BZP and any replacement 'party pills' from the recreational drug market may lead to an increase in the use of illegal drugs.

With the ban on benzylpiperazine (BZP) and related substances, there was a question as to what would happen after BZP became illegal. Would people who used BZP substitute some other substance (legal or illegal) for BZP, or will life simply go on? How popular would any new 'party pills' be, and would there be any attempts to stockpile BZP before the ban comes into effect? Similar questions will be raised with any restrictions that may be placed on new 'party pills'.

BZP-based legal party pills had become increasingly popular in New Zealand over the past few years, to the point that approximately a third of the 18–24 year old demographic had used party pills in the past year. Increasing concerns about the health effects of BZP lead to a series of official reviews, and BZP became illegal on 1 April 2008. Users of BZP were not averse to using other legal and illegal substances, leading to a number of substitution options. Alcohol was a clear candidate with 95% of BZP users also drinking alcohol (almost 90% sometimes drinking alcohol with BZP) and 15% had used nitrous oxide in the previous year. Similarly, levels of illegal drug use were high, with 61% of BZP users having used cannabis in the same year, along with 21% ecstasy, and 16% amphetamines. In terms of likely substitutes, energy drinks and amphetamines both produce a degree of alertness, whereas alcohol, ecstasy, and nitrous oxide are more linked with the 'party' scene.

An additional possibility was that BZP might be stockpiled, so that it would continue to be used during the immediate post-ban phase. New legal 'party pills' have already appeared on the market, and calls for regulation were made within the first month. While some questions addressed in this study are now answerable rather than hypothetical, they continue to be relevant for the new generation of party pills. That is, what would happen if these new products are removed from the market?
The aim of this study then was to examine what impact the impending ban of BZP would have on recreational drug use. This included attempting to determine which of a possible list of the most popularly used recreational drugs (along with energy drinks) would be substituted for BZP, the likelihood of stockpiling BZP, and interest in any new legal party pills.

**Methods**

Participants were initially presented with a list of five statements, and asked to pick the statement that best described them. These were "used to use BZP, but do not any longer", "tried BZP once or twice, but do not any longer", "never used BZP", "used BZP, and may take again", and "used BZP in the last year, and may take again". Participants selecting the first three statements were directed to proceed to the fourth page of the questionnaire, with the remainder to fill out the first three pages.

Participants who were considering taking BZP again were first asked about how often they used BZP on a 1 to 7 scale (1=Less frequently, 2=Every 2–3 months, 3=Monthly, 4=Fortnightly, 5=Weekly, 6=Every 2–3 days, 7=Daily). They were then asked how likely they would be to consume BZP with cigarettes/tobacco, marijuana, alcohol, energy drinks, ecstasy, amphetamines, LSD, hallucinogenic mushrooms, and nitrous oxide, on a 0 to 7 scale, anchored at 0 (Never), 1 (Not at all likely) and 7 (Very likely). They were then asked about how often they used those same substances in general, anchored on the same scale as BZP above. They were then asked how often they thought they would take those substances after BZP is banned on a 0 to 7 scale, anchored at 0 (Never), 1 (Not at all often), and 7 (Very often). Next they were asked to estimate how often they thought they would take those substances if BZP was not being banned on the same scale.

The next question related to whether participants thought the banning of BZP would make them more likely to use illegal drugs (not including BZP once banned), on a 7-point scale anchored at 1 (No) and 7 (Yes). They were then asked about their frequency of use of other substances and whether they would try any new legal high, using the same questions outlined above. They were also asked about their reasons for stopping or not trying BZP rated on a 1 (No influence) to 7 (Large influence) scale: other legal substance better, BZP’s hangover/comedown, BZP’s safety, BZP’s price, price relative to alcohol, ease of access, energy provided, and other illegal substances better.

Volunteers were recruited from participants who had completed a study on attitudes toward conventional, complementary, and alternative medicines, for which they had been paid $15. Participants were offered no additional incentive to participate in this study, and were free to leave having completed only the preceding study. Participants were all studying at the University of Otago, and there were no particular requirements to be in the prior study. The data was collected in July and August 2007. The project was reviewed and approved the University of Otago Human Ethics Committee.

Responses were analysed using SPSS v14.0 software, with analysis of variance (ANOVA) used to determine differences between groups (between subjects) and within groups (repeated measures). For pairwise comparisons, Cohen's $d$ is reported as a measure of effect size where, by convention, values of 0.2, 0.5, and 0.7 are considered to be small, medium, and large effects, respectively.
Results

119 students were surveyed, comprising 62 females and 54 males (3 gender not given), with a mean age of 21.0 (SD=2.5, Range 18-32). Of these, 34.5% (n=41) indicated that they might take BZP in the future, and were thus defined as potential future users (20 females, 20 males, 1 gender not given, mean age=21.0, SD=1.9, Range 18–27).

Potential future users—Fourteen of the 41 potential future users completed an early version of the questionnaire that contained ambiguous questions, which were replaced for later participants. Therefore the following analyses are based on a sub-sample of 27 participants.

This sub-sample was strongly polarised as to whether they were "more likely to use illegal drugs" after BZP was banned. Fifty-four percent responded either 1 or 2 at the 'No' end of the 7 point scale, indicating that they did not think they would be more likely to use illegal drugs following the ban. The remaining 46% responded 5, 6, or 7 ('Yes'), indicating that they thought they were likely to use more illegal substances after the ban. Mirroring this pattern, participants reported on average, an increased likelihood of using Ecstasy after BZP was banned (Table 1). No other predicted use of a substance differed as a function of whether BZP was to be banned. Forty-four percent also reported that they were likely to stockpile BZP prior to the ban.

Table 1. Anticipated future substance use as a function of whether BZP was to be banned [0 to 7 scale, anchored at 0 (Never), 1 (Not at all often), and 7 (Very often); higher scores indicate more likely to use]

<table>
<thead>
<tr>
<th>Substance</th>
<th>Ban</th>
<th></th>
<th>No Ban</th>
<th></th>
<th>F(1,26)</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cigarettes/Tobacco</td>
<td>2.04</td>
<td>0.52</td>
<td>1.89</td>
<td>0.49</td>
<td>1.00</td>
<td>0.06</td>
</tr>
<tr>
<td>Marijuana</td>
<td>2.67</td>
<td>0.41</td>
<td>2.70</td>
<td>0.40</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Alcohol</td>
<td>5.85</td>
<td>0.23</td>
<td>5.70</td>
<td>0.24</td>
<td>2.85</td>
<td>0.12</td>
</tr>
<tr>
<td>Energy drinks</td>
<td>4.04</td>
<td>0.38</td>
<td>3.81</td>
<td>0.36</td>
<td>1.86</td>
<td>0.12</td>
</tr>
<tr>
<td>Ecstasy</td>
<td>1.81</td>
<td>0.41</td>
<td>1.33</td>
<td>0.32</td>
<td>7.85**</td>
<td>0.25</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>0.85</td>
<td>0.37</td>
<td>0.52</td>
<td>0.27</td>
<td>1.41†</td>
<td>0.20</td>
</tr>
<tr>
<td>LSD</td>
<td>0.63</td>
<td>0.20</td>
<td>0.56</td>
<td>0.18</td>
<td>2.08</td>
<td>0.07</td>
</tr>
<tr>
<td>Hallucinogenic mushrooms</td>
<td>0.37</td>
<td>0.17</td>
<td>0.41</td>
<td>0.18</td>
<td>1.00</td>
<td>0.04</td>
</tr>
<tr>
<td>Nitrous</td>
<td>1.11</td>
<td>0.29</td>
<td>1.07</td>
<td>0.29</td>
<td>0.33</td>
<td>0.02</td>
</tr>
</tbody>
</table>

*p<0.01; †F(1,25).

Now, considering the full 41 participants who indicated that they might use BZP in the future, 49% indicated that, after the ban, if they knew a friend who was selling BZP for around the same price as it is now, they would be likely to buy it. Further, 51% indicated they would try any new legal high that might become available, with a further 29% neutral on this question.

Table 2 shows that these participants’ use of BZP was most influenced by the energy it provided and the ease with which it could be purchased. To a lesser extent they were also influenced by being kept alert/awake and its legal status, along with the...
quality of its high, its safety, and the unavailability of other drugs. The price of BZP was the least influencing factor. Despite the imminent ban of BZP, 40% responded 'Yes' to the question "Although BZP will soon be banned, were you thinking of stopping BZP anyway".

Table 2. Reasons for using BZP (higher numbers indicate a larger influence)

<table>
<thead>
<tr>
<th>Reasons for using BZP</th>
<th>Mean¹</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy BZP provides</td>
<td>5.5</td>
<td>5.0–6.0</td>
</tr>
<tr>
<td>Ease of getting BZP</td>
<td>5.4</td>
<td>4.9–5.8</td>
</tr>
<tr>
<td>Kept awake/alert by BZP</td>
<td>5.0</td>
<td>4.4–5.5</td>
</tr>
<tr>
<td>BZP not illegal</td>
<td>4.7</td>
<td>4.1–5.4</td>
</tr>
<tr>
<td>Quality of BZP’s high</td>
<td>4.4</td>
<td>3.9–5.0</td>
</tr>
<tr>
<td>BZP’s safety</td>
<td>4.0</td>
<td>3.3–4.6</td>
</tr>
<tr>
<td>Other drugs unavailable</td>
<td>3.7</td>
<td>3.0–4.4</td>
</tr>
<tr>
<td>BZP cheaper than alcohol</td>
<td>3.0</td>
<td>2.5–3.6</td>
</tr>
</tbody>
</table>

¹Rated on a scale anchored at 1 (No influence) and 7 (Large influence).

Consistent with prior research, at the same time that they were taking BZP participants were also very likely to be drinking alcohol. They were also somewhat likely to be drinking energy drinks, smoking cigarettes, or smoking marijuana (Table 3).

Table 3. Mean frequency of use of other substances with BZP (higher numbers indicate more frequent use)

<table>
<thead>
<tr>
<th>Substance</th>
<th>Mean¹</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>6.0</td>
<td>5.5–6.5</td>
</tr>
<tr>
<td>Energy drinks</td>
<td>3.3</td>
<td>2.6–4.0</td>
</tr>
<tr>
<td>Cigarettes/Tobacco</td>
<td>2.6</td>
<td>1.7–3.4</td>
</tr>
<tr>
<td>Marijuana</td>
<td>2.2</td>
<td>1.5–2.9</td>
</tr>
<tr>
<td>Nitrous oxide</td>
<td>1.3</td>
<td>0.8–1.8</td>
</tr>
<tr>
<td>Ecstasy</td>
<td>1.1</td>
<td>0.6–1.6</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>0.4</td>
<td>0.0–0.8</td>
</tr>
<tr>
<td>LSD</td>
<td>0.1</td>
<td>0.0–0.3</td>
</tr>
<tr>
<td>Hallucinogenic mushrooms</td>
<td>0.1</td>
<td>0.0–0.2</td>
</tr>
</tbody>
</table>

¹Rated on a scale anchored at 0 (Never), 1 (Not at all likely) and 7 (Very likely).

Non-users—Of those who did not plan to use BZP in the future, 11% were former users of BZP, with a further 25% having 'tried' BZP. Only 9% of these participants would consider using a new legal high. Participants' strongest reasons for not using BZP were concerns about its safety, its hangover/comedown, price, and the belief that other legal substances were better (Table 4).

Participants who did not use BZP or intend to in the future also had markedly different levels of use of other substances, relative to potential future users, as can be seen from Table 5. Participants who were currently using BZP or thought they might
use BZP in the future were more frequent smokers (tobacco and marijuana), drinkers, and users of ecstasy, LSD, and nitrous.

Table 4. Reasons for not using BZP for people not intending to use BZP in the future (higher numbers indicate a larger influence)

<table>
<thead>
<tr>
<th>Reasons for not using BZP</th>
<th>Mean</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>BZP's safety</td>
<td>4.5</td>
<td>4.0–5.0</td>
</tr>
<tr>
<td>BZP's hangover/comedown</td>
<td>3.4</td>
<td>2.8–3.9</td>
</tr>
<tr>
<td>Price</td>
<td>2.9</td>
<td>2.5–3.4</td>
</tr>
<tr>
<td>Other legal better</td>
<td>2.7</td>
<td>2.3–3.2</td>
</tr>
<tr>
<td>Energy they provide</td>
<td>1.9</td>
<td>1.6–2.2</td>
</tr>
<tr>
<td>Easy to access</td>
<td>1.8</td>
<td>1.5–2.1</td>
</tr>
<tr>
<td>Other illegal better</td>
<td>1.7</td>
<td>1.3–2.0</td>
</tr>
<tr>
<td>Cheaper than alcohol</td>
<td>1.5</td>
<td>1.3–1.8</td>
</tr>
</tbody>
</table>

*Rated on a scale anchored at 1 (No influence) and 7 (Large influence).

Table 5. Mean frequency of use of various substances as function of being a current or future user of BZP versus non-users (higher numbers indicate greater frequency of use)

<table>
<thead>
<tr>
<th>Substance</th>
<th>Non-users</th>
<th>Users</th>
<th>F(1,103)</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean²</td>
<td>SE</td>
<td>Mean²</td>
<td>SE</td>
</tr>
<tr>
<td>Cigarettes/Tobacco</td>
<td>0.94</td>
<td>0.20</td>
<td>1.89</td>
<td>0.53</td>
</tr>
<tr>
<td>Marijuana</td>
<td>0.71</td>
<td>0.13</td>
<td>1.89</td>
<td>0.30</td>
</tr>
<tr>
<td>Alcohol</td>
<td>4.08</td>
<td>0.18</td>
<td>5.04</td>
<td>0.15</td>
</tr>
<tr>
<td>Energy drinks</td>
<td>3.24</td>
<td>0.20</td>
<td>3.85</td>
<td>0.32</td>
</tr>
<tr>
<td>Ecstasy</td>
<td>0.18</td>
<td>0.06</td>
<td>0.70</td>
<td>0.18</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>0.06</td>
<td>0.04</td>
<td>0.19</td>
<td>0.09</td>
</tr>
<tr>
<td>LSD</td>
<td>0.05</td>
<td>0.04</td>
<td>0.26</td>
<td>0.09</td>
</tr>
<tr>
<td>Mushrooms</td>
<td>0.38</td>
<td>0.13</td>
<td>0.19</td>
<td>0.08</td>
</tr>
<tr>
<td>Nitrous</td>
<td>0.18</td>
<td>0.04</td>
<td>0.59</td>
<td>0.11</td>
</tr>
</tbody>
</table>

*p<0.05; ** p<0.01; *** p<0.001; 1Sample of 27 only; 2Rated on a 0 to 7 scale (0=Never, 1=Less frequently, 2=Every 2-3 months, 3=Monthly, 4=Fortnightly, 5=Weekly, 6=Every 2-3 days, 7=Daily).

Discussion

Just under half of those who indicated they were otherwise likely to use BZP in the future indicated that they would be likely to use more illegal substances as a result of the ban on BZP-based products. In particular, it would appear that they are more likely to use ecstasy. Their interest in trying new legal party pills was also high, and they reported intentions to stockpile BZP prior to the ban.

Of concern is that the withdrawal of BZP might increase use of illegal drugs. In effect, it may be speeding up the so-called 'gateway effect', whereby users of BZP move onto illegal drugs. There has already been evidence of people starting out on BZP and moving onto mostly illegal drugs.

In the Wilkins et al study, a small proportion of all respondents had tried both BZP and illegal substances in their lifetime and reported a relationship between the two. Of
this group 14% had started out using BZP but had moved on to mostly using illegal substances.\textsuperscript{9} Around three times that number (44%) had been mostly using illegal drugs but had substituted BZP for their illegal drug use.\textsuperscript{9} This suggests that the ban may not only increase illegal drug use, but it may also remove an avenue for people to stop taking illegal drugs. Any increased use of illegal drugs may, however, be tempered by cost and availability. Data indicates, however, that the cost of ecstasy is decreasing, and is relatively easily available.\textsuperscript{13} The appearance of new party pills after the exit of BZP from the market may have delayed or mitigated substitution of illegal drugs for BZP. However, any future changes in status for these new substances might increase illegal drug use.

Stockpiling BZP by individuals before the ban would appear to be less of an issue, as it seems unlikely that many people have hoarded any great quantity, with it therefore only slightly delaying cessation of use. If stockpiling was undertaken by those currently trading in other illicit drugs with the intention to on-sell it, this could be problematic, potentially providing new customers for the illicit drug market.

The consequences of the interest in new legal party pills will largely depend on what measures are put in place to test and restrict the new substances. Gee and Fountain have argued that the onus to provide evidence of safety should be placed with the suppliers of such substances,\textsuperscript{14} something the government is looking to adopt.\textsuperscript{12}

A further consideration should be standardisation.\textsuperscript{15} Labelling requirements for alcoholic beverages include a measure of standard drinks. New variants of the same medicine are tested for bioavailability, and typically come in standard dose forms. In contrast, legal party pills have had varying levels of BZP and other active ingredients in them, and presumably also have varying absorption rates, depending on the formulation. An advantage of legal recreational drugs relative to illegal drugs should be standardisation, but at present, it seems likely that the new party pills will be similarly non-standardized.

While serious adverse reactions have been reported at relatively low doses of BZP,\textsuperscript{2} further issues revolve around behavioural choices. Of the 26 BZP overdose cases reported by Theron et al, just 5 had ingested only BZP.\textsuperscript{3} Thirteen had also consumed alcohol, and 8 had consumed an illegal substance (cannabis, ecstasy, methamphetamine) in addition to BZP.\textsuperscript{3} Similar proportions were found in Christchurch hospital, with half of admissions again involving alcohol, 10 of 80 nitrous oxide, and 16 of 80 an illegal substance.\textsuperscript{2} Further reinforcing this pattern of 'suboptimal' decision making, approximately a third (19 of 61) patients re-attended Christchurch Hospital's Emergency Department for a BZP overdose on a separate occasion.

The present study has a number of limitations, with the replacement of ambiguous questions impacting on a relatively small initial sample size. Additionally, it is a convenience sample, but one that is largely in the age group most likely to use legal party pills. The observed level of BZP use in the present sample is very similar to that reported elsewhere in that age group, suggesting a reasonable degree of representativeness.

Self-reported future intentions may also not perfectly predict future behaviour. It is clear, however, that limiting access to BZP or new substances may cause undesired
increases in the use of illegal drugs. To prevent this, developing a flexible framework for assessing and regulating legal recreational drugs should be a priority.

Competing interests: None known.

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References:


High prevalence of gout in patients with Type 2 diabetes: male sex, renal impairment, and diuretic use are major risk factors

Ravi Suppiah, Ajith Dissanayake, Nicola Dalbeth

**Aims** Gout and hyperuricaemia are recognised features of the metabolic syndrome. The objective of this study was to determine the prevalence of gout in patients with diabetes.

**Methods:** We studied 292 consecutive outpatients attending diabetes clinics between August and September 2005. A self-reported history of gout was obtained, and was confirmed by clinical chart review. Information regarding associated comorbidities was also recorded. Current treatments were compared with published EULAR guidelines for the management of gout.

**Results** Gout was confirmed in 0/27 (0%) patients with Type 1 diabetes and 59/265 (22%) of patients with Type 2 diabetes (p<0.01). Prevalence rates varied depending on age and sex, and were highest (41%) in men with type 2 diabetes over the age of 65 years. Multivariate analysis showed that the following variables were independent predictors for gout in patients with Type 2 diabetes: male sex (adjusted OR 4.4, 95%CI 2.1–9.6), impaired renal function (adjusted OR 1.2 for every 10 ml/min reduction in GFR, 95%CI 1.1–1.4), diuretic use (adjusted OR 3.2, 95%CI 1.6–6.6), and high triglycerides (adjusted OR 2.2, 95%CI 1.0–4.7) Only 28/59 (47%) of patients with gout were on urate-lowering therapy. A further 24/59 (41%) met recommended criteria for urate-lowering therapy but were not receiving this medication.

**Conclusion** This study has demonstrated a high prevalence of gout in patients with Type 2 diabetes. Improved recognition of those at high risk of gout is needed to ensure optimal management of these patients.

Gout is an inflammatory arthritis caused by precipitation of intra-articular deposition of monosodium urate crystals. It was one of the earliest diseases to be recognised as a clinical entity, and throughout history it as been associated with rich foods and excessive alcohol consumption. In the past, this lifestyle could only be afforded by the affluent, so gout has been referred to as the ‘disease of kings’. More recently, the diet and lifestyle that predispose individuals to hyperuricaemia and gout have become very common.

The relationship between gout and the metabolic syndrome is well-recognised. Serum uric acid concentrations are strongly correlated with abdominal adiposity, and have been shown to predict the development of Type 2 diabetes, hypertension, cardiovascular disease, and renal failure. Patients with gout have high rates of the metabolic syndrome and Type 2 diabetes compared to individuals without gout. Promotion of renal tubular reabsorption of uric acid by insulin is thought to mediate this relationship.
Despite the documented association between gout and insulin resistance, the prevalence of gout and risk factors for gout in patients with diabetes has not been reported. The aim of this study was to determine the prevalence of gout in patients with Type 2 diabetes. We also sought to identify risk factors for gout in patients with Type 2 diabetes, and to analyse current management of gout in this patient group.

Methods

Study patients—We studied 292 consecutive outpatients with diabetes attending diabetes nurse clinics between August and September 2005 at Counties Manukau District Health Board (CMDHB), South Auckland, New Zealand. The indication for attending clinic was that the patient required secondary level care involving a diabetes nurse specialist to manage their diabetes. The study design was approved as an audit by the Northern X Ethics committee.

Study design—A self-reported history of gout was obtained by diabetes nurse specialists. The diagnosis of gout was then confirmed by primary and secondary care clinical chart review. Duration of diabetes, duration of gout, presence of tophi, and number of gout flares per year were recorded by the nurse specialist.

The type of diabetes was determined by what was recorded in the clinical notes by a diabetes specialist. Baseline and comorbidity data were obtained from the clinical notes. HbA1c, serum uric acid, serum creatinine, and lipid results were obtained from latest available laboratory data. Weight and blood pressure were recorded as part of the clinic visit.

Ethnicity was determined from the National Health Index (NHI) database, and grouped into:

- Māori (New Zealand Māori);
- Pacific people (Cook Island Māori, Niuean, Samoan, Tokelauan, Tongan and Tuvaluan ancestry);
- Indian (Persons of Indian subcontinent descent, including Indian, Pakistani, Bangladeshi, South African Indian, and Fijian Indian);
- Asian (Chinese, Taiwanese, Japanese, Korean, Malaysian and Singaporean Chinese);
- European (European or other ancestry).

Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. The National Cholesterol Education Program Third Adult Treatment Panel (ATP III) criteria was used to define low HDL (<1.04 mmol/L for men; <1.29 mmol/L for women) and high triglycerides (>1.7 mmol/L). Glomerular filtration rate (GFR) was determined using the Modification of Diet in Renal Disease (MDRD) formula:

\[
\text{GFR} = 32788 \times \text{Creatinine (µmol/L)}^{-1.154} \times \text{age}^{0.203} \times \text{constant.}
\]

The constant of 1 for male, and 0.742 for females was used.

Current treatment for gout was compared with European League Against Rheumatism (EULAR) guidelines with regard to urate-lowering therapy and diuretic use. These guidelines state that urate-lowering therapy is indicated in patients with recurrent acute gout attacks, arthropathy, tophi, or radiographic changes of gout. The guidelines also state that urate-lowering therapy should achieve a serum uric acid concentration of 360 µmol/L or less in order to promote crystal dissolution and prevent crystal formation, and that when gout is associated with diuretic therapy, alternative anti-hypertensive therapy should be prescribed.

Statistical analysis—SPSS (v13.0 for Windows) software was used for statistical analysis. Student’s t-tests were used to analyse the differences among means. Chi-squared test was used for differences in proportions. All reported p values are two-tailed; those less than 0.05 were considered statistically significant. Weighted least squares regression was used to calculate age standardised prevalence for each ethnicity. Unadjusted odds ratios (OR) for predictive variables were calculated. A multivariate logistic regression model that included age, sex, ethnicity, renal function, BMI, diuretic use, aspirin use, HDL (low/normal as per ATP III criteria), and triglycerides (high/normal as per ATP III criteria) was used to determine the independent predictive contribution of each variable.
Results

Baseline characteristics—Of the 292 patients in this study, 27 (9.2%) had Type 1 diabetes and 265 (90.8%) had Type 2 diabetes. Patients with Type 1 diabetes were younger (44.6 vs 57.1 years, p<0.001), had a lower BMI (25.9 vs 33.5 kg/m², p<0.001), had better GFR (84 vs. 64 ml/min, p<0.001), and also had lower serum uric acid concentrations (276 vs 416 µmol/L, p<0.001). None of the patients with Type 1 diabetes reported a history of gout.

Prevalence of gout in Type 2 diabetes—Of the 265 patients with Type 2 diabetes, 78 (29.4%) self-reported a history of gout. The diagnosis of gout was confirmed by clinical chart review in 59 patients; a prevalence of 22.3% (95%CI 17.7–27.7). The prevalence of gout in patients with Type 2 diabetes was significantly higher than in patients with Type 1 diabetes (p<0.01). Patients with Type 1 diabetes were not included in further analysis.

For patients with Type 2 diabetes, the sex and age-specific prevalence of gout is shown in Table 1. Overall, men had a higher prevalence of gout (29.5%) compared with women (14.2%), p=0.003. The prevalence of gout also increased with age (Table 1). The prevalence of gout was similar for Pacific people, Māori, and European, but lower in Indian and Asians (Table 2).

Table 1. Sex and age-specific gout prevalence in patients with Type 2 diabetes

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Cases (n)</th>
<th>At risk population (n)</th>
<th>Prevalence (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>0</td>
<td>0</td>
<td>0.0</td>
<td>0.0–56.0</td>
</tr>
<tr>
<td>26–44</td>
<td>3</td>
<td>14</td>
<td>21.4</td>
<td>7.6–47.6</td>
</tr>
<tr>
<td>45–64</td>
<td>22</td>
<td>86</td>
<td>25.6</td>
<td>17.5–35.7</td>
</tr>
<tr>
<td>65–84</td>
<td>16</td>
<td>39</td>
<td>41.0</td>
<td>27.1–56.6</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>0</td>
<td>3</td>
<td>0.0</td>
<td>0.0–56.0</td>
</tr>
<tr>
<td>26–44</td>
<td>2</td>
<td>23</td>
<td>8.7</td>
<td>2.4–26.8</td>
</tr>
<tr>
<td>45–64</td>
<td>10</td>
<td>69</td>
<td>14.5</td>
<td>8.1–24.7</td>
</tr>
<tr>
<td>65–84</td>
<td>6</td>
<td>31</td>
<td>19.4</td>
<td>9.2–36.3</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>0</td>
<td>3</td>
<td>0.0</td>
<td>0.0–56.0</td>
</tr>
<tr>
<td>26–44</td>
<td>5</td>
<td>37</td>
<td>13.5</td>
<td>5.9–28.0</td>
</tr>
<tr>
<td>45–64</td>
<td>32</td>
<td>155</td>
<td>20.6</td>
<td>15.0–27.7</td>
</tr>
<tr>
<td>65–84</td>
<td>22</td>
<td>70</td>
<td>31.4</td>
<td>21.8–43.0</td>
</tr>
</tbody>
</table>

Of the 59 patients confirmed to have gout, 9 (15%) were determined to have tophi. The median number of acute attacks of gout was 1 per year (range 0–30), and the median serum uric acid concentration in this group was 480 µmol/L (range 180–820 µmol/L). The median disease duration of gout was 6 years (range 1–45 years). A diagnosis of diabetes was made before onset of gout in 31/59 (52.5%) patients, concurrently in 4/59 (6.8%) patients, and after onset of gout in 24/59 (40.7%).
Table 2. Age-standardised prevalence of gout by ethnicity in patients with Type 2 diabetes

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Cases (n)</th>
<th>At risk population (n)</th>
<th>Age adjusted prevalence (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Māori</td>
<td>14</td>
<td>52</td>
<td>29.0</td>
<td>16.3–41.8</td>
</tr>
<tr>
<td>Pacific people*</td>
<td>24</td>
<td>90</td>
<td>28.4</td>
<td>18.9–37.9</td>
</tr>
<tr>
<td>European</td>
<td>16</td>
<td>63</td>
<td>27.3</td>
<td>16.0–38.6</td>
</tr>
<tr>
<td>Indian</td>
<td>5</td>
<td>37</td>
<td>13.9</td>
<td>2.2–25.7</td>
</tr>
<tr>
<td>Asian</td>
<td>0</td>
<td>23</td>
<td>0.0</td>
<td>0.0–0.00</td>
</tr>
</tbody>
</table>

*Mostly of Samoan, Tongan, Niuean, or Cook Islands origin.

Risk factors for gout in patients with Type 2 diabetes—Table 3 summarises the characteristics of patients with and without gout in individuals with Type 2 diabetes. In univariate analysis, patients with gout were older (p=0.003), had worse renal function (p<0.001) and more likely to be men (unadjusted OR 2.51, 95%CI 1.37–4.61). They were also more likely to be on diuretics (unadjusted OR 3.8, 95%CI 2.1–6.8) and on aspirin (unadjusted OR 1.93, 95%CI 1.07–3.47).

High triglycerides were more common in patients with gout (69% vs 54%, p=0.014), but there was no difference in other lipid parameters. There was no significant difference in BMI or blood pressure. HbA1c levels were lower in patients with gout (p=0.03), however the mean values were well above treatment targets for both groups. Patients with gout also tended to have had longer Type 2 diabetes disease duration (p=0.06).

Table 3. Characteristics of patients with Type 2 diabetes, with and without gout

<table>
<thead>
<tr>
<th>Variables</th>
<th>Gout (n=59)</th>
<th>No Gout (n=206)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males, n (%)</td>
<td>41 (69%)</td>
<td>98 (47.6%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Age, mean (SD), years</td>
<td>61.1 (10.2)</td>
<td>55.9 (12.3)</td>
<td>0.003</td>
</tr>
<tr>
<td>Body mass index, mean (SD), kg/m²</td>
<td>34.9 (9.0)</td>
<td>33.1 (7.1)</td>
<td>0.118</td>
</tr>
<tr>
<td>Systolic blood pressure, mean (SD), mmHg</td>
<td>128.7 (18.5)</td>
<td>132.2 (18.6)</td>
<td>0.215</td>
</tr>
<tr>
<td>Diastolic blood pressure, mean (SD), mmHg</td>
<td>75.0 (11.6)</td>
<td>77.9 (11.3)</td>
<td>0.088</td>
</tr>
<tr>
<td>Glomerular filtration rate, mean (SD), ml/min</td>
<td>49.9 (25.9)</td>
<td>68.3 (29.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Uric acid, mean (SD), µmol/L</td>
<td>480 (130)</td>
<td>390 (120)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HbA1C, mean (SD), %</td>
<td>8.2 (1.7)</td>
<td>8.8 (1.7)</td>
<td>0.034</td>
</tr>
<tr>
<td>Total cholesterol, mean (SD), mmol/l</td>
<td>4.4 (1.0)</td>
<td>4.8 (3.7)</td>
<td>0.503</td>
</tr>
<tr>
<td>HDL, mean (SD), mmol/L</td>
<td>1.2 (0.3)</td>
<td>1.3 (0.5)</td>
<td>0.354</td>
</tr>
<tr>
<td>Low HDL as per ATP III criteria, n (%)</td>
<td>23 (39%)</td>
<td>88 (43%)</td>
<td>0.608</td>
</tr>
<tr>
<td>LDL, mean (SD), mmol/L</td>
<td>2.1 (0.8)</td>
<td>2.5 (2.1)</td>
<td>0.213</td>
</tr>
<tr>
<td>Total cholesterol/HDL ratio, mean (SD)</td>
<td>3.6 (0.9)</td>
<td>3.8 (1.5)</td>
<td>0.366</td>
</tr>
<tr>
<td>Triglycerides, mean (SD), mmol/L</td>
<td>2.5 (1.5)</td>
<td>2.1 (1.3)</td>
<td>0.061</td>
</tr>
<tr>
<td>High triglyceride as per ATP III criteria, n (%)</td>
<td>41 (69)</td>
<td>110 (54)</td>
<td>0.014</td>
</tr>
<tr>
<td>Duration of Type 2 diabetes mellitus, mean (SD), years</td>
<td>13.7 (10.2)</td>
<td>11.2 (8.6)</td>
<td>0.059</td>
</tr>
<tr>
<td>Diuretic, n (%)</td>
<td>32 (54%)</td>
<td>49 (23.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aspirin, n (%)</td>
<td>37 (63%)</td>
<td>96 (46.6%)</td>
<td>0.042</td>
</tr>
<tr>
<td>Oral hypoglycaemic, n (%)</td>
<td>39 (66%)</td>
<td>172 (83%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Insulin, n (%)</td>
<td>41 (69%)</td>
<td>139 (67%)</td>
<td>0.770</td>
</tr>
</tbody>
</table>
A multivariate regression model was used to identify independent predictors of gout in patients with type 2 diabetes (Table 4). Age, sex, ethnicity, renal function, BMI, diuretic use, aspirin use, low/normal ATP III criteria for HDL, and high/normal ATP III criteria for triglycerides were included in the model. This analysis showed that the following variables were independent predictors for gout in patients with Type 2 diabetes; male sex (adjusted OR 4.4, 95%CI 2.1–9.6), impaired renal function (adjusted OR 1.2 for every 10ml/min reduction in GFR, 95%CI 1.1–1.4), diuretic use (adjusted OR 3.2, 95%CI 1.6–6.6), and high triglyceride (adjusted OR 2.2, 95%CI 1.0–4.7).

Table 4. Multivariate logistic regression analysis for predictors of gout: the model included age, sex, ethnicity, renal function, BMI, diuretic use, aspirin use, low/normal ATP III criteria for HDL, and high/normal ATP III criteria for triglycerides

<table>
<thead>
<tr>
<th>Variables</th>
<th>Adjusted odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4.4</td>
<td>2.1–9.6</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>1.0</td>
<td>0.0–1.8</td>
</tr>
<tr>
<td>Asian</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Indian</td>
<td>0.6</td>
<td>0.2–1.9</td>
</tr>
<tr>
<td>Māori</td>
<td>1.2</td>
<td>0.4–3.1</td>
</tr>
<tr>
<td>Pacific people</td>
<td>1.6</td>
<td>0.7–4.2</td>
</tr>
<tr>
<td>Other factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Every 10-year increase in age</td>
<td>1.0</td>
<td>1.0–1.0</td>
</tr>
<tr>
<td>Every 10 ml/min decrease in GFR</td>
<td>1.2</td>
<td>1.1–1.4</td>
</tr>
<tr>
<td>Aspirin</td>
<td>1.2</td>
<td>0.6–2.5</td>
</tr>
<tr>
<td>Diuretics</td>
<td>3.2</td>
<td>1.6–6.6</td>
</tr>
<tr>
<td>Low HDL</td>
<td>0.7</td>
<td>0.3–1.4</td>
</tr>
<tr>
<td>High triglycerides</td>
<td>2.2</td>
<td>1.0–4.6</td>
</tr>
</tbody>
</table>

Treatment of gout and adherence to EULAR guidelines—Of the 59 patients with gout and Type 2 diabetes, 28 (47%) were on urate-lowering therapy. All of these patients were on allopurinol, with one patient being on benzbromarone in addition to allopurinol. A further 24/59 (41%) patients with gout met the recommendations for urate-lowering therapy based on recurrent attacks of acute gout or presence of tophi, but were not receiving treatment.

Of the 28 patients using allopurinol, only 5 (17%) were achieving a serum uric acid concentration below the saturation point for monosodium urate (<360 µmol/L). Diuretic therapy was used in 32/59 (54%) patients with gout. The majority of these patients 20/32 (63%) were on at least one other antihypertensive agent.
Discussion

This study has shown that patients with Type 2 diabetes are at very high risk of gout. The key predictors for gout identified in this study are renal impairment, diuretic use, and male sex. This is similar to what is observed in the general population, and also in renal transplant recipients.

Diuretic therapy is an important modifiable risk factor in these patients. Use of antihypertensive therapy other than diuretic therapy is likely to reduce the risk of gout in patients with Type 2 diabetes, and should be considered particularly for those with other risk factors such as male sex and renal impairment.

The data regarding ethnicity are particularly interesting in this study. People of Māori and Pacific origin have high rates of gout; a recent community-based study in New Zealand demonstrated that 6.4% of Māori had gout, compared with 2.9% in those of European origin. However, ethnicity was not an independent risk factor for gout in this study, and in fact similarly high rates of gout were found in Māori, European, and Pacific people.

The high prevalence of gout in the three main ethnic groups represented in our study suggests that insulin resistance/metabolic syndrome may be a key risk factor for gout and override other genetic risk factors. However, this hypothesis is not supported by the lower rates of gout found in Asian and Indian patients with Type 2 diabetes. It should also be noted that ethnicity coding in the hospital record is not always accurate, and potential coding inaccuracies should be taken into consideration when interpreting this finding. Swan et al reported a concordance of only 41–89% for self identified ethnicity compared to what is documented in the hospital records.

We recognise that this study has some limitations. Definition of gout remains controversial, and various methods to define this disease have been employed in large observational studies. In our study, gout was defined by a physician diagnosis. This is similar to the definition employed in some studies, whereas others have used self reported rates, and others the 1977 ARA criteria (also known as Wallace criteria).

Using a physician confirmed diagnosis may underestimate the actual prevalence because some of the individuals self reporting gout without a confirmed diagnosis may truly have disease. This study was limited to secondary diabetes care, rather than primary care where many patients with diabetes are treated. These patients may have more severe insulin resistance and renal impairment than patients treated in primary care. However, despite these reservations, we believe that this study is of relevance to both primary and secondary care physicians involved in treating patients with Type 2 diabetes.

There are several implications for individuals with Type 2 diabetes who also have gout. Gouty arthritis may hinder attempts at exercise and weight loss. In addition to the dietary restrictions required for glycaemic control, these patients also need to avoid alcohol and purine-rich foods.

Treatments for acute gout can have adverse effects on disease; for example non-steroidal anti-inflammatory drugs (NSAIDs) may lead to deteriorating renal impairment, and corticosteroids may worsen glycaemic control. This group of patients is also likely to have multiple comorbidities including hypertension, dislipidaemia,
and cardiovascular disease requiring pharmacological treatment. Additional treatment for gout may lead to further polypharmacy in these patients.

We observed that current treatment for gout was suboptimal when compared to the EULAR guidelines. Almost half the patients who met the criteria for urate-lowering therapy were not receiving this medication. Our study did not determine whether patients had evidence of radiographic changes for gout which are included in the EULAR treatment recommendations; hence the number that should have been on treatment may be higher. In those receiving urate-lowering therapy, only a small minority were achieving the treatment target for serum uric acid-lowering. Also, over half the patients with gout were on diuretic therapy.

These data suggest a need for greater awareness, both regarding the high prevalence of gout in this population as well as appropriate treatment strategies for these patients.

In summary, gout is a frequent comorbidity in patients with Type 2 diabetes. We believe that this work highlights the importance of careful assessment of musculoskeletal disease in patients with Type 2 diabetes. Increased recognition of this association and risk factors should lead to improved management of these patients.

**Competing interests:** None known.

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**References:**


Evidence-based resource use by practice nurses in the Greater Auckland region of New Zealand

Karen J Hoare, Jane Steele, Felix S F Ram, Bruce Arroll

Abstract

Aim To determine self-reported use of New Zealand’s Guideline’s Group (NZGG) and BPAC$^\text{NZ}$ resources by practice nurses (PNs) in the Greater Auckland area of New Zealand.

Method A postal survey of all PNs registered on the University of Auckland’s Department of General Practice and Primary Health Care’s database.

Results A total of 419 of 917 (46%) PNs working in 280 general practices returned completed questionnaires. The majority of PNs did not use either the NZGG (53%) or BPAC$^\text{NZ}$ guidelines (57%) and 35% did not use any evidence resources. The main reason these resources were not used was lack of knowledge about them, one-third of PNs had never heard of NZGG guidelines and 42% had never heard of BPAC$^\text{NZ}$ guidelines. Of those who knew of NZGG guidelines, 74% found them useful, (a fair amount’ or ‘very’) and 94% found BPAC$^\text{NZ}$ guidelines useful (a fair amount’ or ‘very’). When PNs knew of these resources, 74% used NZGG guidelines and 69% used BPAC$^\text{NZ}$ guidelines for patient care.

Conclusion PNs who knew of New Zealand Guidelines and BPAC$^\text{NZ}$ found them useful in patient management. Practice nurses are not routinely on the mailing list of these two organisations. Strategies to increase PN awareness of these publicly funded evidence-based resources may increase their use and thus contribute to the reduction in health inequalities between ethnic groups in New Zealand.

Evidence-based practice and the use of clinical guidelines to facilitate clinical effectiveness is one of the seven pillars of clinical governance, defined by Scally and Donaldson as

A system through which NHS organisations are accountable for continuously improving the quality of their services and safeguarding high standards of care, by creating an environment in which clinical excellence will flourish.$^1$

Although conventional texts are available to inform healthcare professionals, access to up-to-date research findings and clinical guidelines is considered best practice when caring for patients.$^2$ A recent survey of 171 Auckland practice nurses illustrated that 28% of the sample felt least competent to give smoking cessation advice despite a readily available guideline at the click a mouse.$^3$

The New Zealand Guidelines Group (NZGG) was established in 1996 by the National Health Committee (NHC) (www.nzgg.org.nz). Initially it was an informal network of expertise producing guidelines and advising on implementation. In 1999 it became an independent incorporated society. It is funded mainly by the Ministry of Health.$^4$
BPAC\textsuperscript{NZ} is an independent organisation which provides evidence-based, cost-effective information for health professionals caring for New Zealand citizens (www.bpac.org.nz). It is funded by DHBNZ (District Health Board New Zealand) which is a sector group comprising representation from all 21 District Health Boards throughout New Zealand, and PHARMAC—the government-funded pharmaceutical agency.\textsuperscript{5}

A survey of PNs' use and attitude to computers conducted 10 years ago, in 1997, illustrated that the majority of PNs who responded to the survey used a computer in the general practice where they worked mainly for storing patients' names and addresses and for recalling patients for follow-up appointments.\textsuperscript{6}

During a 3-month period between November 1999 and February 2000, 499 New Zealand GPs were surveyed to assess their use of evidence databases and while 56\% (n=212) reported ever using the internet in regard to a patient, only 40\% (n=141) reported access to Internet at their practice.\textsuperscript{7}

A survey of Internet use of general practitioners, practice nurses and pharmacists conducted in 2003 in the North Island of New Zealand illustrated that, of 175 GPs and 138 nurses who responded, 51 GPs (29\%) and 17 nurses (12\%) used Internet websites frequently for health information.\textsuperscript{8}

The objective of this study was to estimate the use of NZGG and BPAC\textsuperscript{NZ} resources by PNs in the Greater Auckland region of New Zealand.

Methods

A two-page questionnaire containing 12 questions was sent with a cover letter to 917 practice nurses following a telephone call to the 280 practices and Accident and Medical departments. During the telephone call, JS (research assistant) explained to the PN the objectives of the questionnaire. The PN contacted by telephone was requested to take responsibility to communicate the objectives of the questionnaire to all other PNs within the practice.

The telephone numbers and addresses of the PNs were obtained from a database held at the Department of General Practice and Primary Health Care at University of Auckland. The University of Auckland Ethics Committee approved the research. The survey was carried out from July 2007 till October 2007. The questionnaire was based on a survey of the use of the Cochrane Library by General Practitioners in London.\textsuperscript{9} Respondents answered ‘yes’ or ‘no’ to their use of NZGG and BPAC\textsuperscript{NZ} resources. If they answered ‘yes’, frequency of use was gauged using a modified Likert-scale scoring system. If they answered ‘no’, reasons for not using resources were requested. Usefulness of the resources and reasons for accessing them were also ascertained, along with user-friendliness of the websites. Additionally, an open-ended question asked about use of other sources of evidence.

Results

Of the sample, 419 practice nurses returned the questionnaire—a response rate of 46\%. Table 1 illustrates use of NZGG, BPAC\textsuperscript{NZ}, and other evidence sources.

Over half of the respondents did not use NZGG (53\%) or the BPAC\textsuperscript{NZ} (57\%) guidelines, and 35\% of the sample used no evidence-based resources. Two respondents (0.4\%) used paper versions of NZGG guidelines and 17 respondents (4\%) used BPAC\textsuperscript{NZ} paper resources. Six percent of the sample used evidence resources other than NZGG and BPAC\textsuperscript{NZ}, and 35\% used no resources.
Table 1. Practice nurse use of New Zealand Guidelines (NZGG) and BPAC\textsuperscript{NZ}

<table>
<thead>
<tr>
<th></th>
<th>n=419</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Zealand Guidelines</td>
<td></td>
<td>196 (46%)</td>
<td>223 (53%)</td>
</tr>
<tr>
<td>BPAC</td>
<td>n=419</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>157 (37%)</td>
<td>238 (57%)</td>
</tr>
<tr>
<td>Use NZGG, BPAC\textsuperscript{NZ}, and other resources</td>
<td>n=419</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>57 (14%)</td>
<td>147 (35%)</td>
</tr>
<tr>
<td>Use other evidence-based resources (not NZGG or BPAC\textsuperscript{NZ})</td>
<td>n=419</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>27 (6%)</td>
<td>147 (35%)</td>
</tr>
</tbody>
</table>

Table 2 illustrates the frequency with which NZGG and BPAC\textsuperscript{NZ} resources were used by the respondents. The majority of the sample who did use NZGG used it seldomly, whereas the majority who used BPAC\textsuperscript{NZ} guidelines used it occasionally (more than four times each year).

Eighteen percent of the sample used NZGG frequently and 23% used BPAC\textsuperscript{NZ} frequently; 13% of the sample used NZGG regularly (almost every week) and 9% of the sample used BPAC\textsuperscript{NZ} regularly.

Table 2. Frequency of use of NZGG and BPAC\textsuperscript{NZ} websites

<table>
<thead>
<tr>
<th>Frequency</th>
<th>NZGG n=196</th>
<th>BPAC\textsuperscript{NZ} n=157</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seldom (1–4 times per year)</td>
<td>66 (34%)</td>
<td>39 (25%)</td>
</tr>
<tr>
<td>Occasionally (more than 4 times per year)</td>
<td>59 (30%)</td>
<td>49 (31%)</td>
</tr>
<tr>
<td>Frequently (monthly)</td>
<td>35 (18%)</td>
<td>36 (23%)</td>
</tr>
<tr>
<td>Regularly (almost weekly)</td>
<td>25 (13%)</td>
<td>14 (9%)</td>
</tr>
<tr>
<td>Other</td>
<td>11 (6%)</td>
<td>7 (4%)</td>
</tr>
</tbody>
</table>

Table 3 indicates the reasons NZGG and BPAC\textsuperscript{NZ} resources weren’t used by the sample. One-third of the sample had never heard of NZGG and 42% of the sample had never heard of BPAC\textsuperscript{NZ} guidelines. A similar percentage (6 and 5, respectively) were aware of the resources, but did not understand their purpose. Eleven percent were unable to use NZGG because of time restraints, and 5% said the same in relation to BPAC\textsuperscript{NZ} resources.

Seventeen (4%) felt they had no use for NZGG and 11 (3%) had no use for BPAC\textsuperscript{NZ} guidelines. Eighteen (4%) of the sample stated that they did not have access to the Internet. There was no question asking whether access to a computer was from work or home.
Table 3. Reasons given for not using NZGG or BPAC\textsuperscript{NZ}

<table>
<thead>
<tr>
<th>Frequency</th>
<th>NZGG n=419</th>
<th>BPAC\textsuperscript{NZ} n=419</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never heard of it</td>
<td>140 (33%)</td>
<td>175 (42%)</td>
</tr>
<tr>
<td>Aware of it but do not understand it</td>
<td>25 (6%)</td>
<td>23 (5%)</td>
</tr>
<tr>
<td>Aware of it but unable to use it due to time restraints</td>
<td>47 (11%)</td>
<td>23 (5%)</td>
</tr>
<tr>
<td>Aware of it but do not feel to have any use for it</td>
<td>17 (4%)</td>
<td>11 (3%)</td>
</tr>
<tr>
<td>Other</td>
<td>21 (5%)</td>
<td>28 (7%)</td>
</tr>
</tbody>
</table>

Table 4 illustrates the reasons given for using NZGG and BPAC\textsuperscript{NZ} resources. Some respondents did indicate more than one use. The majority of the respondents stated that both websites were used for patient management: 74% for NZGG and 69% for BPAC\textsuperscript{NZ}. Over one-third (39%) used NZGG for a course they were studying and 20% used BPAC\textsuperscript{NZ} for the same reason. A similar percentage of respondents (21% and 23%, respectively, for NZGG and BPAC\textsuperscript{NZ}) used the resources for research.

Table 4. Reasons for using NZGG and BPAC\textsuperscript{NZ}

<table>
<thead>
<tr>
<th>Variables</th>
<th>NZGG n=196</th>
<th>BPAC\textsuperscript{NZ} n=157</th>
</tr>
</thead>
<tbody>
<tr>
<td>Information to help with a course you are studying</td>
<td>76 (39%)</td>
<td>31 (20%)</td>
</tr>
<tr>
<td>Information to help with a course/seminar you conducted</td>
<td>21 (11%)</td>
<td>7 (4%)</td>
</tr>
<tr>
<td>Research</td>
<td>45 (23%)</td>
<td>33 (21%)</td>
</tr>
<tr>
<td>Patient management</td>
<td>146 (74%)</td>
<td>109 (69%)</td>
</tr>
<tr>
<td>Other</td>
<td>25 (13%)</td>
<td>20 (13%)</td>
</tr>
</tbody>
</table>

Table 5 illustrates that of the sample who knew of the websites, the majority found them useful: 36% said ‘a fair amount’ for NZGG and 46% for BPAC\textsuperscript{NZ}. Thirty-eight percent found NZGG ‘very’ useful and 48% found BPAC\textsuperscript{NZ} ‘very’ useful.

Table 5. How useful respondents found the resources

<table>
<thead>
<tr>
<th>Usefulness of resources</th>
<th>NZGG n=196</th>
<th>BPAC\textsuperscript{NZ} n=157</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not at all</td>
<td>10 (5%)</td>
<td>9 (6%)</td>
</tr>
<tr>
<td>A little</td>
<td>35 (18%)</td>
<td>17 (22%)</td>
</tr>
<tr>
<td>A fair amount</td>
<td>71 (36%)</td>
<td>73 (46%)</td>
</tr>
<tr>
<td>Very</td>
<td>75 (38%)</td>
<td>50 (48%)</td>
</tr>
</tbody>
</table>

Table 6 illustrates how user-friendly the respondents who knew of the BPAC\textsuperscript{NZ} website found it; most of the respondents (49%) stated ‘a fair amount’ and 24% stated ‘very’.
Table 6. How user-friendly practice nurses (of those who had used it) found BPAC\textsuperscript{NZ} (n=157)

<table>
<thead>
<tr>
<th>User-friendliness of BPAC\textsuperscript{NZ}</th>
<th>Number of practice nurses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not at all</td>
<td>0</td>
</tr>
<tr>
<td>A little</td>
<td>19 (12%)</td>
</tr>
<tr>
<td>A fair amount</td>
<td>77 (49%)</td>
</tr>
<tr>
<td>Very</td>
<td>37 (24%)</td>
</tr>
</tbody>
</table>

Appendix 1 illustrates other evidence-based websites utilised by the respondents. The authors assigned the websites listed by the respondents to the category evidence-based. The assignment of some of the websites was arbitrary as not enough information was given by the respondents.

**Discussion**

This is the first study in New Zealand to examine the use of two premier evidence-based resources, specific to the New Zealand population, by PNs. It was a large sample of 917 practice nurses and nearly half of the sample returned the questionnaire (a response rate of 46%). This return rate was achieved by a telephone call to 280 practices prior to the mail-out of the questionnaires—an evidence-based strategy used to increase response rates to questionnaires.\textsuperscript{10} There was only one mail-out of questionnaires and the response rate is similar to that of other studies with a single mailout to health professionals.

If this sample is representative of PNs in Greater Auckland, less than half of the sample access NZGG or BPAC\textsuperscript{NZ} resources to provide care for patients. One-third of the sample did not access any websites. The situation has improved since a survey conducted in 2003 when only 12\% of PN’s reported accessing websites for health information.

The authors of the 2003 study cited one of the limitations as the small sample size of PN’s (128) and that GPs were asked to pass on the questionnaire to the PNs. Our study sent questionnaires directly to PNs. A qualitative study of Flemish (Belgian) nurses found that they do not achieve a sufficient level of mastery in applying evidence-based nursing, taking time to read on duty was difficult and in some cases felt to be ethically wrong.\textsuperscript{11}

An online survey of 4451 nurses in the UK during June 2006, illustrated that 72\% of the sample accessed the Internet more than once per week from their workplaces; 267 (6\%) of the nurses worked from general practice settings.\textsuperscript{12}

The UK has had a uniform IT strategy since the publication of *Information for Health* in 1998.\textsuperscript{13} Concern about the lack of progress in achieving the aims of the strategy led to the launch of the *National Programme for Information Technology* (NPfIT) in 2002 with the appointment of a Director General of IT and a top-down approach to procurement and implementation.\textsuperscript{14}

This approach, along with the statutory duty of clinical governance required of all NHS staff,\textsuperscript{15} has undoubtedly led to the greater use of evidence-based resources by UK PNs than currently seen in Belgium or New Zealand.
The strengths of this study are the sample size and the use of a validated questionnaire from a previous UK study. Limitations include no individual information collected to correlate age, postgraduate education, and experience with use of NZGG and BPAC\textsubscript{NZ} resources. The questionnaire did not explicitly ask about paper-based resources of NZGG or BPAC\textsubscript{NZ} and so some respondents may have inadvertently denied knowledge of the web resources but used paper based copies. However, this is probably limited to only a few PNs as those that did use paper resources did annotate the questionnaire accordingly.

Of concern are the numbers of PNs who have never heard of these websites; 33\% (140) of the sample had never heard of NZGG and 42\% (175) had never heard of BPAC. Seventeen (4\%) felt they had no use for NZGG and 11 (3\%) had no use for BPAC.

Although it is encouraging that the numbers of PNs who access health information websites is increasing, there are still many who do not. Many PNs may not subscribe to paper copies of BPAC\textsubscript{NZ} and so be unaware of the web resource. PNs are governed by the Health Practitioners Competence Assurance Act (2003) and one of the principles of the code of conduct for nurses is to maintain standards of practice.\textsuperscript{16}

The majority of the sample (73\%) who knew of the BPAC\textsubscript{NZ} website found it user-friendly. The Ministry of Health, using public funds, supports NZGG to produce clinical guidelines for all healthcare professionals. Similarly, DHBNZ and PHARMAC are publicly funded bodies who support BPAC\textsubscript{NZ}.

One of the aims of the Primary Health Care Strategy (PHCS) is for nurses to work in different ways to reduce the inequalities in health between ethnic groups in New Zealand.\textsuperscript{17} The inequalities are significant; the difference in mortality between Māori and non-Māori is worse than that between non-Hispanic Whites and non-Hispanic African Americans in the US.\textsuperscript{18}

One way to achieve the aim of the PHCS is for all health professionals to adhere to best practice and clinical guidelines. Well organised, evidence-based primary care can compensate for considerable social disadvantage.\textsuperscript{2} Resources are required to improve utilisation and increase awareness of NZGG and BPAC\textsubscript{NZ} resources amongst PNs not only in the Greater Auckland region but throughout New Zealand.

Competing interests: None known.

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References:

## Appendix 1

<table>
<thead>
<tr>
<th>Name of resource</th>
<th>Numbers reporting use of this resource</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACC (NZ Government)</td>
<td>2</td>
</tr>
<tr>
<td>American Diabetes Association</td>
<td>1</td>
</tr>
<tr>
<td>ARPHS</td>
<td>1</td>
</tr>
<tr>
<td>American Journal of Nursing</td>
<td>1</td>
</tr>
<tr>
<td>Asthma Foundation</td>
<td>5</td>
</tr>
<tr>
<td>Asthma Guidelines Starship–ACH</td>
<td>1</td>
</tr>
<tr>
<td>Auckland University database</td>
<td>1</td>
</tr>
<tr>
<td>Australian Nursing Guidelines</td>
<td>1</td>
</tr>
<tr>
<td>Best Practice Magazine</td>
<td>4</td>
</tr>
<tr>
<td>Bandolier</td>
<td>1</td>
</tr>
<tr>
<td>Best Treatment</td>
<td>4</td>
</tr>
<tr>
<td>British Medical Journal</td>
<td>7</td>
</tr>
<tr>
<td>British Nursing Journal</td>
<td>1</td>
</tr>
<tr>
<td>CADS website</td>
<td>1</td>
</tr>
<tr>
<td>Chronic management guidelines</td>
<td>1</td>
</tr>
<tr>
<td>Classes/ seminars/lectures</td>
<td>4</td>
</tr>
<tr>
<td>Clinical evidence handbook</td>
<td>3</td>
</tr>
<tr>
<td>Clinical evidence.com</td>
<td>4</td>
</tr>
<tr>
<td>Cochrane Library database including Joanna Briggs</td>
<td>6</td>
</tr>
<tr>
<td>Diabetes NZ Guidelines online/protocol/courses</td>
<td>8</td>
</tr>
<tr>
<td>Ebsco research data base</td>
<td>1</td>
</tr>
<tr>
<td>GP Weekly magazine</td>
<td>1</td>
</tr>
<tr>
<td>IMAC Immunisation guidelines</td>
<td>9</td>
</tr>
<tr>
<td>Mayo clinic</td>
<td>2</td>
</tr>
<tr>
<td>National Heart Foundation</td>
<td>4</td>
</tr>
<tr>
<td>NHS Guidelines</td>
<td>2</td>
</tr>
<tr>
<td>New Zealand Medical Journal</td>
<td>1</td>
</tr>
<tr>
<td>NICE Guidelines</td>
<td>2</td>
</tr>
<tr>
<td>Paediatric Society of NZ</td>
<td>1</td>
</tr>
<tr>
<td>Respiratory Foundation NZ</td>
<td>1</td>
</tr>
<tr>
<td>Travel health—CDC website</td>
<td>4</td>
</tr>
<tr>
<td>UK Guidelines</td>
<td>1</td>
</tr>
<tr>
<td>WHO/Centre E-B Nursing</td>
<td>2</td>
</tr>
<tr>
<td>WONS</td>
<td></td>
</tr>
<tr>
<td><a href="http://www.prodigy.com">www.prodigy.com</a></td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>90</strong></td>
</tr>
</tbody>
</table>
When should I do rural general practice? A qualitative study of job/life satisfaction of male rural GPs of differing ages in New Zealand

Tom Noonan, Bruce Arroll, David Thomas, Ron Janes, Raina Elley

Abstract

**Aims** There is a shortage of rural general practitioners in New Zealand (NZ), and many are approaching retirement. This qualitative study was undertaken to investigate the perceived advantages and disadvantages of rural general practice at various stages of family life of male NZ-trained GPs.

**Methods** Semi-structured interviews were conducted with 12 male NZ-trained rural GPs from the Waikato and Northland regions during December 2006. Major themes relating to rural general practice as a career were identified and analysed with respect to the family life cycle: no children yet, pre-school children, high school children, or ‘empty nest’.

**Results** Trends in the frequency of themes, and changes in the sentiments within each theme across different stages of family life were noted.

**Conclusion** Based on the frequency of themes and sentiments, a conceptual picture of the influences of stages of a male rural GP’s family life on the GP are discussed.

The New Zealand medical workforce is having difficulty in attracting and retaining doctors, and this is particularly true in rural areas. In addition, the existing general practice workforce is aging at a significant rate.¹

Over the last few years various steps have been taken to address the rural workforce shortage; however despite these measures, the majority of rural General Practitioners (GPs) in NZ are still overseas-trained.¹,² Due to these workforce shortages, numerous studies into rural general practice have been performed, both in New Zealand and abroad.

The existing literature within New Zealand and internationally regarding rural General Practice has typically focused on the demographics of the population served by the GP or the intrinsic properties of the practice itself. Various aspects of the practice and patients that cause satisfaction or dissatisfaction in GPs have been documented.³

Suggested *advantages* of rural general practice include positive aspects of a rural community, better therapeutic relationships with patients, and the satisfaction from practicing “real medicine”.⁴–⁶

Suggested *disadvantages* include factors such as excessive work hours (especially oncall), demanding rural communities, and difficulty finding locum relief.⁴–⁶ Certain factors, such as the rural community, had both positive and negative aspects.
Investigations into the satisfaction/dissatisfaction of rural GPs have indirectly looked at the life of a rural GP’s family. There have also been investigations into the effects and support needs of the rural GP's family, with numerous stressors being identified. These studies have identified common themes such as community demands on family, social difficulties of the family, professional isolation of the spouse, and education problems for children.

Although it was implied, no specific means were used to isolate and examine the dynamic nature of these factors; there was no specific evaluation at different family life stages of the rural GP.

Female GPs in rural practice have some unique stressors and rewards. These include role strain between childcare and doctor, security concerns when oncall, and stress caused by the types of problems sometimes presenting to a female GP.

Case studies dealing with specific issues raised by family members of rural GPs have been documented. These illustrated efforts to address the issues raised by the family members of several GPs, such as spouse employment, limited social interaction with others in the community, and so on.

Attitudes towards rural general practice amongst junior doctors have been studied though not yet to a degree where perceived barriers to entering practice have been confidently deduced.

An ambition amongst students is to practice in a specialty with a good “work versus lifestyle” balance. Clearly this requires information about the interaction of family and work life to be available. This study provides information on the perceived advantages and disadvantages of rural general practice according to the views of male GPs at various stages of family life.

Method

Participants in this study were male, non-Māori, New Zealand-trained GPs, with a Rural Ranking Scale (RRS) score of at least 35 points (the RRS is a measure of the rurality of a GP, encompassing factors such as oncall frequency and distance to the nearest base hospital).

Māori GPs were excluded based on the advice of Associate Professor Papaarangi Reid (Auckland University; personal communication), who considered that the aims of the study did not confer any significant generalisability to Māori. Female GPs were excluded principally because funding limitations restricted the sample size and geographical extent of the study making it difficult to include sufficient numbers of female GPs. Overseas-trained doctors were excluded to focus the study on NZ-trained rural GPs.

A list of rural general practices in Northland and Waikato was obtained from the New Zealand Institute of Rural Health. Using this list, and public domain information such as telephone books and primary health organisation (PHO) websites, the contact details of each practice were obtained, along with the names of doctors.

The New Zealand Medical Council database was then used to confirm the country and year of graduation of individual rural GPs. The year of graduation gave a rough estimate of the GP’s age.

This contact list was stratified by year of graduation into 10-year bands (since 1995, 1985–1994, 1975–1984, and 1965–1974) and a number of GPs were randomly sampled from each group. These categories were used in an attempt to sample GPs from a variety of stages of family life.

Only one GP per town was selected; and once selected, all other GPs from that town were excluded. This allowed a wide geographic and age spread of the participants to be obtained.

A total of 12 GPs were approached by phone to take part in the study, with all 12 agreeing to do so. Each GP received a $150 gratuity as compensation for the time taken to take part in the study.
All GPs were interviewed in their practice by one of the authors (TN). The interviews were recorded on audiotape, transcribed, and copies returned to the participants for corrections.

Semi-structured interviews were conducted, beginning with several closed background questions. This enabled the interview to be modified, and to allow for analysis of different demographic groups. The remaining interview consisted of eight broad questions, designed to elicit elaborated comments and stories.

For questions that were more abstract, brief prompting was used to elicit discussion if this was not spontaneously forthcoming. Prompting was, however, reserved for situations only where an apparently important point had not been raised. Prompts were based on previously interviewed GPs and from information from other studies.

At the end of the interview, each GP was asked if there were any other points they felt were important to raise that have not yet been elicited by previous questions.

Interviews were then transcribed and saved as a Word document. Personally identifiable and location-specific references were removed from each transcript (such as names of spouses and towns). Audio CDs of their interviews were made and, along with the typed transcript, were sent to each participating GP. GPs were given the opportunity to confirm the validity of the transcription and to remove and/or edit the transcript. At the end of each transcript was a section for the GP to add any additional comments that may have been stimulated by reading the transcript.

Each participant was coded according to the answers provided in the background questioning (e.g. age, marital status, age of children in the family). The most important code was the stage of the family based on the age of the children: pre-school, primary school, high school, or children having left home. If the GP had children at different stages of schooling they were placed into the group corresponding to the oldest child living at home. All of the male GPs interviewed had children.

Each interview was listened to and the transcripts read multiple times to become immersed in the data and to understand the context of each statement. It was clear that there were several recurring major themes amongst the transcripts.

Once all transcripts were coded, all comments within each theme were examined, looking for relationships to other themes, and attempting to build a conceptual hierarchy into which interrelating themes would fit.

These hierarchies and individual themes were not watertight and as a result, some sentiments fell between or across several themes, and several individual comments were found in multiple themes. Several matrices were constructed examining the frequency that each theme was raised with respect to particular demographics of the GPs. We used NVivo (version 7) software to assist in analysing the data.

Results

Several common themes emerged from the interviews. For ease of understanding these have been broken down into those pertaining to the physical environment, small communities, family, and self.

Physical environment

Benefits of rural living—There were numerous references made to the benefits of living in a rural setting. These benefits included more contact with natural environments, and better recreational opportunities.

Community

Belonging to a community—Generally the GPs felt the community where they worked was a positive place to live and work.

Limitations of living in a small community—Practicing in a small town caused unique stressors and pressures on GPs and their families. These included a sense of
feeling trapped, having limited social networks, people expecting on-street consultations, and a sense of being ‘owned’ by the community as well as professional and social isolation of spouse and limited family opportunities.

Family

Visibility in small communities—A negative aspect noted was the high visibility of rural GPs and their families in small rural communities. Due to the apparent high status in the community of the GP, their family is usually well known, and the responses of people in everyday life often reflected their role as a GP.

Poor quality of secondary schooling—The lack of quality secondary school education in the local area was a serious concern for the GPs, with a few notable exceptions. Many GPs stated that once their children reach high school they would consider leaving the area where they currently practice. These findings are consistent with findings from other studies that have reported that many GPs leave rural practice once their children reach high school.4

Support from family—The role of the family in supporting the GP appeared to be critical in allowing the GP to continue to deal with the pressures of work. Participants reported that this support gave them a broader perspective on life, and reinforced the traditional family unit.

Rural areas being a positive place to raise children—Many references were made to the advantages of raising children in a rural community. Factors such as a closer community, environmental, and recreational factors (in particular) were mentioned.

Stress on family and family relationships suffering—The direct influence of the amount of time needing to be spent away from their family put strain on family relationships. The indirect effects of a demanding job also rubbed off on family members causing further problems.

Burden of oncall impacting family time—Having to be available to attend a call caused significant problems for many GPs when planning family outings. There was also a resentment of being called away from their family at other times, such as during meals.

Self

Adequate remuneration—Based on previous studies,4 it was anticipated that responses regarding remuneration would state that rural GPs were underpaid. However this was not the case, with the overall impression being that a career as a rural GP is well remunerated.

Variety in rural general practice—The work of the rural general practitioner is diverse, with significant differences between practices. However there were several key aspects of rural practice that the GPs reported to be rewarding. Many of the GPs noted they derived deep satisfaction and enjoyment from their work. Some aspects of the variety of rural practice included; dealing with “real” medicine and emergencies, providing extended scope of care, enjoyment from being oncall, developing a broader perspective on patients, and the community knowing and trusting the GP.
Being oncall—Undoubtedly the most consistent and pervasive disadvantage raised was the oncall duty. Negative aspects included having to be available at all times, having to adequately perform the next day, doing “out of rostered” call, and inadequate remuneration for oncall work.

Financial pressures from running a small business—Many of the GPs reported stress involved in running a business, something medical school had not prepared them for.

Overwork causing burnout and depression—The continual pressures and workload of being a rural GP, and the inability to effectively unload this stress, resulted in burnout or depression for many of the GPs.

Dimensions of themes

The following themes were noted to have significant variation between the different stages of life, both in the frequency of comments and the sentiments expressed.

Attitudes to being oncall—For GPs in the youngest age groups with young families, attitudes to oncall work were positive, or at worst ambivalent. Indeed, the GPs enjoyed the challenge and variety of work encountered during on-call work.

…great sense of enjoyment I get out of my job. I do enjoy ironically being on call, and going out to some minor trauma and that sort of stuff

The same disadvantages of oncall work were acknowledged by GPs of all ages, but the attitudes towards the significance of these disadvantages was significantly less for younger GPs.

This positive attitude dropped off as children entered school, with attitudes shifting to that of deep resentment of oncall work.

But I find as I get older, even more so, the after hours is more distasteful, more stressful, and less remunerative than it ever was. If I get rid of one thing it would be getting rid of after-hours 24/7

The negative attitudes towards oncall dropped off slightly for GPs whose children had left home, with attitudes being more of a pragmatic acceptance of this burden.

Depression and burnout—This seemed to be a much more common sentiment for those with primary school-aged children than for any other group.

I was working long hours, heaps of call and I was a young GP and I had the two young children then a baby in 2 years. Towards the end of that, my boss kept asking me to do extra stuff. In the end I blew up really, I couldn’t handle it, just collapsed, so had to leave there

Visibility in a small community—A lack of personal identity unrelated to their role as a doctor was a significant issue for both the GP and for their family. Acknowledgement of this factor was limited for younger GPs, with increasing awareness as time in practice increased. A retrospective acknowledgement that this had been previously been an issue was notable for those GPs whose children had left home.

…as they are teenagers and they seek to establish their own identity, they have to somehow deal with the fact that Dad is the local GP and a known figure to everyone in the community

Family relationships suffering—Both the direct influence of time away from the family, and the indirect influences of a job of a rural GP putting strain on family
relationships were present for all stages. There was, however, a trend in that GPs with pre-school aged children seemed to suffer worst from this, with progressively less of an effect.

**Discussion**

This is the first NZ study to examine the advantages and disadvantages of rural general practice from the perspective of where the rural GP is in relation to the family lifecycle.

There are numerous possible explanations for the observed differences in the perceptions of the advantages and disadvantages at various stages of family life.

The original observation that lead to the development of this study was that of GPs leaving rural practice when their children entered high school. From analysis of the themes and various quotes found in this study, it appears as though a combination of several factors appear to come together at this stage of life and trigger many GPs to leave rural practice.

The combination of several themes: perspective on life, environmental opportunities, and the advantages (and both the advantages and disadvantages) of being oncall can be used to build a picture of the attitudes of young GPs with a preschool family. The satisfaction with the rural environment lend themselves to the idea of the young GP being energetic and enthusiastic, following the cliché “work hard and play hard”. After several years, however, this enthusiasm seems to drop, with the challenges of raising children and continual demands of the job beginning to take their toll. This is illustrated by the decline in enjoyment derived from being oncall, but continual acknowledgment of the difficulties of call.

As their children enter school, there is a decreased satisfaction with the rural environment and an apparent disregard for the prior opinion of the positive aspects of raising children in a rural environment with primary school-aged children. It is therefore not surprising that by the time the GP’s family is at primary school there is a greatly increased prevalence of feelings of burn out, exhaustion, and depression.

A challenging career did not appear to be sufficient to warrant leaving practice, however. An impression gained from the interviews was that the GPs would tolerate working in difficult conditions, but will not tolerate a situation that has significant negative effects on the family. The salient example of this situation is when the GP’s children enter high school, which was often considered to be of low quality in the rural areas.

It is obvious from the comments that different priorities influence career choice at different stages of rural GPs family life. Primary school education in rural areas is perceived as more than adequate. However many GPs perceived that rural high school education was not as good as that available in urban centres and this caused them to see this as an issue which could prompt them to consider relocating. Once older children have moved out of the house, it appears that the burden of being oncall is the main factor influencing rural GPs to consider relocating.
Finally there were numerous references made to spending 10 years in rural practice, then moving on. This 10-year period often coincided with the children entered high school.

The hypothesis of poor quality high school education being the trigger to leave a difficult but tolerable career is supported by the observations made on those GPs with children at high school. These GPs had quality secondary school education in the immediate surrounding area, eliminating this trigger. After discussion around schooling issues, it was found that many of these GPs would have considered leaving the area had the education been of poor quality.

A strength of this study is that all 12 GPs approached agreed to be interviewed. Having a medical student with an interest in rural general practice do the interviews may have been less threatening that a GP colleague, yet more acceptable than a non-medical interviewer.

The limitations of this study are a result of several factors.

The interviewer was a medical student with limited experience in qualitative interviewing. During the initial introductions, the interviewer (TN) told the rural GPs he had an interest in entering rural general practice. Thus this could have influenced respondents to avoid negative answers that might give a bad impression of rural general practice, or to respond more positively to some questions.

In developing this study, much background reading on the rural New Zealand general practice was performed. This no doubt influenced the preconceptions about the nature of rural general practice before the study began. The semi-structured questionnaire format for the study may have enabled some of these preconceptions to influence the discussion with the GPs.

Due to the personal nature of many of the questions, it was necessary for some empathic connection between the interviewer and the GP to be established. There will have been variations in the level of comfort that each GP has with the interviewer, conceivably affecting the degree to which the GPs were forthcoming with the more personal issues raised.

It was also noted that several social taboos were encountered during the study, these potentially interfering with the intrinsic validity of results. One such taboo was that of one’s work life negatively affecting one’s family. On several instances self-censorship of a spontaneously forthcoming disadvantage was noted. Several transcripts were also altered by the participants to remove references to these negative effects.

It was apparent that the same trouble that has affected prior studies into rural general practice was also a factor in this study; the enigma of the “typical rural general practice”. The heterogeneity of practice situations was such that the findings of the study may not be generalisable until confirmed by other similar studies.

This study did not interview GPs who have recently left rural practice. It is likely that these GPs would have a different spectrum of concerns, or at least have a different opinion of the relative importance of each concern.

By necessity, the sample size of GPs was limited to 12. This does confer some uncertainty regarding the extrinsic validity of the variation in themes found. However
the nature of the retrospective questioning in the interviews did help to partly address this limitation.

Only GPs who had their details listed in sources readily accessible in the public domain were contacted. This may have resulted in a biased selection of GPs who had not chosen to have their name withdrawn from such public domain sources, possibly due to unique disadvantages for them.

Many of the issues raised during this study are reflected in other local and international literature, though the interactions of these themes with various stages of family life have not been studied in depth in any literature we could find. An awareness of these issues for potential rural general practitioners may enable them to develop strategies to prevent them from succumbing to the same difficulties as previous generations of GPs have.

Competing interests: None known.

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References:


Clozapine and myocarditis: a case series from the New Zealand Intensive Medicines Monitoring Programme

Geraldine R Hill, Mira Harrison-Woolrych

Abstract

Aim To examine a New Zealand case series of clozapine-associated myocarditis.

Methods All cases of myocarditis in the Intensive Medicines Monitoring Programme’s (IMMP) clozapine database were identified and reviewed.

Results 25 cases of myocarditis associated with the use of clozapine have been reported to the IMMP. The majority of cases (84%) were male and the mean age was 35.5 years. Myocarditis occurred at daily clozapine doses ranging from 12.5 mg to 500 mg. Eighty percent of the cases developed within 1 month of starting the medicine, although in three cases the onset was more than a year after commencing clozapine. Of the 25 cases, 2 patients died.

Conclusions This New Zealand case series of clozapine-associated myocarditis is similar to a recent Australian case series. Clozapine-associated myocarditis most often occurs within 1–2 months of starting clozapine, but it may develop at any time while on the medicine, and can occur even at very low doses. A data-linkage study using national morbidity and mortality datasets could estimate the incidence of clozapine-associated myocarditis in New Zealand.

Clozapine, marketed in New Zealand as Clozaril® (Novartis), is an atypical antipsychotic medicine indicated in patients with treatment-resistant schizophrenia. Clozapine has been shown to be more effective than typical neuroleptic medication for the treatment of schizophrenia, but because of the risk of agranulocytosis (which occurs in about 1% of patients in the first year of treatment) use of clozapine is limited to patients who have been non-responsive to, or intolerant of, at least two other antipsychotic agents.

Royal Australian and New Zealand College of Psychiatrists' clinical practice guidelines for the management of schizophrenia and related disorders recommend that clozapine be introduced as soon as treatment resistance to at least two antipsychotics has been demonstrated.

The first case of myocarditis in a patient taking clozapine was reported in the literature in 1980, however, it was not recognised as an adverse reaction to clozapine until 1999 when Killian et al reported 15 cases of myocarditis (5 fatal) and 8 cases of cardiomyopathy (1 fatal) that had been notified to the Australian Adverse Reactions Advisory Committee (ADRAC) from among 8000 patients who had taken clozapine between January 1993 and March 1999.

The incidence of clozapine-associated myocarditis reported by Killian et al was about 1 in 500 patients treated with clozapine, or 96.6 cases per 100,000 patient-years. The
incidence has since been reported as 5.0, 16.3, and 43.2 cases per 100,000 patient years in the US, Canada, and UK, respectively. In 2001, a Bayesian neural network analysis by the World Health Organization’s programme for international drug monitoring, which received data from national pharmacovigilance centres in 60 countries, demonstrated a statistically significant association between clozapine and myocarditis that was much stronger than the association between any other antipsychotic agent and myocarditis.

In February 2002, Novartis issued a ‘Dear Health Care Provider’ letter informing doctors of changes made to the boxed warning in the product data sheet to draw doctors’ attention to the risk of myocarditis. Haas et al recently reported a series of 116 cases of suspected myocarditis associated with use of clozapine in Australia during the period 1993–2003. They reported an estimated incidence between 0.7% and 1.2% of treated patients. The median time to onset was 17 days among those for whom treatment dates were known and the majority (88%) of cases developed myocarditis within 6 months of starting clozapine.

Clozapine has been available in New Zealand since 1993. A clozapine register is operated by Novartis to monitor weekly blood tests, a practice which, in the United States, has been shown to reduce the number of deaths from agranulocytosis. Monitoring of clozapine by the Intensive Medicines Monitoring Programme (IMMP) commenced in December 2000.

The aim of this study is to describe the New Zealand experience of clozapine-associated myocarditis by examining a series of cases reported to the IMMP.

Methods
The IMMP carries out post-marketing surveillance on selected medicines by conducting prospective observational cohort studies using prescription event monitoring (PEM). The cohort for each monitored medicine is established using prescription data collected at regular intervals from virtually all community and hospital pharmacies nationwide. Information collected includes the name, address, National Health Identification (NHI) number, gender and date of birth of the patient, doctor identification, date of dispensing, medicine name and formulation, dose, and quantity of medicine dispensed.

The IMMP has monitored four of the atypical antipsychotic medicines available in New Zealand: clozapine, olanzapine, quetiapine, and risperidone. A system of enhanced spontaneous reporting has been utilised to monitor these medicines. Accordingly, reports of adverse reactions were obtained through spontaneous reporting by doctors, nurses, pharmacists and pharmaceutical companies. All clinical events are assessed and coded by medical assessors using terms from a dictionary based on WHOART (World Health Organization Adverse Reaction Terminology). Causality assessment is performed for each event to determine the relationship with the medicine. For this case series, all cases in the IMMP database coded as “myocarditis” associated with clozapine were identified and reviewed. This term was only used when the diagnosis of myocarditis was confirmed by the reporter and/or by record linkage with NZHIS (New Zealand Health Information Service) databases where myocarditis was recorded as a discharge diagnosis.

The processes and practices of the IMMP have been set up to comply with the New Zealand Health Information Privacy Code and the Privacy Commissioner has been advised of the purpose and methods of the programme. The programme has ethical approval and as this study used routine IMMP methods additional ethical approval was not required.
Results

**IMMP case reports**—Table 1 summarises the details of 25 case reports of myocarditis associated with clozapine reported to the IMMP between March 2000 and 15 November 2007. Fifteen cases were reported by the pharmaceutical company and the remaining 10 cases were reported spontaneously by the patient’s doctor.

**Patient demographics**—Of the 25 cases, 3 (12%) were female, 21 (84%) were male, and 1 was of unknown gender. The age of patients ranged from 17 to 72 years with a mean age of 35.5 years (median 30.5 years). Ethnicity data were available for 24 of the 25 cases: 17 (68%) patients were NZ European, 5 (20%) were NZ Maori, 1 (4%) was a Pacific Islander, and 1 was of other ethnicity. Patients were treated for myocarditis mainly in tertiary referral centres throughout New Zealand. About-two thirds of patients (17 of 25) were treated in the Auckland region.

**Dose of clozapine**—The dose of clozapine at the time of the adverse event was recorded for 20 patients. The dose ranged from 12.5 mg daily (for an elderly patient) to 500 mg daily. Among patients for whom dose was recorded, the mean daily dose was 256 mg and the median daily dose was 238 mg.

**Time to onset/treatment duration**—Information on the time from start of clozapine treatment to onset of myocarditis was available for 24 of the 25 cases. Twenty cases (80%) began within 1 month of starting clozapine, 1 case presented 2.5 months after starting clozapine, and 3 cases presented more than a year after starting the medicine (including 1 which presented more than 9 years after starting treatment).

**Outcome**—Two patients (8%) died from clozapine associated myocarditis and 23 patients survived this event (although 2 died at a later date). Whether or not clozapine was continued at the time of the myocarditis event was reported for all patients in this series. Of the 23 patients who survived, clozapine was stopped in 21 patients and continued in 2 patients. In 14 of the 21 patients who stopped clozapine there was evidence of recovery following withdrawal of the medicine (positive dechallenge). Of the remaining 7 patients, the outcome following withdrawal of clozapine was unknown for 5 patients, and 2 patients had not yet recovered at the time of reporting.

**Causality assessment**—Causality assessment was performed for all 25 cases on the basis of the available information reported to IMMP. In 14 cases, the relationship of myocarditis with clozapine was assessed as ‘probable’ as all these patients had a positive dechallenge (as described above). For the remaining 11 cases the relationship was assessed as ‘possible’.

**Concomitant use of another atypical antipsychotic medicine**—Four (16%) of the cases were known to be taking another atypical antipsychotic (2 risperidone, 1 quetiapine, and 1 quetiapine plus olanzapine) in addition to clozapine at the time myocarditis developed. These were in addition to patients who were down-titrating from other atypical antipsychotic medicines whilst starting clozapine, in whom concomitant atypical medicines were not recorded as concomitant medication.
### Table 1. Summary of myocarditis cases reported to IMMP

<table>
<thead>
<tr>
<th>Case</th>
<th>Source of report</th>
<th>Age</th>
<th>Sex</th>
<th>Daily dose (mg)</th>
<th>Onset (days)</th>
<th>Action</th>
<th>Outcome</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Spontaneous</td>
<td>53</td>
<td>M</td>
<td>400</td>
<td></td>
<td></td>
<td>Died</td>
<td>Also taking risperidone</td>
</tr>
<tr>
<td>2</td>
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<td>M</td>
<td>200</td>
<td>7</td>
<td>Withdrawn</td>
<td>Recovered</td>
<td></td>
</tr>
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<td>100</td>
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<td>Withdrawn</td>
<td>Recovered</td>
<td></td>
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<tr>
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<td>M</td>
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<td>300</td>
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<td>Withdrawn</td>
<td>Recovered</td>
<td>Also taking olanzapine and quetiapine</td>
</tr>
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<td>Company</td>
<td>28</td>
<td>M</td>
<td>100</td>
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<td>Withdrawn</td>
<td>Recovered</td>
<td>Also had cardiomyopathy</td>
</tr>
<tr>
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<td>Company</td>
<td>30</td>
<td>M</td>
<td>200</td>
<td>12</td>
<td>Withdrawn</td>
<td>Recovered</td>
<td>Also taking quetiapine</td>
</tr>
<tr>
<td>9</td>
<td>Spontaneous</td>
<td>25</td>
<td>M</td>
<td>200</td>
<td>12</td>
<td>Withdrawn</td>
<td>Recovered</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Company</td>
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<td>M</td>
<td>225</td>
<td>13</td>
<td>Withdrawn</td>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Spontaneous</td>
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<td>M</td>
<td>14</td>
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<td>Died</td>
<td></td>
</tr>
<tr>
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<td></td>
</tr>
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<td>M</td>
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<td>Not yet recovered</td>
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</tr>
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<td>300</td>
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<td>F</td>
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<td>M</td>
<td>500</td>
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<td>Recovered</td>
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</tr>
</tbody>
</table>
Discussion

We have presented a New Zealand case-series of clozapine-associated myocarditis which includes 25 patients whose information has been reported to IMMP from March 2000 until July 2007.

Demographic data from these New Zealand cases are generally similar to those reported in other case series. The recent Australian review (Haas et al) of 116 cases of suspected myocarditis associated with the use of clozapine (between 1993 and 2003) reported that 77.6% of cases were male and the median age was 30 years. This is comparable to the male preponderance (84%) and median age of 30.5 years observed in our series.

Most of the cases of myocarditis reported to the IMMP (80%) developed within one month of commencing clozapine treatment. This is consistent with other case series. In the original Australian report by Killian et al, all 15 cases of myocarditis developed within 1 month of starting clozapine. In the larger, more recent series by Haas et al, 79% of cases developed within 1 month of starting clozapine and nearly 90% developed within 6 months of initiating clozapine therapy. However, it should be noted that clozapine-associated myocarditis occurred in several cases more than a year after starting treatment and the diagnosis should therefore not be overlooked in patients who have been on the medicine for some time. It should also be noted that one of the cases in this series developed myocarditis while taking a very low clozapine dose of 12.5 mg daily.

The proportion of cases in which myocarditis had a fatal outcome (8%) is similar in this case series to that reported in the recent Australian case series in which 12 (10.3%) of 106 patients with clozapine-associated myocarditis died. Similarly, the proportions of patients in the Australian series who had recovered, had not yet recovered at the time of reporting, and in whom the outcome was unknown were also comparable to those reported in this New Zealand series.

Clozapine-associated myocarditis is thought to be a drug-induced, acute hypersensitivity (type I, IgE-mediated) reaction, although other mechanisms have also been proposed including a type III allergic reaction or a direct toxic effect on the heart. Genetic variation and environmental differences have also been postulated to explain variable incidence rates in different countries. A case-control study is currently underway in Australia to examine risk factors for myocarditis. The study aims to identify possible genetic markers, in particular polymorphisms in the genes that code for enzymes involved in clozapine metabolism and the generation of the immune response.

The IMMP relies on data provided by the reporting doctors and the pharmaceutical company. While reporting rates are high, it is likely that more cases of clozapine induced myocarditis occurred than were reported to the IMMP. Cases were only included in this case series if the report included a diagnosis of myocarditis.

The methods used in this study were similar to methods used recently by Haas et al to describe the Australian case-series of suspected clozapine-associated myocarditis.
However, unlike the earlier study by Killian et al.,\textsuperscript{5} strict criteria for case-definition based on clinical and histological evidence were not applied.

Further examination of all clozapine reports in the IMMP database for events which may be presenting symptoms of myocarditis (such as fever, tachycardia, eosinophilia, sudden death) might identify more cases of myocarditis associated with clozapine. A further record-linkage study using national morbidity and mortality datasets would provide a fuller picture of the incidence of clozapine-associated myocarditis in New Zealand.

**Funding statement:** This work was supported by the NZ Ministry of Health (Medsafe) who provide the majority of IMMP funding for post-marketing surveillance. The IMMP has also received general unconditional donations towards monitoring from pharmaceutical companies, including Novartis, the sponsor of Clozaril in NZ. However, pharmaceutical companies have no role in the analysis or interpretation of IMMP data, or in the decision to submit articles for publication.

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**Acknowledgement:** We thank all the New Zealand doctors who actively support the IMMP.

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**References:**

7. Coulter DM, Bate A, Meyboom RH, et al. Antipsychotic drugs and heart muscle disorder in international pharmacovigilance: data mining study. BMJ. 2001;322:1207-9. See also BMJ Website extra for explanation of Bayesian Neural Network Analysis at [http://www.bmj.com/cgi/content/full/322/7296/1207/DC1](http://www.bmj.com/cgi/content/full/322/7296/1207/DC1)


Pharmacovigilance in New Zealand: the role of the New Zealand Pharmacovigilance Centre in facilitating safer medicines use

Desireé L Kunac, Mira Harrison-Woolrych, Michael V Tatley

Abstract

The New Zealand Pharmacovigilance Centre (NZPhvC) is the national centre responsible for monitoring adverse reactions to therapeutic products in New Zealand (NZ). The NZPhvC operates three pharmacovigilance programmes and this article explains how each of these programmes operate, focuses on their strengths and limitations, and looks to the future for medicines safety monitoring in NZ.

Pharmacovigilance has been defined as “the science and activities relating to the detection, assessment, understanding, and prevention of the adverse effects of pharmaceutical products”. Pharmacovigilance is particularly concerned with post-marketing surveillance of adverse drug reactions (ADRs); an important objective being the early detection of previously unrecognised ADRs including drug interactions to better inform patient care and ultimately improve patient safety.

Despite clinical trials prior to licensing, rare or delayed ADRs are often unknown at the time a pharmaceutical product enters the market. This is because such trials are limited in time and number of patients, usually have an efficacy rather than safety focus, and are usually performed in selected patient groups.

The infamous ‘thalidomide tragedy’ that occurred overseas around 1960, highlighted (internationally) the importance of monitoring the safety of medicines once a product is marketed for general use and was a catalyst for the formation of national schemes for collecting information about emerging ADRs.

New Zealand (NZ) implemented a national surveillance scheme in 1965 and was one of the founding members of the World Health Organization (WHO) International Drug Monitoring Programme when it was established in 1968. Today, the ‘New Zealand Pharmacovigilance Centre’ (NZPhvC) is the national centre responsible for monitoring adverse reactions to therapeutic products in NZ.

The purpose of this paper is to provide an overview of how the NZPhvC, through operation of three programmes, contributes to the safer use of medicines in NZ. As the functions of the NZPhvC are dependent upon all those who report adverse reactions, it is important to raise awareness of the programmes operating within the Centre and explain how operation of these programmes contributes to the safer use of medicines in NZ.

The New Zealand Pharmacovigilance Centre (NZPhvC)

The NZPhvC is located in the Department of Preventive and Social Medicine at the University of Otago, Dunedin and contracted by the Ministry of Health (Medsafe) to provide an ADR reporting programme. The aims of the NZPhvC are to identify any side effects of a medicine as early as possible; to determine the frequency of such adverse effects and which patient groups may be at highest risk of the adverse event;
and to report these findings to Medsafe which in turn takes appropriate action leading
to the safer use of medicines in NZ.

The NZPhvC currently utilises a multifaceted approach to ADR detection and
management and operates three main programmes:

- Centre for Adverse Reactions Monitoring (CARM), which is the national
  spontaneous reporting programme established in 1965;
- Intensive Medicines Monitoring Programme (IMMP) introduced in 1977
  which primarily monitors selected newly marketed medicines; and
- Intensive Vaccine Monitoring Programme (IVMP) which commenced in 2004
  to monitor the safety of the meningococcal B vaccine (MeNZB™) during roll
  out of the national Meningococcal B Immunisation Programme.

An overview of the pharmacovigilance activities undertaken by the NZPhvC is
illustrated in Figure 1 and detail regarding each of the key elements is provided
below.

Sources of data

Centre for Adverse Reactions Monitoring (CARM)—The CARM spontaneous
reporting programme is a voluntary, nationwide, structured system for the reporting of
suspected adverse events to medicines. Reports are encouraged from all healthcare
professionals (e.g. doctors, pharmacists, dentists, midwives), coroners, and
pharmaceutical companies as well as consumers regarding any prescription or over-
the-counter (OTC) medicine (including herbal and alternative medicines and dietary
supplements), and vaccines.

CARM encourages reporting of any unexpected event thought to be medicine or
vaccine related, including those of clinical concern, all adverse events to new
medicines, all serious allergic reactions and drug interactions. CARM encourages
reporters to report and document ADRs which meet the above criteria even when they
are unsure if the event is related to use of a medication.

Reports may be submitted to CARM in a variety of ways. A standard reporting card
(Figure 2), designed to capture all relevant information is available as hard copy or is
accessible online (http://carm.otago.ac.nz/). Once completed the card may be
forwarded to CARM by freepost, facsimile, or email. Reporters may also telephone
with a verbal report.
Figure 1. Overview of pharmacovigilance activities undertaken by the New Zealand Pharmacovigilance Centre (NZPhvC)

Sources of Data
- Health care professionals, coroners, consumers, pharmaceutical companies
- selected newly marketed medicine(s)
- all medicines (including vaccines, herbal and alternative medicines)
- child immunised with MeNZB™ at sentinel practice
- pharmacy prescription data
- follow up questionnaires to prescriber
- CARM ADR Report Card
- feedback to reporter
- electronic transfer of consultation details

NZPhvC processes
- IMMP
  - Clinical evaluation and causality assessment
  - incidents reactions
- CARM
  - reports prioritised
  - serious events to MWS
- IVMP
  - On-line Clinical evaluation and causality assessment

Risk communication
- MARC (Medicines Adverse Reactions Committee)
- MedSafe
- World Health Organisation (WHO)
- Data Management Group
- Prescriber update, revisions to data sheets etc

Safety reviews and data analysis

CARM = Centre for Adverse Reaction Monitoring; ADR = adverse drug reaction; IMMP = Intensive Medicines Monitoring Programme; IVMP = Intensive Vaccines Monitoring Programme; MWS = Medical Warnings System.
Figure 2. CARM reporting card for adverse reactions

![CARM Reporting Card](https://example.com/carm-reporting-card)

**Patient Details**

<table>
<thead>
<tr>
<th>Surname:</th>
<th>First Names:</th>
<th>NH No:</th>
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<tr>
<th>Address:</th>
<th>Date of Birth:</th>
<th>Sex:</th>
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<tr>
<th>Ethnicity:</th>
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</table>

**All Medicines in Use**

* Asterisk Suspect Medicines include over-the-counter (OTC) and alternative medicines.

<table>
<thead>
<tr>
<th>Medicine or Vaccine + Batch no. (and brand name if known)</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Date Started</th>
<th>Date Stopped</th>
<th>Reason for Use</th>
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<tbody>
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**Description of Adverse Reaction or Event**

Date of onset: _____________

**Recovery**

- Recovered [ ]
- Not yet recovered [ ]
- Not yet recovered but Improved [ ]
- Unknown [ ]
- Fatal [ ]
- Date of Death: _____________

**Severity**

- Yes [ ]
- No [ ]
- Rechallenged? [ ]
- Yes [ ]
- No [ ]

**Other Factors**

- Renal disease [ ]
- Allergy [ ]
- Other Medical Conditions: _____________
- Hepatic disease [ ]
- Nutritional Suppl or OTC use: _____________
- Industrial Chemicals: [ ]

**Reporter**

- Please tick as appropriate: Doctor [ ], Pharmacist [ ], Dentist [ ], Nurse [ ], Other [ ]

<table>
<thead>
<tr>
<th>Name:</th>
<th>Signature:</th>
<th>Address:</th>
<th>Phone:</th>
<th>Date:</th>
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</tbody>
</table>

Send completed form to CARM

Freepost 112002, CARM, PO Box 913, Dunedin or Fax: (03) 479 7150
Intensive Medicines Monitoring Programme (IMMP)—The main impetus for creation of the IMMP in 1977 was the international recognition that spontaneous reporting had proved inadequate in recognising the serious oculomucocutaneous syndrome with the beta-blocker practolol—and due to the lack of a denominator for events, the extent of the problem was unknown. Thus an additional programme was instigated which would collect both medicine exposure data (from prescription records) and adverse events (safety outcome) data.

The IMMP uses Prescription Event Monitoring (PEM) methodology to conduct prospective observational cohort studies on selected new medicines. Medicine exposure data are captured from prescription records for the monitored medicines. The IMMP receives prescription data directly from virtually all dispensing pharmacies (from both hospital and community settings) throughout New Zealand. The data are used to establish patient cohorts which provide denominator populations for calculating the incidence of adverse events.

The IMMP prescription/exposure data may also provide useful demographic information about patients prescribed the monitored medicines and the patterns of usage of these medicines. Importantly, demographic data can be used to identify particular characteristics that may place a patient at increased risk of developing an adverse reaction.

The IMMP obtains safety outcome data from multiple sources. Adverse events are identified primarily from follow-up questionnaires sent to doctors at specific times after the medicine was prescribed. In addition, adverse events are identified from spontaneous reports sent to CARM, from prescription data and increasingly from record linkage to national mortality and morbidity databases. This intensive methodology is more proactive than the passive methods of the CARM spontaneous reporting programme.

A further difference is that the IMMP asks health professionals to report all new clinical events (of any type or severity) since starting the medicine, rather than reporting only suspected ADRs. Therefore, reporting is made without any prejudgment on the relationship of the event to the medicine, providing greater opportunity for identification of signals of previously unrecognised ADRs.

Intensive Vaccine Monitoring Programme (IVMP)—Although vaccine ADR data are collected and monitored via the CARM scheme, the IVMP was implemented by the NZPhvC in 2004 to proactively monitor the safety of a new meningococcal B vaccine (MeNZB™) during roll-out of the national Meningococcal B Immunisation Programme.

The IVMP system was designed to provide an early alert mechanism for serious adverse events following immunisation. The IVMP formed part of an intensive multifaceted safety strategy, led by the Ministry of Health’s Data Management Group (DMG), to ensure the vaccine’s safety as the MeNZB™ Programme rolled out in NZ.

The IVMP system is based on the IMMP methodology but uses an innovative process of electronic data capture, transfer, and assessment. Since 19 July 2004 when the
Immunisation Programme began, the IVMP has prospectively monitored the safety of MeNZB™ in a cohort of NZ children receiving immunisations in primary care in selected (sentinel) practices.

Clinical data is routinely collected at the sentinel practice in their Practice Management Software (PMS). For children in the cohort, data on all immunisations administered (which forms the denominator for events) and all subsequent health consultations at the vaccinee’s own practice in the 6 weeks following an immunisation are extracted and electronically transferred via a secure link to the NZPhvC for analysis. The data extraction operates automatically within the PMS with no extra compliance burden for the practice. At the NZPhvC, all health consultation visits in the 6 weeks following MeNZB™ immunisation are electronically assessed to identify all clinical events.

**Assessment of data at NZPhvC**

**CARM report assessment and feedback**—Upon receipt by the NZPhvC, each CARM ADR report card is assigned a unique CARM number, then checked and scanned onto the CARM database so that an electronic image of the report and any supporting information is available for ‘read only’ access by NZPhvC staff. In addition, each report is logged into a tracking database to ensure timely progress of the reports through the report evaluation system.

The reports are prioritised, so that the more serious adverse events receive early attention, and are then sorted by suspect medicine with reports pertaining to IMMP medicines being considered by the IMMP personnel, meningococcal B vaccine reports directed to the IVMP team and reports for all other medicines and vaccines considered by CARM staff (Figure 1).

- Clinical evaluation

  At the NZPhvC, each CARM ADR report undergoes clinical evaluation by a medical assessor. The terms included in the report are evaluated by a medical assessor and coded to standardised terms from the World Health Organization Adverse Reaction Terminology (WHOART) dictionary to ensure consistency in use of the data held in the database.

  This dictionary organises terms under System-Organ Class (SOC) headings, with sub-hierarchies within each SOC to facilitate analysis. Each event is then assessed for severity, seriousness, and outcome (Table 1). The term ‘severe’ is used to describe the intensity (severity) of a specific event, whereas the term ‘serious’ relates to the patient/event outcome.\textsuperscript{10,11}

- Case follow-up

  The reporter is contacted in cases where further clarification or information is required—such as laboratory data, patient outcome data (if patient not yet recovered at time of report), or for verification of findings. In cases of deaths, post-mortem and/or coroners' reports are also requested and these events are considered by the Medicines Adverse Reactions Committee (MARC), (refer next section).
### Table 1. Causality categories\(^{10}\) (all points need to be reasonably complied with)

<table>
<thead>
<tr>
<th>Causality Categories</th>
<th>Definition</th>
</tr>
</thead>
</table>
| **Certain**          | Event or laboratory test abnormality with plausible time relationship to drug intake  
                       | Cannot be explained by disease or other drugs  
                       | Response to withdrawal plausible (pharmacologically, pathologically)  
                       | Event definitive pharmacologically or phenomenologically using a satisfactory rechallenge procedure if necessary |
| **Probable**         | Event or laboratory test abnormality with reasonable time relationship to drug intake  
                       | Unlikely to be attributed to disease or other drugs  
                       | Response to withdrawal clinically reasonable  
                       | Rechallenge not necessary |
| **Possible**         | Event or laboratory test abnormality with reasonable time relationship to drug intake  
                       | Could also be explained by disease or other drugs  
                       | Information on drug withdrawal lacking or unclear |
| **Unlikely**         | Event or laboratory test abnormality with a time relationship to drug intake that makes a connection improbable (but not impossible)  
                       | Diseases or other drugs provide plausible explanations |
| **Unclassified**     | Event or laboratory test abnormality  
                       | More data for proper assessment essential or additional data under examination |
| **Unclassifiable**   | Event or laboratory test abnormality  
                       | Judgement cannot be made because information is insufficient or contradictory and which cannot be supplemented or verified |

In the IMMP and IVMP, Certain, Probable and Possible are termed *Reactions* whilst Unlikely, Unclassified and Unclassifiable are termed *Incidents*.

<table>
<thead>
<tr>
<th>Severity</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe</td>
<td>Recovered without sequelae</td>
</tr>
<tr>
<td>Not severe</td>
<td>Recovered with sequelae</td>
</tr>
<tr>
<td>Seriousness</td>
<td>Not yet recovered</td>
</tr>
<tr>
<td>Not serious</td>
<td>Died—due to adverse reaction</td>
</tr>
<tr>
<td>Congenital abnormality</td>
<td>Died—drug may be contributory</td>
</tr>
<tr>
<td>Hospitalisation</td>
<td>Died—unrelated to drug</td>
</tr>
<tr>
<td>Persisting disability</td>
<td>Died</td>
</tr>
<tr>
<td>Life-threatening</td>
<td>Unknown</td>
</tr>
<tr>
<td>Death</td>
<td></td>
</tr>
<tr>
<td>Intervention to prevent permanent impairment</td>
<td></td>
</tr>
</tbody>
</table>

- **Causality assessment**

The degree of association (causality) between the suspect medicine(s) and the reported event is determined according to WHO definitions\(^{10}\) (Table 1). These definitions, based on a modification of the Karch and Lasagna\(^{12}\) method, are utilised by national monitoring centres internationally to facilitate sharing of data.

Judgements regarding causality can be extremely difficult, so standardised causality criteria are followed when making this assessment. The criteria consider the nature of the event, its timing, the dose of the medicine being...
taken, possible confounding factors, and information on dechallenge or rechallenge with the suspected medicine (Table 1).

Current evidence from a diversity of published data sources, evidence in the CARM database and when appropriate, interrogation of the WHO database (into which National Monitoring Centres such as CARM pool their data to improve signal recognition) are also considered. In challenging cases, opinions of experts may be sought. A causality assessment of ‘certain’, ‘probable’, or ‘possible’ assigned to an event identifies a reaction, whereas an adverse event deemed ‘unlikely’ to be causally associated with the medicine are considered unrelated. In the IMMP and IVMP, these events are termed incidents (events considered to be, with the information available, incidental to drug use). All information, irrespective of their causal status, is retained in the database to add weight to the evidence that might signal a previously unrecognised potential association should further reports of the same kind be received.

- Feedback

For each CARM spontaneous report, the sending of individual acknowledgement and feedback letters from the NZPhvC to the reporter have become an established routine in NZ. These responses acknowledge the importance of the reporter’s role and efforts and therefore are aimed at providing useful feedback. The letters typically report on the Centre’s causality assessment, the number of similar reports in NZ and/or WHO, plus any other additional information such as at-risk groups and prevention issues that may be relevant or topical.

Comments from reporters indicate that these letters are positively received, often providing further value for the prescriber and patient.

- Medical Warnings System (MWS)

A major advantage of the CARM scheme is that through the National Health Index (NHI) and the Medical Warnings System (MWS), both of which are managed by the New Zealand Health Information Service (NZHIS), individual patient safety benefits are achieved.

Each person in NZ is assigned a unique NHI number and the NHI is an index of health information associated with that unique number. This means that individuals can be positively and uniquely identified for the purposes of treatment and care and for maintaining medical records. The MWS is designed to warn those who access the system (currently almost exclusively hospitals) of any known risk factors that may be important when making clinical decisions about care for that patient.

For severe and life-threatening reactions, CARM records warning or danger alerts for medicines for individual patients against their National Health Index (NHI) number in the MWS. Therefore, when the individual is next seen, and the system is accessed at a hospital, the information is displayed and incorporated into that facility’s ‘alert’ mechanism aimed at protecting the patient from harm. This system is unique to NZ.
IMMP data assessment—The events identified for IMMP medicines, whether from follow-up questionnaires, spontaneous reports, prescription data, or NHI data, undergo a similar clinical evaluation and causality assessment by a medical assessor as for the CARM reports described above. Those events deemed to be a ‘reaction’ are also entered into the CARM database (Figure 1).

IVMP data assessment—For the IVMP system, a medical assessor clinically evaluates all MeNZB™-related CARM reports and for each child immunised at a sentinel practice, and identifies clinical events through review of each health consultation record electronically received in the 6 weeks following each immunisation.

Assessment and coding of all identified clinical events is undertaken in a similar manner as outlined above, but using a paperless system with assessments performed online and on-screen. The IVMP database therefore holds MeNZB™ event information identified through both the CARM scheme and through the IVMP electronic data capture and transfer system.

Comparison of NZPhvC programmes

The CARM spontaneous reporting programme provides a crucial source of data and this programme is complemented by the IMMP and IVMP which utilise a proactive approach to identification of clinical events. Each of the three programmes operated by the NZPhvC has a number of benefits and limitations, as summarised in Table 2.

Table 2. The benefits and limitations associated with each of the three programmes operated by the New Zealand Pharmacovigilance Centre (NZPhvC)

<table>
<thead>
<tr>
<th>NZPhvC Programme</th>
<th>Benefits</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARM Centre for Adverse Reaction Monitoring (Spontaneous reporting method)</td>
<td>Relatively inexpensive Examination of the patterns of reactions—reinforce established knowledge, stimulus for prescriber reminders Useful for detecting rare adverse reactions Useful for generating signals (hypotheses that a particular medication may cause a particular ADR) Continual safety monitoring of a product</td>
<td>Under-reporting—major weakness of all spontaneous reporting systems Selective reporting due to differing thresholds for reporting amongst health professionals (reporting bias) Lack of denominator for events so not able to provide incidence rates Poor at detecting delayed ADRs Rates of reporting influenced by publicity</td>
</tr>
<tr>
<td>IMMP Intensive Medicines Monitoring Programme (Prescription event monitoring type method)</td>
<td>Extremely useful method of signal detection Denominator for events known so enables calculation of rates and estimates of risks for particular events Provides insight into reasons for cessation of therapy Patients may be monitored for several years allowing the opportunity for longer term effects to be identified</td>
<td>Labour intensive—for reporters completing follow-up questionnaires and for IMMP staff Can only monitor a few medicines at any one time For low usage products, can take some time to establish a cohort of adequate size and takes longer to identify less common adverse reactions</td>
</tr>
<tr>
<td>IVMP Intensive Vaccines Monitoring Programme (Computerised prescription-event monitoring type method)</td>
<td>Benefits as for IMMP Rapid source of data Real time results and reporting Minimal compliance burden on sentinel practices Resource savings with automated data capture and assessment System could be adapted to monitor new medicines or vaccines in the future</td>
<td>Potential data overload due to ease of dataflow Requires experienced database personnel to design, maintain and extract data from the database Accurate data linkage relies on the correct National Health Index number being used Varying detail provided in consultation notes which may influence the number of events identified</td>
</tr>
</tbody>
</table>
Overall, this multifaceted approach generates enormous synergies that facilitate not only a greater yield of reports and events, but also a wider range of events upon which to base medication safety decisions. Consequently NZ has one of the highest reporting rates per capita as compared to other national programmes internationally.13

In addition, the NZPhvC programmes provide direct individual patient safety benefit when events reported to any programme are assessed as significant enough to require a medical warning.

**Aggregated data analysis and risk communication**

**Within New Zealand**—The NZPhvC undertakes regular safety reviews and data analysis to identify any significant patterns of adverse reactions. Information from CARM and IMMP are routinely provided to Medsafe and considered by the Health Ministry’s Medicines Adverse Reactions Committee (MARC), which meets quarterly to discuss medication safety issues.

Issues typically presented to MARC by the NZPhvC include: previously unrecognised ADRs (especially those of clinical concern), clusters of reports for particular events, signals from current literature and those of international interest, reactions arising where prescriber feedback and education opportunities are identified, or where changes to the product data sheet are required.

Advice from MARC to the regulator of medicines, Medsafe, may contribute to decisions around revisions of medicine data sheets or other regulatory actions. Often the issues highlighted by MARC result in or form the basis of publications, including information that is disseminated to healthcare professionals via the ‘Prescriber Update’ bulletin which is accessible online.14

Additional reports are compiled for IMMP medicines. These reports may be signal identification, specific indepth studies, record linkage studies, or monitoring summaries. These processes are described in detail in previous publications.4,7

Data from the IVMP system is also analysed at regular intervals and standardised key reports on emerging patterns and trends of events are provided to the Data Management Group (DMG), with oversight by an Independent Safety Monitoring Board (ISMB).

**International collaboration**—The NZPhvC contributes anonymised data, together with national monitoring centres from over 80 member countries, to the database of the WHO’s International Drug Monitoring Programme.13 This facilitates identification of new and or rare reactions and global drug safety monitoring. Responsibility for leading and managing this Programme is undertaken by the Uppsala Monitoring Centre (UMC) in Uppsala, Sweden.

Through the WHO International Drug Monitoring Programme, other international networks and via the link with Medsafe, the NZPhvC is able to keep abreast of the latest concerns around drug safety as they emerge, whilst access to the international database serves to complement the local experience of adverse reactions to medicines.
Discussion

Importance of current pharmacovigilance processes in New Zealand

The CARM spontaneous reporting programme established over 40 years ago continues to be a valuable national resource allowing early identification of new adverse reactions and rare reactions as well as assessment of local patterns of reactions and risk factors for adverse reactions.

NZ has one of the highest reporting rates per capita as compared to other international spontaneous reporting programmes. This is probably due to the provision of individual feedback letters to reporters; the fact that there is one nationally recognised centre for ADR reports for the full spectrum of therapeutic products including vaccines and complementary and herbal preparations; that the NZPhvC also operates other post marketing surveillance programmes such as the IMMP and IVMP resulting in the Centre becoming synonymous with drug safety issues; that NZ is a small country with a good reporting culture and that the NZPhvC is perceived as independent of the regulator.

Whilst the CARM programme provides a core source of useful data for the Centre, the inherent weaknesses of spontaneous reporting programmes—namely under-reporting and the lack of a denominator for events—means that the magnitude of risk cannot be determined.

The IMMP, which utilises prescription event monitoring methodology, overcomes many of these shortcomings and also provides an extremely useful method of signal detection. Examples of signals recently identified through this programme include: sibutramine and memory impairment, sibutramine and QT prolongation, risperidone and epistaxis, alopecia and quetiapine, and COX-2 inhibitors with dysrhythmias.

The IVMP system further enhances the IMMP methodology through automated data capture and assessment which has enabled efficiencies that have realised resource savings in time and data preparation at the practice level. The IVMP has served as a successful pilot for wider implementation in the future.

Future of medicines safety monitoring in New Zealand

Initiatives to enhance and strengthen current NZPhvC processes—The current processes in the NZPhvC are clearly valuable and effective, but there are always opportunities for improvement. There is a need for enhanced approaches that exploit advances in information technology, and the development of improved signal identification strategies. Such initiatives include:

- Healthcare professional electronic reporting;
- Improved electronic report processing and data extraction strategies;
- Enhancement of signal recognition algorithms and capability;
- Strategies to improve reporting of adverse events associated with complementary and alternative medicines, herbal preparations, and dietary supplements;
• Identification of opportunities to interact to mutual advantage with other programmes that relate to adverse medication event issues;

• Incorporating the electronic data capture and transfer elements of the IVMP into the IMMP processes;

• Targeted reporting initiatives, whereby particular health professional groups are actively targeted to provide regular reports. Other suitable targets for stimulated reporting may include particular medications (or medicine classes) about which there may be an issue, or populations (such as the paediatric age group) that are not currently well represented in the CARM database; and

• Consideration of enhanced consumer reporting of ADRs.

Initiatives to broaden into medication safety - medication error recognition and prevention—Historically, pharmacovigilance centre activities have focused on ADRs which are largely non-preventable events that occur with the proper use of a medicine. However, it has become widely recognised that errors in medication use are also an important cause of medication-related patient injury. Importantly, because these events are associated with error, they are preventable events and thus amenable to prevention strategies. Medication safety aims to identify system faults to enable improvements in medication use systems to prevent future errors. Clearly classical pharmacovigilance approaches can be seen as representing only part of the problem.

In many countries, separate pharmacovigilance and medication safety organisations exist, but as there is often considerable overlap between activities, the WHO World Alliance for Patient Safety is presently looking at ways in which greater collaboration may occur between pharmacovigilance and medication safety (error prevention) organisations.21

In NZ, there is currently no coordinated national mechanism for medication error recognition and prevention. Current resources restrict the focus of NZPhvC activities to ADRs. In the future, to facilitate the safest use of medicines for New Zealanders, both nationwide pharmacovigilance and medication safety approaches are needed. In a country the size of NZ, this could ideally be achieved through broadening the pharmacovigilance activities of the NZPhvC. The opportunity exists for NZ to showcase this model to the rest of the world.

Conclusions

Current pharmacovigilance activities undertaken by the NZPhvC facilitate individual patient safety benefits, benefits for the NZ population and contribute to global medicines safety initiatives. However to facilitate the safest use of medicines for the NZ population into the future, pharmacovigilance activities need to be enhanced and complemented with nationwide medication safety approaches to enable recognition and prevention of medication errors alongside ADRs at a national level.
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Kava hepatotoxicity: a European view

Rolf Teschke, Alexander Schwarzenboeck, Ahmet Akinci

Abstract

Kava was well tolerated and considered as devoid of major side effects only until 1998 when the first report of assumed kava hepatotoxicity appeared. Causality of hepatotoxicity for kava ± comedicated drugs was evident after the use of predominantly ethanolic and acetonic kava extracts in Germany (n=7), Switzerland (n=2), United States (n=1), and Australia (n=1) as well as after aqueous extracts in New Caledonia (n=2). Compliance regarding the recommendation for daily kava dose and duration was ascertained in only a few patients, including 2 from Germany and Switzerland.

Since 450 millions of daily doses of kava extracts equating to 15 millions of monthly doses were sold in Germany and Switzerland, hepatotoxicity by kava appeared to be rare—similar to other herbal remedies, dietary supplements, and synthetic drugs. Risk factors were found in most patients and include daily kava overdose, prolonged therapy, and comedication with up to 5 other herbal remedies, dietary supplements, and synthetic drugs.

Kava hepatotoxicity was not reported until 1998, thus raising the question of inferior quality of the kava raw material at times of the kava boom later on. Insufficiently defined regulatory guidelines to produce kava extracts are of some concern. Open questions refer not only to kava cultivars, but also to analytical methods and definitions of extract media and contents. Future strategies should therefore focus on the solution of a standard methodology of ascertaining quality that can assure a high degree of reliability in conjunction with actions by regulators, physicians, manufacturers, and producers. A medical advisory is also recommended as part of the labelling.

The use of aqueous extracts of kava rhizome has a long tradition in the South Pacific islands, being well tolerated and considered devoid of major side effects until recently.\(^1\)

Treatment of anxiety syndromes of light and moderate grades with ethanolic and acetonic kava extracts was common worldwide. In a systematic (Cochrane) review, kava extract significantly reduced symptoms compared with placebo when Hamilton anxiety scores are considered.\(^2\) However, since 1998, reports have appeared in various countries linking newly recognised liver diseases with the treatment by kava extracts of ethanol,\(^3–5\) acetone,\(^3–5\) or water.\(^6\)

Based on its ad-hoc causality evaluation, the German regulatory agency\(^5\) issued a ban of kava extracts,\(^5\) and other countries followed.\(^4\) A worldwide discussion emerged, focusing mainly on the question to what extent kava is potentially hepatotoxic and whether the regulatory ban was justified.\(^3,4,7–16\) Kava hepatotoxicity has now been characterised.\(^16\) There is supporting evidence that treatment with kava extracts used
within regulatory recommendations may carry only a very low risk of hepatotoxicity in analogy to many other herbal remedies, dietary supplements, and synthetic drugs. Of more concern is the nonadherence of the patients to the regulatory recommendations with the consequence of high daily doses and/or prolonged treatment, rendering the patients more susceptible to severe kava hepatotoxicity including acute liver failure and requirement for a liver transplant.

The present review will focus on recent advances in the highly debated field of kava hepatotoxicity, discussing the results of quantitative causality assessments evaluated in patients with assumed kava hepatotoxicity, and dealing with other issues of contention. It appears that major issues have to be addressed by regulatory agencies, physicians, manufacturers, and producers.

**Common grounds**

Despite worldwide discussions regarding toxic liver disease in assumed causal relationship with kava use, few essential points can be regarded as valid assumptions that are accepted by most of the involved parties:

- There is general agreement that ethanolic and acetonic extracts of kava may be hepatotoxic in a very few patients similar to other herbal remedies, dietary supplements, and synthetic drugs, provided treatment follows the regulatory recommendations with respect to maximal daily dose and duration of treatment.\(^3\)\(^4\)\(^9\)\(^16\)

- It was recognised early that most of the patients have used kava daily overdosed and/or for prolonged periods.\(^3\)\(^4\)\(^16\) In view of poor adherence to regulatory recommendations of kava therapy, kava hepatotoxicity is basically a preventable disease, at least to a major extent.

- Comedication with up to 5 additional synthetic drugs, herbal remedies, and dietary supplements was recognised early in most patients.\(^3\)\(^5\)\(^16\)

- Aqueous kava extracts may also be associated with rare hepatotoxicity.\(^6\)

**Issues of contention**

There are major points of contention between the involved parties of regulators, physicians, manufacturers, and producers:

- How sophisticated and how relevant are ad-hoc causality assessments by regulatory agencies in the cases of assumed kava hepatotoxicity?

- Was it impossible or impracticable for regulatory agencies to clearly define desired characteristics of kava extracts regarding extraction medium, amount of various components, and the most appropriate kava cultivar to be used?

- How intensive was the control of the used raw material by the manufacturers regarding the quality of the kava cultivar and the part of the kava shrub meeting the regulatory requirements?

- What approach was undertaken by the producers supplying the manufacturers with kava cultivars of best quality?
Causality assessment

Causality of liver disease in assumed relationship with the use of kava extracts has been assessed by the German health agency (BfArM, Bundesinstitut für Arzneimittel und Medizinprodukte, Bonn) and its Swiss counterpart (Swissmedic, SM; Schweizerisches Heilmittelinstitut, Department Pharmacovigilance, Berne, formerly Interkantonale Kontrollstelle Schweiz, IKS) on an ad-hoc basis—but the results of most of the evaluated cases were not reproducible by scientists,^3,4,7,9,16^ Medicines Control Agency (MCA, London), and European Medicines Agency (EMEA, London).^3,4^ In face of the ongoing discussion regarding the relationship of liver disease and the use of kava,^3,4,8–15^ a new approach for causality evaluation has been undertaken.^16^ A thorough assessment of the temporal as well as causal association was pursued using quantitative criteria of CIOMS (Council for International Organizations of Medical Sciences) published by Danan and Bénichou.^17^ The CIOMS system was derived from an international consensus meeting of experts who defined various parameters such as time to onset, course of improvement of laboratory data, risk factors, concomitant drugs, search for nondrug causes, previous information on hepatotoxicity of the drug, and response to readministration. It provides with each of these parameters a range of scores, and the total score is computed and then may be divided into ranges that represent a causality being either highly probable, probable, possible, unlikely, or excluded.

The scales of CIOMS were also used for causality assessment regarding all comedicated drugs in temporal association with the observed liver disease. Only one single comedication with the highest score was included in the analysis, provided the therapy consisted of 2 or more drugs and/or dietary supplements. The CIOMS scale has been well validated and is universally accepted.^16^

German and Swiss cases

German and Swiss regulatory ad-hoc causality assessments of liver disease in assumed relationship with the treatment by ethanolic and acetonic kava extracts^5^ have been discussed worldwide.^3,4,7–15^ Using the CIOMS scale,^17^ causality was established for kava ± comedication in 2 patients who adhered to the regulatory recommendation for the treatment (maximal 120 mg kavapyrones per day for not longer than 3 months) and in 7 others who failed to follow.^16^ Risk factors were daily overdoses, prolonged treatment, and comedication. Between 1992 and mid-2002, 450 millions of daily kava doses were sold in Germany and Switzerland, corresponding to 15 millions of monthly doses. Obviously, kava hepatotoxicity was rare in these countries.

Australian cases

There is one single case report from Australia of a fatal hepatic failure induced by a natural therapy containing kava.^18^ Kava was taken at a daily overdose of 180 mg kavapyrones for 3 months. The second ingredient was Passiflora incarnata and there was a third as yet unidentified compound.^4,18^
In a comprehensive study, heavy use of aqueous kava extracts was associated with greatly increased activities of \( \gamma \)-glutamyl transpeptidase and a concomitant decrease of bilirubin levels.\(^\text{19}\) In another report, \( \gamma \)-glutamyl transpeptidase and alkaline phosphatase were increased with normal alanine aminotransferase and bilirubin.\(^\text{20}\) Thus, no evidence is provided for hepatocellular injury in these cases in contrast to those patients who used ethanolic or acetonic kava extracts.\(^\text{16}\)

However, the laboratory constellation of increased \( \gamma \)-glutamyl transpeptidase\(^\text{19,20}\) and alkaline phosphatase\(^\text{20}\) deserves further pathogenetic evaluation regarding possible cholestasis or hepatic enzyme induction.

**New Caledonian cases**

Two cases with hepatic injury due to traditional aqueous root extracts of an unknown kava cultivar have been published.\(^\text{6}\) The weekly intake was 18 g kavapyrones in 1 patient and unknown in the other one. Treatment lasted for 4 and 5 weeks. Comedication was declared for patient 1 (but not for patient 2) and included lisinopril, phenobarbital, and fenofibrate.

There is some concern that these cases may potentially be related to the use of low quality kava.\(^\text{15}\) Certainly, hepatotoxicity is an extremely rare observation after the use of aqueous kava extracts, as evidenced by the two patients from New Caledonia and also the high quantities of kava commonly consumed in the South Pacific.

In a study with 27 heavy consumers of an aqueous kava extract, increased \( \gamma \)-glutamyl transpeptidase in the presence of normal or minimally elevated transaminases were found,\(^\text{6}\) reflecting low grade of hepatocellular injury associated with cholestasis or hepatic enzyme induction.

**Other international cases**

Hepatotoxicity has primarily been suspected worldwide in 83 patients in assumed causal relationship with the use of kava.\(^\text{4}\) Liver diseases of only some patients were causally related to the use of kava, as outlined in the present review. In most cases, however, causality was unlikely or not probable and/or documentation was insufficient to establish causality.\(^\text{3,4,7,9,16}\)

There is one case report from the United States linking acute hepatitis and subsequent requirement for liver transplantation with the use of kava.\(^\text{21}\) Various contradictory statements are made regarding the product containing kava, St Johns wort, and other herbs.\(^\text{4,21}\)

Comedication included Ibuprofen found in the urine.\(^\text{21}\) In this case daily overdoses of kava, 240 mg kavapyrones, were taken for a prolonged period of 4 months.

**Characteristics of kava hepatotoxicity**

The evaluation of 9 patients from Germany and Switzerland with a causal relationship of various degrees between ethanolic or acetonic kava extracts and liver disease reveals that kava hepatotoxicity has some typical characteristics:

- Kava hepatotoxicity may occur after daily doses of 45–1,200 mg kavapyrones and a therapy ranging between 1 week and 12 months (regulatory
recommendations restricted kava therapy to a maximum of 120 mg kavapyrones daily for not longer than 3 months);

- All patients, with two exceptions, failed to follow the regulatory recommendations for kava treatment; used high daily kava doses and/or experienced a long duration of treatment, features all considered as risk factors;

- Under these conditions, kava hepatotoxicity was confirmed in a single patient by a positive kava re-exposure test;

- Comedication was another risk factor for the development of kava hepatotoxicity;

- Kava treatment, excessively exceeding regulatory recommendations, may be associated with the risk of life-threatening acute liver failure requiring LTX;

- Under kava use, within the recommendations, hepatotoxicity occurred in 2 patients with a causality for kava ± comedication and a good outcome following kava and comedication cessation;

- Kava hepatotoxicity may exhibit high serum levels of ALT compared to ALP and is characterised by liver cell necrosis, hepatitis, or both;

- The ratio of males:females was 1:4;

- Four out of 9 patients used an acetic and the others an ethanolic kava extract;

- Half of the patients took kava erroneously for depression, a clear regulatory contraindication since kava is ineffective in this particular disease;

- In the majority of patients (6/9) ,causality of hepatotoxicity for kava was graded as only possible and thus weak; and

- Kava hepatotoxicity is the result of an idiosyncratic reaction of the metabolic rather than the immunologic type.

The analysis of the 2 patients from the United States\textsuperscript{21} and Australia\textsuperscript{18} shows that both used a preparation with various herbs as ingredients including kava, but no reference was given for the extraction medium used. Otherwise characteristics are similar to those of the German and Swiss cases:

- Kava hepatotoxicity occurred after daily overdoses of 180–240 mg kavapyrones;

- The duration of therapy was partially prolonged, 3–4 months;

- Comedication was present in 1 of 2 patients; and

- The patients were females.

Assessment of the 2 patients from New Caledonia revealed the use of aqueous kava extracts.\textsuperscript{6} The clinical courses were similar to those from Germany, Switzerland, Australia, and the United States:
• Kava hepatotoxicity was evident after weekly use of 18 g or an unknown amount of kavapyrones contained in aqueous kava extracts, hardly comparable to the daily maximum of 120 mg derived from ethanolic or acetonic extracts as regulatory upper limit in Germany;
• The treatment was short duration of 4 and 5 weeks;
• Comedication was declared in 1 of 2 patients; and
• The patients were females.

Taken together the characteristics of all 13 patients from Germany, Switzerland, the United States, Australia, and New Caledonia with established causality for kava ± comedicated drugs, it appears that hepatotoxicity by kava occurs independently from the medium (ethanol, acetone, or water) used to prepare the kava extract.

Specific considerations

There are major concerns regarding possible risk factors for kava hepatotoxicity.\textsuperscript{3,4,7,15,22} For a long time multiple different kava cultivars were known,\textsuperscript{7,23} but no effort has been made to clearly define the best kava cultivar to be used. Neither regulators nor manufacturers or producers have had any interest regarding this question, and as a result they did not consider that the various cultivars may differ in their specific positive and negative effects, including those with possible hepatotoxic ones.\textsuperscript{16}

Some discussions center around the question whether, instead of the rhizome, aerial parts of the kava plant which may contain hepatotoxic substances could have been used in the manufacturing process.\textsuperscript{12,16,24} Ethanol, acetone, and water are preferentially being used as media for kava extracts, but there is no regulatory statement which medium may be superior. This is certainly challenging in view of the fact that kava extracts with all these three media are associated with the risk of hepatotoxicity. Similarly, various solubilisers such as macrogol, craspovidon, mentha oil, methyl acryl acid polymer, and polysorbate polyols have been included in the extracts, but lacking a regulatory recommendation of the best one to use.

The regulatory recommendation for the maximal daily dose of 120 mg kavapyrones is not sufficiently qualified since the analytical method for quantification is not described. As there are major quantitative differences, for instance, between TLC and HPLC, accuracy is lacking.\textsuperscript{15} There is also no regulatory definition of the desired percentage of each of the kavapyrones in the extracts.

Kava hepatotoxicity is best described as an idiosyncratic reaction of the metabolic type, but the clinical relevance of comedication is unclear.\textsuperscript{16} Most of the patients had a comedication with related causality in some cases. Kavapyrones inhibit various isoenzymes of cytochrome P450 which may be the clue for the development of hepatotoxicity when both kavapyrones and drugs are present.\textsuperscript{25} It remains to be established, however, whether kavapyrones initiate hepatotoxicity by comedicated drugs or vice versa. Hopefully kava cultivars are found with a suitable composition of various kavapyrones lacking major interactions with cytochrome P450 isoenzymes.
Regulatory agencies

Future steps should include:

- Regulatory prescription guidance to minimise risk; and
- Regulatory definitions regarding not only the optimum of kava cultivar, part of plant, extraction medium and solubiliser, but also standardisation of the analytical method for quantification and optimal proportion of various kavapyrones as extract ingredients.

Physicians

Essential is:

- Advice to the patient regarding maximal daily dose and duration of treatment, possible hepatotoxicity, avoidance of comedication, and recognition of depressive disorders as contraindication; and
- Thorough quantitative causality assessment in case of assumed liver injury.

Manufacturers

Requirements include:

- Adherence to regulatory guidelines; and
- Quality control of raw material.

Producers

Quality control of the raw material is essential regarding:

- Planting and distributing the best kava cultivar according to regulatory guidelines;
- Selective use of the plant part according to regulatory guidelines; and
- Destroying unwanted kava plant parts and cultivars of low quality.

Conclusion

Ethanolic, acetonic, and aqueous kava extracts may be potentially hepatotoxic in rare instances as are other herbal remedies, dietary supplements, and synthetic drugs. Risk factors may include daily overdose, prolonged treatment, comedication, and raw material of low quality. When risk factors are being removed, kava hepatotoxicity may well be a preventable disease, at least to a major extent.

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Necrotizing fasciitis due to *Vibrio parahaemolyticus*

Gary Payinda

**Abstract**

A report of a fatal case of necrotizing fasciitis of the leg due to *Vibrio parahaemolyticus* infection. This organism frequently causes minor infections in seawater-exposed wounds. In this case the patient died due to fulminant sepsis caused by necrotizing fasciitis, despite surgical debridement. This case serves as a reminder for targeted antibiotic coverage for *Vibrio* in any serious saltwater-related infection, and as an illustration of the rapid and severe systemic toxicity associated with *Vibrio parahaemolyticus* necrotizing fasciitis, even in the setting of minor initial skin findings.

**Case report**

The patient was a 79-year-old male who abraded his right leg on a boat anchor while fishing in the Pacific Ocean off the coast of northern New Zealand. The patient presented to a community emergency department complaining of a painful leg infection as well as nausea, vomiting, subjective fevers, decreased urine output, and dizziness of one day’s duration. He denied headache, neck stiffness, dysuria, diarrhoea, or rectal bleeding. He had a history of atrial fibrillation and was on long-term low dose prednisone for polymyalgia rheumatica.

On examination he was alert despite tachycardia, fever, and hypotension. His pulmonary, abdominal, and neurological examinations were normal. Skin findings comprised a minor cellulitis on the right lateral leg, with no necrosis, fluctuance, or crepitance.

The patient's initial hypotension resolved with a fluid challenge. He was started on an intravenous beta-lactam antibiotic and admitted. His white blood cell count was 16,000/mm$^3$ and a right leg X-ray revealed no gas in the soft tissues.

Overnight his condition worsened, and he developed a 2×5 cm haemorrhagic bulla on this right leg centred over a 6×12 cm area of erythema. His hypotension returned and his oliguria continued despite aggressive hydration. Sixteen hours after presentation, he was transferred to a tertiary centre for surgical debridement and ICU care.

Intraoperatively he required inotropic support and was found to have necrotizing fasciitis of his right leg. Fasciotomy and moderate debridement of the lateral compartment was performed, and he was returned to the ICU intubated and ventilated. He developed disseminated intravascular coagulation (DIC), and continued to require pressors, and haemodialysis. He was treated with hydrocortisone, cefuroxime, and metronidazole.

His respiratory function improved, his WBC normalised, his fevers abated, and he was extubated. A second look surgery revealed no further soft tissue necrosis. His blood cultures were negative, but his bulla aspirate culture was positive for *Vibrio*.
parahemolyticus. His antibiotics were adjusted to piperacillin/tazobactam and ciprofloxacin. However despite maximal treatment, his renal failure, DIC, and septic shock persisted for several days, and on his sixth hospital day he suffered a respiratory arrest, failed resuscitation attempts, and died.

Discussion

Necrotizing fasciitis (NF) is a rapidly spreading inflammatory infection extending along fascial planes and causing secondary necrosis of the subcutaneous tissues. It can occur at a site of trauma or surgery, or idiomatically in otherwise healthy individuals. The vast majority of cases of NF cases are caused by Group A haemolytic streptococci, although staphylococcal and mixed aerobic/anaerobic infections frequently occur.

Mortality with NF is approximately 70%, with an increased prevalence among individuals in their third and fourth decade, and a 2:1 male-to-female predominance, however cases have been reported in all age groups.1 Incidence is higher among diabetics and abusers of alcohol or drugs. Patients typically appear moderately-to-severely septic, though they can also appear deceptively well. Skin findings can include cellulitis, necrosis, and hemorrhagic bullae, though exceptional cases can have completely normal appearing overlying skin.

Pain out of proportion to skin findings, tenderness beyond the bounds of the erythema, and haemorrhagic bullae are hallmarks of necrotizing fasciitis. Diagnosis is made surgically, upon fasciotomy, or with the aid of MRI, CT, or ultrasound scans which can reveal fascial thickening, deep-tissue gas, stranding, or fluid collections.2,3 Plain radiography and laboratory testing are frequently not helpful in differentiating severe cellulitis from necrotizing fasciitis. The treatment of necrotizing fasciitis is surgical debridement, along with IV hydration and broad-spectrum antibiotics which cover Gram-positives, Gram-negatives, and anaerobes, until culture results and sensitivities are known.

Necrotizing fasciitis caused by Vibrio parahaemolyticus has been reported three times in the medical literature.4-6 The related species, Vibrio vulnificans, is more frequently implicated in severe wound infections. Vibrio parahaemolyticus is a halophilic (or salt-requiring) Gram-negative rod widely distributed in brackish seawater, usually associated with a self-limited diarrheal illness, frequently after eating undercooked shellfish.

Less commonly, it can cause an infection when an open wound is exposed to seawater. Treatment for significant Vibrio parahaemolyticus infections is with tetracyclines, quinolones, or third-generation cephalosporins.

In this case, Vibrio parahaemolyticus infection was not suspected until bulla aspirate culture results became available, on the fourth hospital day. Antibiotic coverage until that point was quite broad, but did not cover Vibrio.

The essential treatment for necrotizing fasciitis, surgical debridement, had been performed but was insufficient to save this patient. Other factors that worsened this patient's prognosis include chronic steroid immunosuppression, advanced age, and...
severe sepsis upon presentation, later progressing to complete renal failure and frank shock despite treatment.

This case serves as a reminder for targeted *Vibrio* coverage in any infected saltwater-contaminated wound, and as an illustration of the rapid and severe systemic toxicity associated with *Vibrio parahaemolyticus* necrotizing fasciitis, even in the setting of minor initial skin findings.

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Allergic reaction to blue cheese: serendipity or actual causation?

Rayin N Kulambil Padinjakara, Khaled Ashawesh, Vinod Patel

Cutaneous allergic reactions in the form of urticaria are a condition commonly encountered in everyday clinical practice. Often we clinicians fail to identify the precipitating cause. A thorough history and a high index of suspicion are useful in identifying the potential triggering factor.

We report a case of allergic reaction after consuming blue-veined cheese.

Case report

A 40-year-old man attended Accident and Emergency Department with a 2-day history of worsening shortness of breath, difficulty of swallowing, and generalised itchy skin rashes. He is known to react to penicillin and denied taking any recent medications.

He recollected that the itching started immediately after consuming a meal comprising of papaya, mangoes, and a newly found brand of blue cheese. The patient had consumed mangoes and papayas several times in the past as well as most brands of cheeses commonly available in the UK supermarkets.

Figure 1 shows multiple erythematous skin rashes
Physical examination revealed multiple erythematous annular rashes with some of the lesions resembling target lesions of erythema multiforme (Figure 1). He was treated with intravenous steroids, antihistamines, and nebulised salbutamol.

We contacted the food standards agency and were advised that Penicillium species are used in the manufacture of blue cheeses but these fungi are not known to produce penicillin and they were not aware about penicillin allergic patients reacting to blue cheeses. However, we advised the patient to avoid taking blue cheeses as it may trigger another reaction.

The patient remained in the hospital for 5 days and his condition slowly improved. Two months later, he was contacted by telephone and remained asymptomatic without further problems.

Discussion

Antibacterial properties of the fungus Penicillium chrysogenum was first observed by Sir Alexander Fleming in 1928. Since then a few more species of Penicillium were also found to produce penicillin. The known penicillin producers are P. chrysogenum (previously known as P. notatum), P. nalgiovense, P. dipodomis, P. griseofulvum, and P. flavigenum. Interestingly, many fungi belonging to Penicillium genus are also used as starters in the manufacture of blue cheeses.

Uniform colonisation of the cheese by Penicillium fungi prevents the growth of unwanted micro-organisms and also imparts a characteristic flavour to the cheese. Famous examples are P. roqueforti in Roquefort cheese as well as P. camemberti in Camembert and Brie cheeses. However, these fungi do not have the necessary genes for penicillin production.

Penicillin in the food chain should be avoided as it can lead to antibiotic resistance and some authors have pointed it out as a potential causative factor in chronic urticarial reactions; it can also lead to allergic reactions in penicillin-sensitive individuals.

Allergic reactions in penicillin-sensitive individuals have been reported after consuming milk, chicken, pork, and beef containing small amounts of penicillin. However, there are no such reports in the literature after consuming cheese. It is difficult to prove that the cheese our patient consumed contained penicillin or antigenically similar compounds, as there was no sample left out for analysis. As per the advice of Food Standards Agency, we urged the patient to contact the Environmental Agency about this incident.

We propose that the allergic reaction in our patient was triggered by either contamination of the cheese with penicillin or antigenically similar compounds produced by the Penicillium species used in the manufacture of the cheese.
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Malignant melanoma: hidden behind a black veil

Keith Winters

Cutaneous melanoma is a malignant neoplasm arising from epidermal melanocytes. The earliest description is in the writings of Hippocrates in the 5th Century BC. Individuals most susceptible to the development of melanoma are those with fair complexions, red or blond hair, blue eyes, and freckles, with a history of sunburn, especially in early life.\(^1\)

Other risk factors associated with increased risk include family history of melanoma, presence of atypical moles (dysplastic naevus), a giant melanocytic naevus, a small to medium-sized congenital melanocytic naevus, the presence of higher than average number of ordinary melanocytic naevi, and immunosuppression.\(^2\) It demonstrates somewhat unpredictable behaviour, which varies from spontaneous regression to rapid progression and death.

Recurrence or metastatic spread after 5-year surveillance is well documented. The incidence of melanoma in Australasia has been reported between 30 and 40 per 100,000, and is doubling every 10 to 15 years,\(^3\) presumably related to increased recreational sun exposure.

In 1999, there were 231 deaths related to melanoma in New Zealand.\(^4\) It accounts for almost all the deaths from skin cancer. The most important prognostic factor is stage at time of presentation. The American Joint Committee on Cancer/International Union Against Cancer (AJCC/UICC) staging is employed based on the TNM system. Once the Breslow’s depth exceeds 0.76 mm, there is a significant chance of metastatic spread.

The 10-year survival rate for a nodular tumour between 0.76 mm and 1.5 mm is estimated at 90.7%.\(^5\) The treatment is primarily surgical, with excision margins of 1 cm for every millimetre of invasion, to a probable maximum of 2 cm.\(^6\) Other treatment modalities have not been shown to alter survival.

Case report

A 73-year-old Caucasian male was referred by his family doctor in April 1989 to the Plastics Department at Hutt Hospital, following the excision of a 1.1 mm nodular melanoma from the posterior aspect of his left knee. He was an active farmer, and other than bilateral knee joint and left hip joint replacements for osteoarthritis, had no other medical problems. He did not smoke, and there was no family history of melanoma. He underwent a further wide local excision with 2 cm margins and followed up in the melanoma clinic for 5 years, with no evidence of recurrence or metastases.

In March 1998, he was referred back to the clinic with a nodular recurrence within the scar of the excision site. This was re-excised and repaired with partial thickness skin...
graft. In August of 1999, a fixed mass in the left inguinal region was found on routine follow-up.

Fine-needle aspirate (FNA) was suspicious of melanoma, and a CT scan showed a large mass extending close to the iliac vessels and involving the lateral end of the inguinal ligament. He underwent an urgent block dissection 10 days later. It was noted at the time of surgery that the tumour appeared to involve most nodes, encased the iliac vessels and extended into the spermatic cord.

A sub-total dissection was performed, and he was referred for postoperative radiotherapy. The pathologists reported no evidence of tumour, with reactive nodes containing numerous histiocytes full of fine granular black pigment (Figure 1).

Figure 1. Low power slide showing pigment granules within histiocytes in the lymph nodes (×200 magnification; H&E stain)

The pigment was assumed to originate from the debris of his hip replacement, and the patient was reassured. Almost exactly 2 years later, a nodule was noted on the lower end of the inguinal scar. A repeat FNA showed scar tissue, but a formal excision was arranged to be certain. This was performed 7 days later under a general anaesthetic. The 1 cm by 2 cm mass excised was suspicious of melanoma, with black pigmentation and an invasive margin involving the underlying sartorius muscle. Histological analysis revealed metastatic melanoma!

He is currently undergoing radiotherapy to the inguinal region for residual tumour, some 14 years after the original diagnosis of melanoma.

Discussion

Malignant melanoma has developed a reputation as a nasty and unpredictable cancer. Similar to other cancer surveillance regimes, we usually follow patients for 5 years after the excision of a melanoma. Recurrence after this period is well recognised, with 10–15% of first time recurrence occurring after 5 years.

Prosthetic wear particles are generated by the abrasion at the prosthesis/cement interface. Langkamer et al have shown that metal debris from a hip implant may
disseminate through the whole body by lymphatic spread. They may be carried by macrophages in the perivascular lymph spaces and/or in the form of free particles. Metal particles usually appear as fine grey-black birefringent granules, 0.5–5 µm in size. There are few cases in literature. Basle et al reported four cases of lymphadenopathy from prosthetic wear particles which mimicked pelvic malignancy. Yoshitaka et al reported a case of inguinal lymphadenopathy from prosthetic wear particles which mimicked pelvic malignancy. Basle et al reported four cases of lymphadenopathy from prosthetic wear particles which mimicked pelvic malignancy.10 Yoshitaka et al reported a case of inguinal lymphadenopathy from prosthetic wear particles which mimicked pelvic malignancy.10 Yoshitaka et al reported a case of inguinal lymphadenopathy from prosthetic wear particles which mimicked pelvic malignancy.10 Given the possibility of metastatic spread in this case, it may have been prudent to institute radiotherapy despite the histology report. Whether the 2-year delay would have made a difference to the outcome is questionable.

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**References:**

Acute pretibial myxoedema following thyroidectomy for Graves’ disease

Akheel A Syed, Nigel A G Jones, Petros Perros

A 37-year-old man developed shiny, erythematous, indurated lesions on both shins (Figure 1) following total thyroidectomy for thyrotoxic Graves’ disease associated with thyroid eye disease. His serum free thyroid hormone concentrations were maintained stably within normal limits before and after surgery by carbimazole and thyroxine dual therapy in a block-and-replace regime. However, his thyrotropin receptor antibody (TRAb) titre post-thyroidectomy was 15 times above the upper limit of the reference range, compared to 7.7 times above the upper limit of the reference range at initial presentation before initiation of antithyroid treatment.

Figure 1. Bilateral erythematous, non-pitting, oedematous plaques of thyroid dermopathy on the anterior and lateral aspects of the legs (Panel A)

Note the induration seen in profile view (Panel B)

The dermopathy is pretibial myxoedema, a characteristic lesion that results from excessive deposition of hyaluronic acid and chondroitin sulphate in the dermis. Although the precise nature of this extra-thyroidal phenomenon remains uncertain, it is thought that TRAbs stimulate skin fibroblasts to generate abnormally large amounts of glycosaminoglycans. 1

Acute development of pretibial myxoedema following radioiodine treatment for thyrotoxic Graves’ disease has been associated with very high TRAb titres post-radioiodine. 2 Similarly, very high TRAb activity in response to thyroid antigens released during surgery may have caused the postoperative flareup of the dermopathy in our patient, although his thyroid eye disease remained stable, and was managed conservatively.
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References:
Bertillon's Nomenclature of Disease and of Cause of Death (part 1)

Written by Dr Colquhoun, Dunedin, and published in N Z Med J. 1907;5(23).1–2.

The Bureau of Census and Statistics of the Commonwealth of Australia have done great service in publishing and issuing free to all interested in the subject, a pamphlet dealing with the work of an International Commission which met at the instance of the French Government, in 1906, to consider the nomenclature of disease and the statistics of the cause of death in different countries.

The delegates represented Germany, Bavaria, Dresden, The Argentine, Austria, Belgium, Bolivia, Chili, Denmark, Sweden, Spain, United States, France, Greece, Ecuador, Honduras, Hungary, Italy, Mexico, Monaco, Norway, Netherlands, Paraguay, Russia, Salvador, Switzerland and Uruguay—twenty-six States—Great Britain and the Colonies not being included. The delegates agreed to recommend to their Governments the adoption of the nomenclature held in the City of Paris and they also agreed that their classification should be reviewed every ten years, the first to take place in 1910.

As the system in use in New Zealand is the English classification, it is desirable that we should consider its efficiency, and it is not too early, if we wish to take any part in the review of 1910, for the medical profession in New Zealand to take this matter into consideration.

It is obvious that there must be close agreement between the systems of various nations in reporting causes of death if the results are to have any comparative value. As far back as 1853, the Statistical Congress at Brussels, Commissioners D'Espine of Geneva and Farr of London to present proposals for nomenclature for International use, Farr's scheme was the one practically adopted. It classes as far as possible most diseases, according to their anatomical location and not according to their nature. Beside their classification, there were also headings for general diseases, malformation, diseases of infancy, of old age, those caused by violence and well defined diseases. This is the classification which has been adopted by the Congress and elaborated according to Bertillon's scheme for Paris.
New treatments for dementia?

“Dementia is perhaps the cruellest manifestation of ageing, inexorably melting away all that which makes us individual and human”

These striking words begin the first of three editorial commentaries on two new treatments reported recently in *The Lancet*. The writer points out that increased life expectancy has its down side and that currently 1% of the UK population has dementia. Even worse, it is predicted the numbers will double in the next 30 years.

The first new treatment for Alzheimer’s disease, from Russia, is dimebon, a drug with weak cholinesterase, weak glutamatergic, and neuroprotective activity. Well, dimebon was better than placebo at 26 weeks. However, a small numbers trial with a very short follow-up. We will have to wait. The second report concerns immunisation of patients with Alzheimer’s disease with full-length amyloid-β peptide (Aβ42). This immunotherapy is capable of clearing amyloid plaques from the brain. And it did clear them but it did not affect progressive neurodegeneration.


Transdermal versus oral hormone replacement therapy (HRT), and gallbladder disease

There is evidence for an increased risk of gallbladder disease in postmenopausal women using HRT. Oestrogen administered transdermally avoids first pass metabolism in the liver and it has been suggested that it might have a lesser effect on the risk of gallbladder disease than oral oestrogen.

Nearly 20,000 women with gallbladder disease in England and Scotland over a 5-year period were studied. Current HRT users were more likely to be admitted for gallbladder disease compared with never users (relative risk 1.64), but risks were substantially lower within the transdermal group compared with the oral HRT group (p<0.001). Interesting; however, it appears to translate to one cholecystectomy avoided in every 140 users in the transdermal group. (This article is an abridged version of a paper that was published on bmj.com. Cite this article as *BMJ* 2008;337:a386.)


Daily versus as-needed inhaled corticosteroid for mild persistent asthma in childhood

This paper from Finland reports on a randomised trial involving 176 children with newly detected asthma. One group had regular budesonide inhalation, another were given budesonide as required, and the third arm had regular disodium cromoglycate supplemented with budesonide as deemed necessary.
Their results confirmed that continuous treatment with inhaled corticosteroids is associated with significantly better asthma control than treatment with disodium cromoglycate or intermittent treatment with inhaled corticosteroids.

The authors and an editorial commentator recommend regular daily budesonide. The down side is a growth arrest and the children may be 1-2 cm shorter than their peers for some years on their way to adult height.


**Strep sore throat—10 days treatment still the best**

Tonsillopharyngitis caused by group A β-haemolytic streptococcus (GAS) is one of the most common bacterial infections in the community, particularly among children aged 5 to 15 years.

The authors of this paper are concerned that although the traditionally recommended antibiotic treatment is a 10-day course of penicillin V, administered 2 or 3 times daily, patient adherence to the full course of treatment is suboptimal. The reason for this is that resolution of symptoms often occurs well before 10 days.

This meta-analysis involves 11 randomised controlled trials comparing short versus long (10 days) courses of antibiotics, most with penicillin V or a cephalosporin.

The result—both microbiological eradication of GAS and clinical remission were inferior in the shorter course treatments. So back to the gold standard—10 days of penicillin V.


**Proton pump inhibitors, osteoporosis, and fractures?**

Proton pump inhibitors (PPI) efficiently inhibit the production and intragastric secretion of hydrochloric acid, which is believed to be an important mediator of calcium absorption in the small intestine.

Hence there is the possibility that prolonged usage might lead to osteoporosis and fractures. There is some published evidence of this and the authors of this observational study have matched 15,792 cases of osteoporosis-related fractures with 47,289 controls and compared their long-term usage of PPI. They acknowledge that confounding factors such as other drugs, comorbidities, and lifestyle are involved and have gone to considerable trouble to eliminate these from their analysis. They conclude that exposure of 7 or more years was associated with increased risk of an osteoporosis-related fracture (adjusted OR 1.92, p=0.011).

The obvious corollary is that powerful drugs should be used for specific purposes and not used frivolously, particularly for prolonged periods.

Election issues

On September 26th, the New Zealand Herald printed the results of a poll.

The main concern with voters is the economy (28%). Law and order was again second (17.8%), followed by tax cuts (16.5%), leadership (12.3%), hospital waiting lists (10.3%), and global warming (6%).

The hospital waiting lists are a government concern. When Pete Hodgson was Minister of Health, he was quoted as saying that although the private sector played an important role, the government believed “the private provision of health is always more expensive in the long run.” For that reason, he said, it wanted the public health system to dominate.

He did acknowledge the public system falls short by nature. “No public health system in the world that is free of charge can deliver the real or perceived public need for elective surgery.”

The key word in all that is the word “perceived.” Not only are we paying for your operation; one of our operatives will tell you whether or not you even need it. As of this week, I could find no reference to private surgery anywhere on the Labour Party website. What I did find was a boastful display of publicly-funded “achievements” dated 2005.

The National Party, by contrast, wants “smarter” use of private hospitals. In fact it is pledged to maintaining health spending by the government at current high levels, and its tepid support for private surgical practice is not a ringing endorsement. In its September 2007 Health Discussion Paper it mentioned public-private partnerships, which are invariably horses pulling in different directions.

National Party strategists said this:

Concerns are often raised that specialists working in both the public and private sector have an incentive to under-perform in the public hospitals in order to increase more lucrative private work.

Where does the New Zealand Medical Association stand in this debate? I wouldn’t know. When last heard from, it wanted “more explicit definition of the boundaries between the public and private sectors.” The doctors, it appears, feel unable to say anything until somebody can tell them what they are talking about.

I think I can help the NZMA with its concerns. If you want a thing done, you reach for your cheque book and you go and find somebody to do it. If you don’t have the money, you wait in the queue, where people try to scramble past each other.

The health system is now self-privatising. Many patients walk, or hobble, or are led to the private specialist and the private hospital, where business has never been better.

Roger M Ridley-Smith
Retired GP
Wellington
The responses of alternative practitioners when approached about common childhood illnesses

There has been much debate of late in the New Zealand Medical Journal around alternative practitioners. I was interested to see what the response would be from chiropractors, homeopaths, and acupuncturists to an approach concerning medical conditions in which these treatments have no proven benefits.

Five of each type of practitioner (or fewer if there were not 5)—from the 6 largest cities in New Zealand, who listed either an email address or website on the Yellow Pages website—were selected using a random number generator.

An email was sent from a fictitious grandmother who stated that she had a 7-year-old grandson who suffered from recurrent ear infections and a 13-year-old granddaughter who had asthma. The practitioner was asked if they could recommend something that was proven to work for these conditions and the approximate cost. The response rate after 1 month was 45% (33 out of 73). The use of a fictitious patient is the only way to determine the real-life advice that is given and has been used in similar surveys.1,2

It is beyond the scope of this letter to undertake a detailed systematic review of these three alternative treatments for these two common paediatric conditions. However, the evidence is perhaps best summarised in the book Trick or Treatment by the world-leading authority on evidence-based complementary medicine, Professor Edzard Ernst.3 His review of the literature shows that there is no good evidence that homeopathy can treat any condition; that chiropracty may have small benefits in certain musculoskeletal disorders; and that acupuncture may have small benefits in patients with pain or nausea. This view is consistent with the conclusions of the many major reviews that have been undertaken.4–8

There is no good evidence, and in fact no plausible scientific rationale, to support the use of these treatments for asthma or recurrent ear infections.

The results of the email responses are summarised in Table 1.

Table 1. Responses from chiropractors, homeopaths, and acupuncturists

<table>
<thead>
<tr>
<th>Alternative practitioners</th>
<th>N (total=35)</th>
<th>Suggested an appointment (n,%)</th>
<th>Gave prices (n,%)</th>
<th>Suggested they could treat asthma (n,%)</th>
<th>Suggested they could treat ear infections (n,%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chiropractors</td>
<td>13</td>
<td>12 (92%)</td>
<td>11 (85%)</td>
<td>9 (69%)</td>
<td>8 (62%)</td>
</tr>
<tr>
<td>Homeopaths</td>
<td>9</td>
<td>9 (100%)</td>
<td>6 (67%)</td>
<td>9 (100%)</td>
<td>9 (100%)</td>
</tr>
<tr>
<td>Acupuncturists</td>
<td>13</td>
<td>12 (92%)</td>
<td>11 (85%)</td>
<td>9 (69%)</td>
<td>8 (62%)</td>
</tr>
</tbody>
</table>

This survey identified that almost all practitioners suggested that the children should have an appointment with them. All of the homeopaths suggested that they could effectively treat both asthma and ear infections, and around two-thirds of
Chiropractors and acupuncturists suggested that their treatments would work. A number of chiropractors and acupuncturists suggested that the children be brought in for an assessment, even though they did not directly claim that their treatment would help.

Charges for the initial consultation ranged from free to $160, with an average of around $60. For follow-up visits, the charges ranged from $7.50 to $85, with an average charge of around $50, with little difference between the three types of practitioners. Despite never having seen the children, many practitioners recommended a long course of treatment, with one acupuncturist recommending 10 treatments and 30 days of herbal remedies, at a total cost of $810 per child.

The responses generally had a pseudoscientific tone, although no replies referenced any scientific studies.

Some of the more interesting comments from chiropractors included:

- *I personally haven’t seen any children with these conditions not respond phenomenally well to chiropractic care;*
- …great response through boosting body function;
- …certainly have wonderful results.

Comments of note from some of the homeopaths included:

- …works brilliantly for ear infections;
- …hundreds of remedies for ear infections and asthma;
- homeopaths have a success rate nearing 80%.

There are many ethical, regulatory, and safety issues associated with alternative medicine practitioners giving health advice and treating patients; this survey provides local data which contributes to the debate and raises major concerns.

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References:


Health Practitioners Disciplinary Tribunal – Not Guilty (Med07/72D)

Charge

The Doctor was charged with professional misconduct by the Director of Proceedings. The charge alleged that:

1. On or about 28 September 2000 when the Doctor operated on his patient to repair a major degree of cystocele, he failed to perform a procedure designed to repair this cystocele (namely a vaginal anterior repair or an abdominal paravaginal repair), but instead performed a Burch colposuspension, which is a procedure used to treat urodynamic stress incontinence;

2. Between 20 February 2001 and 22 November 2001 when his patient presented with urinary incontinence he performed various procedures on his patient without first performing urodynamic studies to ascertain the cause of the incontinence. In particular:
   a. On or about 28 February 2001 he injected macroplastique;
   b. On or about 27 November 2001 he performed a SPARC sling procedure and injected collagen;

3. Between 19 February 2002 and 28 January 2003 when his patient presented to him with incontinence on five times, he failed at any time to perform urodynamic studies in order to ascertain the cause of her incontinence.

Explanation of procedures

A cystocele is a protrusion of the bladder into the anterior vaginal wall, and in severe cases the protrusion extends through the vaginal opening. The condition is a result of weakening of the support structures of the bladder base.

A Burch colposuspension is a retropubic suspensory operation, involving suturing the vaginal fornices to the Cooper’s ligaments on each side. It is primarily intended to treat stress incontinence.

Macroplastique and collagen are “bulking agents” placed submucosally at bladder neck/proximal urethra.

Urodynamic studies are an objective test of bladder and bladder outlet function. Urodynamics assess the detrusor muscle stability and sphincter competence. Abnormalities of either can lead to urinary outflow disorders.

Finding

The Tribunal found the Doctor not guilty of professional misconduct.

Background

The issues that arose in this case are in the fields of urology (female incontinence) and gynaecology (pelvic floor dysfunction).
On 19 September 2000 the Doctor met Mrs S, a seventy year old woman. He recorded:

- She did not have stress incontinence, and did not have any other urinary problems.
- She had a very large cystocele that was nearly coming through the introitus of the vagina.
- The vault of the vagina was still high and she had only a small rectocele which was not troubling her.
- He recommended cystoscopy, excision of the urethral mucosal prolapse, and a laparoscopic Burch colposuspension. He stated that if the whole cystocele was not completely eliminated by the Burch procedure, then a high anterior repair would be performed as well. He said it was very important to fix the bladder neck properly otherwise she could have stress incontinence post operatively.

On September 2000, the Doctor performed a cystoscopy which revealed nothing abnormal, excised the urethral mucosa prolapse, and performed the laparoscopic Burch colposuspension.

Mrs S returned to see the Doctor on 17 October 2000 and 31 October 2000. By the latter date she was experiencing severe urge problems and leaking on change of position, but no stress incontinence. The Doctor prescribed Imipramine (a tricyclic antidepressant used to facilitate urine storage). She was reviewed again on 29 November 2000; there was again urge incontinence, which the Doctor dealt with by way of anticholinergic medications.

Mrs S presented to the Doctor on 20 February 2001 with incontinence. He noted that she “trickles urine all the time – wet at night”. There was some urine in the vagina. He queried whether there was a vesicovaginal fistula. He decided to undertake a flexible cystoscopy.

The cystoscopy was performed the next day by the Doctor where he reported a normal bladder but fluid (presumably urine) in the vagina. He was still suspicious of a fistula and considered it appropriate to examine her under general anaesthetic. He did this examination on 28 February 2001. No fistula was shown. The Doctor reported the bladder neck was slightly open. He therefore concluded she had intrinsic sphincter deficiency, so he injected three ampoules of macroplastique peri-urethrally.

On 15 March 2001, Mrs S reported ongoing incontinence, which despite treatment from the Doctor continued through until the end of October 2001. By 31 October 2001, there was a “continuous flow of urine non stop”. On 22 November 2001, the Doctor performed a SPARC sling procedure, and peri-urethral collagen injections.

Reviews were undertaken on 27 November 2001 and 21 December 2001 by which time continence had returned. The Doctor discharged Mrs S back to her GP. Unfortunately, it was necessary for Mrs S to see the Doctor again, from 30 July 2002 onwards, because she experienced episodes of incontinence at times. The Doctor maintained a conservative (non surgical) regime, with medication and physiotherapy.
The intention was to wait for 12 months following the SPARC sling procedure, and then to review the possibility of further macroplastique injections.

In the course of 2003, Mrs S moved to another centre; on 29 January 2003, the Doctor referred Mrs S to another urologist, who specialised in incontinence issues.

The other urologist advised urodynamic investigations (which the Doctor had not at any time undertaken) to determine the cause of the leakage. In April 2003, the other urologist found that the mesh which had been used in the SPARC sling had eroded the dome of the bladder, and it was thought this could account for some of the symptoms. He surgically removed the mesh and some of the bladder, and redid the SPARC sling procedure on 14 April 2003, having first undertaken videourodynamics. In the course of the urodynamic studies, a moderately severe intrinsic sphincter deficiency and type III stress urinary incontinence were reported.

**Reason for findings**

There was no dispute that in fact the Doctor undertook a Burch colposuspension, and did not undertake a vaginal anterior repair or abdominal paravaginal repair. The issue raised by Particular 1 was whether he should have undertaken such a repair.

The Tribunal accepted the opinion of the experts to the effect that undertaking the Burch colposuspension without a concurrent vaginal repair was a deviation from accepted practice. The Tribunal also noted that the Doctor accepted this conclusion when he gave evidence.

There was no controversy over the factual basis for Particulars 2 and 3. It was a fact that no urodynamics studies were performed between 20 February 2001 and 22 November 2001 (Particular 2) and between 19 February 2002 and 28 January 2003 (Particular 3).

The Tribunal considered the first procedure mentioned in Particular 2, the injecting of macroplastique on 28 February 2001. In theatre, the Doctor was able to confirm there were normal ureterograms bilaterally, and that the leakage was from the urethra itself. Without waking her, he proceeded with the macroplastique injections. In the Tribunal’s view this was an appropriate response. The Doctor had suspected there might be a urinary fistula, and if there had been, it needed to be identified and managed urgently. Accordingly, the Tribunal did not consider it to have been negligent in those circumstances not to undertake urodynamics first.

The Tribunal considered the situation for the second procedure mentioned in Particular 2, (the insertion of the SPARC sling) and Particular 3 was different. The Tribunal accepted the consistent evidence from all the experts that the requirement to undertake urodynamics was important, particularly before the surgical procedure undertaken in November 2001, but also during 2002 to early 2003, when the problems persisted.

The Tribunal concluded that in respect of Particulars 2 and 3 there was a deviation from accepted practice.

The Tribunal was satisfied that there was a departure from acceptable professional standards in respect of each particularised allegation (apart from the suggestion that urodynamics should have been performed prior to the injection of macroplastique on
28 February 2001). The Tribunal was satisfied that the departures amounted to negligence.

The Tribunal was required to make a qualitative evaluation of the extent of the departure from the accepted standards. Although there were undoubtedly some worrying aspects of the management of the case, the Tribunal was not persuaded, by a narrow margin, that the departures were so significant as to justify the imposition of penalties to protect the public, or to maintain professional standards.

It was evident, from the difficulties that the experts had in evaluating the extent to which a departure from relevant standards had occurred, the matter was finely balanced.

The Tribunal was not satisfied that discipline was warranted. Accordingly, the charge of professional misconduct was not established. The Tribunal recorded, however, that in its opinion the case was an entirely proper one to be placed before it, and for the complex issues to be fully tested, examined and determined.

The full decisions relating to the case can be found on the Tribunal web site at www.hpdt.org.nz (Reference No: Med07/072D)
Ross Alexander Fairgray

Many health professionals remember Ross Fairgray with affection.

As Medical Superintendent of Christchurch Hospital, Fairgray "went the extra mile" to make staff feel valued.

When junior staff arrived from overseas, he met them at the airport, brought them home for dinner, helped them settle into their flats, ensuring they had everything they needed.

His son, Dr Andrew Fairgray, says his father was considerate towards others and totally without pretension.

The former GP, obstetrician, and anaesthetist who became an outstanding health administrator died in Christchurch recently. He was 79.

Fairgray was born and raised in Auckland. He attended Mount Albert Grammar School and Auckland University, before completing his medical studies at Otago University. He graduated in 1954 and became a resident medical officer at Tauranga Hospital in the Bay of Plenty.

He married Iris Brown and they settled in Tauranga, a place they both loved. They had four children. Daughter Liz says her mother was an academic and noted sportswoman whose dedication to her husband made his career possible.

After 2 years at the Tauranga Hospital, Fairgray went into general practice in the town. He worked also in obstetrics and anaesthesia. His son says he was a popular family doctor and enjoyed the work. However, he had difficulty saying "no" to anyone and his workload became too much. "He wore himself out."

He took a lesson from a fellow GP and close friend who died at 40 from overwork. He returned to Otago University in 1967 and completed a Diploma in Public Health, which qualified him for hospital administration.

The family then moved to Auckland, where Fairgray took the position of Deputy Medical Superintendent at Middlemore Hospital. He won the keenly sought post of Medical Superintendent at Christchurch Hospital in 1969 and the family made its last move.

Fairgray led the medical sector of public health in Canterbury for the next 20 years, until his retirement in 1989. These were decades of major change, with the rebuilding of Christchurch Hospital and the restructuring of administration, from the North Canterbury Hospital Board to the Canterbury Area Health Board, and with the rising influence of non-medical managers.
His titles changed with the restructuring. His responsibilities encompassed management of Christchurch Hospital, including medical officers' appointments and duties and patient care services, and overseeing all Canterbury public hospitals.

Liz says her father addressed an acute shortage of house surgeons on his arrival in Christchurch by writing to every medical school in the Commonwealth, extolling the virtues of the city. Many new staff arrived in subsequent years.

Medical Staff Association chairwoman Ruth Spearing said in a eulogy that his personal kindness helped Canterbury retain staff and there was no further shortage. He had a major role in developing "the most collegial group of hospitals in New Zealand".

Pat Cotter, of the Medical History Trust, says Fairgray was "a very good doctor, a really nice guy and an outstanding manager". He always knew exactly how the hospitals were functioning because "he spoke to the cleaners". Liz says this reflected her father's strong Christian beliefs and "Leftish" politics. "He loathed injustice and inequality." He was a strong proponent of women's rights, she says.

He was a firm believer in a publicly provided health system. His inability to offer services he saw as "desirable" for patients, because of budget restrictions, frustrated him. He agonised over conflicting calls for funding.

Andrew says his father was a mentor to many. People frequently visited in the evenings to discuss work and non-work matters and seek his advice. He was astute and "no pushover" for anyone trying to put one across him. "He was no socialite but he had an incredible number of loyal friends," Andrew says.

Fairgray turned down a plum position in national health administration, in Wellington, because his family was happy in Christchurch. Liz says he was devoted to wife and family. Even when his kidney disease made him so weak he could barely stand, he travelled to watch his grandchildren play hockey.

Illness was cruel to a man who had been so active. He was a prominent cross-country runner in his youth and always a keen walker. He remained a member of a walking group until recent years. He enjoyed sailing and often crewed in yacht races around Banks Peninsula. He took up skiing at 50.

He loved his garden and for many years rose each day at 6am, working for 2 hours among his 200 rosebushes, then riding his bike from home, in Fendalton, to the hospital.

Ross Alexander Fairgray, born Auckland, December 14, 1928; died Christchurch, September 3, 2008. Survived by wife Iris, daughters Susan, Elizabeth and Helen, son Andrew, and eight grandchildren.

This obituary entitled Widely revered medical chief originally appeared in The Press newspaper (Christchurch) on September 20 and was written by Mike Crean. We are also grateful to Bruce Rennie of The Press. The photo appeared on the funeral programme.