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This Issue in the Journal

Antimicrobial consumption at Auckland City Hospital: 2006–2009
Rob Ticehurst, Mark Thomas

The spread of antimicrobial-resistant bacteria is a major challenge for human health in the coming years. Prudent use of antimicrobial drugs will help to slow the spread of these antimicrobial resistant bacteria. An audit of antimicrobial consumption by adult inpatients at Auckland City Hospital between 2006 and 2009 shows that the level of consumption is comparable to or less than that in Australian and Scandinavian hospitals. This shows that the antimicrobial stewardship programme at Auckland City Hospital is working well. The results provide a local standard for comparison with other New Zealand hospitals.

Demographic variation in community-based MRSA skin and soft tissue infection in Auckland, New Zealand
Stephen R Ritchie, John D Fraser, Eric Libby, Arthur J Morris, Paul B Rainey, Mark G Thomas

This study aimed to estimate the burden of skin and soft tissue infection caused by Staphylococcus aureus (S. aureus), and to determine the effects of ethnicity and age on the rate of skin and soft tissue due to the relatively dangerous methicillin-resistant Staphylococcus aureus (MRSA) bacteria in the Auckland community. S. aureus is a very common cause of disease in the community and the incidence of infection with MRSA subtypes varies with ethnicity. Māori and Pacific people had higher rates of non-multiresistant MRSA infection compared with New Zealand European and Asian people while elderly New Zealand European people had much higher rates of multiresistant MRSA infections compared with people from other ethnic groups.

Nasal carriage of Staphylococcus aureus in healthy Aucklanders
Nicola Best, John D Fraser, Paul B Rainey, Sally A Roberts, Mark G Thomas, Stephen R Ritchie

Prior studies have found that Māori and Pacific people are at increased risk of disease caused by the bacteria S. aureus, which is a common cause of serious disease and death in New Zealand. We identified healthy, asymptomatic nasal carriers by performing nasal swab cultures from healthy population volunteers, who also completed a brief questionnaire. The proportion of people who carried S. aureus did not differ significantly between ethnic groups. Indicators of social deprivation did not differ between nasal carriers and non-carriers. Ethnic variation in the prevalence of S. aureus nasal carriage does not contribute to an increased risk of disease caused by S. aureus.
Impact of universal hepatitis B vaccination on antenatal hepatitis B prevalence in the Midlands region of the North Island, New Zealand
Michael Addidle

This study looks back at hepatitis B tests done over the past 12 years on antenatal women on the midlands region of New Zealand. The results show that the universal hepatitis B vaccination, commenced in 1988 is now positively impacting on the number of antenatal women who test positive for hepatitis B, with a gradual decrease in prevalence over the past 12 years.

Molecular epidemiology and susceptibility profiles of Clostridium difficile in New Zealand, 2009
Sally Roberts, Helen Heffernan, Nadia Al Anbuky, Christopher Pope, Susan Paviour, Tracey Camp, Terri Swager

This study looked at the strains of Clostridium difficile causing diarrhoea in patients in New Zealand hospitals. One of the main objectives was to determine if a particular hypervirulent strain, called ribotype 027, was present in New Zealand. This strain is associated with an increase in the incidence and severity of Clostridium difficile disease in North America and the United Kingdom. Over a 5-month period, 101 isolates from 97 patients across New Zealand were examined. There was a wide range different types but the hypervirulent strain was not detected. Antimicrobial resistance was also uncommon.

Pertussis (whooping cough) epidemiology in Waikato, New Zealand: 2000–2009
Richard Wall, Anita Bell, Jason Theobald

This study examined the pertussis (whooping cough) cases in the Waikato region between 2000 and 2009. The rate of pertussis was higher in the Waikato region than nationally during the decade. Pertussis epidemics occurred in the Waikato in 2000 and 2004, at the same time as national epidemics occurred. There were no differences found in the gender, ethnicity or socioeconomic status of people with pertussis during an epidemic or a non-epidemic period. The proportion of pertussis cases occurring in people aged 25 years and over has increased from 2000 to 2009.
Antibiotic prescribing: time for national surveillance?

Justin Beardsley, Tim Blackmore

Antibiotic resistance is topical again, because of startling reports describing nearly-impossible-to-treat infections caused by multi-resistant Gram-negative bacilli and tuberculosis. Indeed, antibiotic resistance was the focus of the recent World Health Day, with the headline *Antimicrobial resistance: no action today, no cure tomorrow.* In particular, the need for “stewardship by government” of surveillance and prudent antibiotic use was emphasised.¹

This makes the article by Ticehurst and Thomas² in this issue of the *NZMJ* particularly timely because it is the first systematic description of antibiotic use in a New Zealand (NZ) hospital. The data presented allow comparison with overseas antibiotic usage patterns and serve as an excellent starting point for collecting and comparing data from other NZ hospitals. This type of surveillance is essential for antibiotic stewardship, as it provides a baseline, and suggests areas for targeted interventions.

We hope that other hospitals will also recognise the value of knowing antibiotic usage patterns and therefore collect and report data consistently. Meaningful surveillance allows the effectiveness of antimicrobial stewardship to be properly assessed between NZ hospitals. Because it is a retrospective, non-interventional study, it is impossible to assess the effectiveness of the Auckland District Health Board hospitals’ stewardship programme itself from the report by Ticehurst and Thomas.

A NZ-wide survey of antibiotic use would be a powerful tool for demonstrating which interventions are most effective in reducing inappropriate antimicrobial consumption and improving patient outcomes. Further, when combined with national antibiotic resistance data, it would allow NZ hospital clinicians to compare themselves to their counterparts around the globe.

As described by Kuster et al, benchmark reporting methods should be standardised, precise and clear. For example, it is recommended that the first and final days of an admission are counted as one: counting them as two can affect DDD/100 inpatient days estimates by up to 26%.³ The methods used in Ticehurst report are not clear in that regard, but other reports from NZ should follow the same method once clarified. To facilitate future comparisons, basic hospital demographics such as mean length of stay, total number of bed-days, number of patient admitted and total number of admissions should also be reported.³

Sweden has a highly organised and effective national antibiotic stewardship programme. They have limited both overall antibiotic consumption and consumption of broad-spectrum agents and have low rates of multi-drug resistant organisms.⁴ Their data collection, reporting, accuracy and the philosophical approach are laudable, but whether NZ should follow their specific antibiotic choices as suggested by Ticehurst and Thomas, is debatable: we believe NZ recommendations should be guided by local microbiological data.
Ticehurst and Thomas steer clear of discussing costs, yet antibiotics are usually one of the most expensive pharmaceutical classes used in hospitals. The proposal for PHARMAC to take over hospital pharmaceutical purchasing, which would include antibiotics, to reduce drug acquisition costs will bring a new focus on antibiotic costs and stewardship.

The Centers for Disease Control (CDC) website Get Smart for Healthcare has summarised numerous publications showing that stewardship is cost-effective and, in an era of restrained healthcare expenditure, these savings should motivate managers and clinical leaders alike.

Despite being mostly limited to the pharmaceutical costs, these studies have shown that stewardship programmes more than pay for themselves. Reductions in the length of stay have been shown with the management of community acquired pneumonia, providing significant cost savings. Numerous articles have shown the relationship between antibiotic use and the frequency of multi-drug resistant bacteria, providing yet more reasons to get rational about antibiotics.

Stewardship is about using the right antibiotic, via the right route, at the right time and for the right length of time: few should object to these goals in principle. The difficulty is how best to implement a stewardship programme whilst maintaining goodwill and buy-in from medical colleagues who often have their favourite antibiotics. Unfortunately, education without restrictive interventions is ineffective. Effective stewardship requires a team approach, with drug chart review by a ward pharmacist and a senior experienced clinician motivated to encourage colleagues to prescribe antibiotics more effectively.

Information technology has also been used to restrict prescribing of selected antibiotics. Care bundles for antimicrobials have been described, where prescribers are required to document the indication for their choice of antibiotic, consider the microbiological evidence or request further investigations and plan for duration of treatment and monitoring. Adopting such a care bundle requires up to date antibiotic guidelines, and compliance with the bundle means that basic principles of therapy are adhered to: the bundle itself provides quality markers for audit.

The effectiveness of antibiotic care bundles on patient outcome are yet to be assessed, but they are simple and have been shown to be effective in preventing ventilator associated pneumonia, central venous catheter associated bloodstream infections and others.

NZ is a small country with some regional differences, but it is important that there is consistency in the delivery of healthcare: hospital antibiotic prescribing is no exception. This article should stimulate other hospitals to publish or report their antibiotic usage data in a standardised way. This will open up further discussion about how best to use antibiotics in the NZ hospital environment, and expose areas resistant to educational approaches.

Finally, as a word of caution, the most inappropriate antibiotic “use” is not using an effective antibiotic for someone who would benefit. We need to avoid wasting broad-spectrum antibiotics on those who don’t need them, without holding back for those with sepsis caused by resistant organisms.
A balance must be struck, but are we ready for national antibiotic surveillance and reporting against a national antibiotic guideline?

Competing interests: None.

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Antimicrobial consumption at Auckland City Hospital: 2006-2009

Rob Ticehurst, Mark Thomas

Abstract

Aims We aimed to determine the level of antimicrobial consumption by adult inpatients at Auckland City Hospital (Auckland, New Zealand) and to compare our findings with those in other developed nations.

Methods We used the computerised records of the central Auckland District Health Board (ADHB) pharmacy to measure the amount of antimicrobials dispensed to inpatients (excluding psychiatric units, day stay units and outpatient clinics) during 2006 to 2009. The total weight of each antimicrobial dispensed was used to determine the number of defined daily doses (DDDs) dispensed. The Information Management and Technical Services department of ADHB provided data on the number of admissions and inpatient days, and these data, together with information from the 2006 census, were used to calculate antimicrobial consumption for adult inpatients measured in DDDs/100 admissions, DDDs/100 inpatient days and DDDs/1000 population.

Results Total antimicrobial consumption by adult inpatients increased from 74 DDDs/100 inpatient days in 2006 to 80.3 DDDs/100 inpatient days in 2009. The level of consumption did not vary greatly with the season. The total level of consumption was very similar to that seen in adult inpatients in hospitals in Australia and Scandinavian countries. The level of consumption of fluoroquinolones, third or fourth generation cephalosporins, carbapenems and vancomycin (antimicrobial classes that are not available for unrestricted use in Auckland City Hospital) was comparable to or less than that seen in adult inpatients in hospitals in Australia or Scandinavian countries. Beta-lactamase susceptible penicillins (such as benzyl penicillin and phenoxyethylpenicillin) comprised a relatively small proportion of total penicillin use and beta-lactamase inhibitor combinations (predominantly amoxicillin/clavulanate) a relatively large proportion of total penicillin use, when compared with Scandinavian hospitals.

Conclusion The antimicrobial stewardship programme at Auckland City Hospital has resulted in a generally prudent level of consumption in recent years. Opportunities exist to improve the pattern of antimicrobial prescribing in the expectation that this will help to slow the spread of antimicrobial resistance in our community.

Increasing rates of resistance to widely used antimicrobial medicines in common bacterial pathogens pose a growing health threat. Infections due to these resistant pathogens frequently require treatment with medicines which may need to be administered intravenously rather than orally, may be associated with increased risk of toxicity, and may be less effective and more expensive than previously used agents. In a small but worrying proportion of patients the pathogen may be resistant to all
available antimicrobial agents and infections that previously were curable may have no effective treatment.\textsuperscript{1}

The major factor driving the evolution and spread of antimicrobial resistance is antimicrobial use. A number of other factors, such as demographic context (overcrowding, inadequate hygiene, etc), associated illnesses (especially those that result in some immune compromise and/or repeated hospital admissions) and failure to attend to hand hygiene, immunisation and other measures intended to reduce transmission of infection from person to person, also contribute to the spread of resistant microbes, but in general are less important than antimicrobial use.

A large number of studies have demonstrated strong associations between the volume of antimicrobial agents consumed and the rates of resistance in common bacterial pathogens to commonly used antimicrobial agents. Such associations have been seen at the level of the individual patient,\textsuperscript{2} at the level of the hospital and its surrounding community\textsuperscript{3} and at the national level.\textsuperscript{4,5}

The strong relationship between the volume of antimicrobial agents consumed and the rate of resistance to many antimicrobial agents should be a powerful motivating force to ensure that these agents are used wisely. Many surveys have shown that antimicrobials are very frequently overused and there is considerable potential for reductions in the volume of antimicrobials commonly prescribed for a range of conditions.\textsuperscript{6}

The type of antimicrobial commonly prescribed also has an effect on the rates of resistance to antibacterial agents. Prescription of antimicrobial agents with either a very broad antimicrobial spectrum or a low genetic barrier to the development of resistance is associated with increased rates of resistance in common bacterial pathogens.

Marked differences have been found between prescribing patterns at the level of the individual doctor and at the national level. Interventions intended to change the type of antimicrobial prescribed for various infectious syndromes have been associated with reductions in the rate of resistance in common pathogens.\textsuperscript{7–9}

The hospitals of the Auckland District Health Board (ADHB): Auckland City Hospital (ACH), Starship Children’s Hospital (SSH) and Greenlane Clinical Centre (GCC), provide secondary healthcare to the residents of central Auckland (approximately 450,000 people in 2009) and tertiary healthcare to the wider Auckland region population (approximately 1,436,400 people in 2009) for some services (e.g. neurosurgery, ophthalmology, cardiac surgery) and to the total New Zealand population (approximately 4,315,800 people in 2009)\textsuperscript{10} for other services (e.g. liver, heart and lung transplantation).

We have retrospectively measured antimicrobial consumption within the ADHB hospitals during the years 2006–2009. We anticipate that our results will provide a baseline for comparisons with other New Zealand hospitals, and with future prescribing within the ADHB hospitals. We also anticipate that the results will identify opportunities to encourage changes in antimicrobial prescribing that might either slow or reverse the rising rates of infection with resistant bacteria.
Methods

All medications prescribed for inpatients of ACH, SSH or GCC are purchased by the central ACH pharmacy. The computerised records for antimicrobial dispensing from this central pharmacy were accessed for the years 2006 to 2009. The amount of antimicrobials dispensed in each of these years was measured for each clinical unit involved in inpatient care.

Medications dispensed to patients within psychiatric wards, outpatient clinics, day stay units, etc were not included. Antimicrobial agents were aggregated into the following classes in accordance with the Anatomic Therapeutic Chemical (ATC) classification: tetracyclines (J01AA), penicillins with extended spectrum (J01CA), beta-lactamase sensitive penicillins (J01CE), beta-lactamase resistant penicillins (J01CF), combinations of penicillins, including beta-lactamase inhibitors (J01CR), first-generation cephalosporins (J01DB), second-generation cephalosporins (J01DC), third-generation cephalosporins (J01DD), fourth-generation cephalosporins (J01DE), monobactams (J01DF), carbapenems (J01DH), trimethoprim and derivatives (J01EA), intermediate acting sulphonamides (J01EC), combinations of sulphonamides and trimethoprim (J01EE), macrolides (J01FA), lincosamides (J01FF), other aminoglycosides (J01GB), fluoroquinolones (J01MA), glycopeptides (J01XA), polymyxins ((J01XB), steroid antibacterials (J01XC), imidazole derivatives (J01XD), nitrofuran derivatives (J01XE) and other antibacterials (J01XX08).

The total weight of each antimicrobial dispensed was used to calculate the consumption using the defined daily dose (DDD) measurement unit.

The Information Management and Technical Services department of the ADHB provided data on the total number of admissions and inpatient days for adults admitted to ACH or GCC (ophthalmology inpatients only), and for children admitted either to SSH or to the Neonatal Intensive Care Unit (NICU) in ACH; and for adults admitted to: the Department of Critical Care Medicine (DCCM:14 beds), the Cardiovascular Intensive Care Unit (CVICU:12 beds), the four adult general medical wards (100 beds), the two adult general surgical wards (50 beds), the adult haematology ward or the bone marrow transplant unit (20 beds) and the adult liver and kidney transplant ward (34 beds). The number of people resident within the area for which the ADHB provides secondary healthcare was obtained from the 2006 census. These data were used to calculate annual rates of DDD/100 admissions, DDD/100 inpatient days and DDD/1000 inhabitants/day.

Results

The total monthly consumption of antimicrobial agents, and the total monthly number of inpatient days, for adults admitted to ACH or GCC (total 902 inpatient beds) and for children admitted to SSH or NICU (total 281 inpatient beds), during 2006 to 2009, are shown in Figure 1.

Overall, the total consumption of antimicrobials (measured in adult DDDs/month) by adult inpatients was approximately four times greater than that by paediatric inpatients. For both children and adults there was relatively little variation in either the total monthly consumption of antimicrobial agents or the total number of inpatient days between the winter months (June, July, August) and the summer months (December, January, February).
Figure 1. Total consumption of antimicrobial agents (DDD) and total number of inpatient days for adult patients (ACH and GCC) and for paediatric patients (SSH and NICU), by month during 2006-2009

Note: In the absence of an accepted method of measuring paediatric DDDs, the total monthly consumption of antimicrobial agents by adult inpatients, and by paediatric inpatients, was measured in adult DDDs.

Figure 2 shows the relative contribution made by each inpatient unit to the total antimicrobial consumption by adult patients in ACH and GCC during 2009. The emergency medicine department and assessment planning unit (10%), the general medical wards (16%), the general surgical wards (9%) and the care for the elderly and rehabilitation wards (7%) together consumed approximately 40% of the total adult inpatient consumption. Between them the DCCM and the CVICU were responsible for approximately 3% of the total adult inpatient consumption.

The annual consumption of antimicrobial agents within ADHB hospitals by antimicrobial class for the years 2006 to 2009 is shown in Table 1. The average annual increase in total antimicrobial consumption during the four year period from 2006 to 2009 was approximately 3.2% for DDD/100 admissions, approximately 2.7% for DDD/100 inpatient days and approximately 4.3% for DDD/1,000 inhabitants/day.

Significant changes were apparent in the consumption of some antimicrobial classes during the same four year period. The annual consumption of carbapenems (measured in DDD/100 inpatient days) increased by approximately 50% in both 2007 and 2008 and then declined by approximately 20% in 2009. The annual consumption of fluoroquinolones and of glycopeptides increased by approximately 130% and 190%
respectively in 2007 but the annual consumption of both of these classes then declined over the next 2 years.

**Figure 2. Total annual consumption of antimicrobial agents (DDD) by adult inpatients in the various clinical units of ACH during 2009**

The annual consumption of antimicrobial agents by adult inpatients in the general medicine wards, general surgery wards, liver and kidney transplant ward, haematology ward, DCCM and CVICU, for the years 2006 to 2009 are shown in Figure 3. It shows that total antimicrobial consumption in the general medicine, general surgery, and liver and kidney transplant wards was relatively stable during this four year period (approximately 80–100 DDD/100 inpatient days), with low levels of consumption of some restricted antimicrobials (third and fourth generation cephalosprins, carbapenems, vancomycin and fluoroquinolones).

Relatively high levels of consumption of third and fourth generation cephalosprins (approximately 60 DDDs/100 inpatient days), and of glycopeptides (approximately 8 DDDDs/100 inpatient days) were seen on the haematology ward, where cefepime (a 4th generation cephalosporin) is a component of the empiric treatment of patients with neutropenic fever, and vancomycin is commonly used in the treatment of patients with intravascular cannula-related sepsis. An increase in the consumption of carbapenems was seen in most wards during the four year period, in response to an increase in the prevalence of infections due to extended spectrum beta-lactamase (ESBL) producing Gram-negative bacilli.
Figure 3. Consumption of antimicrobial agents (DDD/100 inpatient days) in the general medicine wards (A), general surgery wards (B), liver and kidney transplant ward (C), haematology ward (D), DCCM (E) and CVICU (F), for the years 2006 to 2009

Note: The y-axis is truncated in the same manner for all six graphs.

Discussion

This audit has shown that the total annual antimicrobial consumption by adult inpatients within the ADHB hospitals during 2006 to 2009 was comparable to the average levels of inpatient consumption in Sweden, Norway, Denmark, Ireland, and Israel during 2008. It was considerably less than the average levels of inpatient consumption in hospitals in France and Italy during 2008 (Figure 4).
The approximately 3% annual increase in total antimicrobial consumption by adult inpatients within the ADHB hospitals between 2006 and 2009 was comparable to that seen recently in Scandinavian hospitals. Total annual antimicrobial consumption, measured in DDD/1,000 inhabitants/day, increased by 2.6% per year in Swedish hospitals between 2000 and 2008,\textsuperscript{13} by 7% in Danish hospitals between 2007 and 2008\textsuperscript{14} and in Norwegian hospitals by 1.2% between 2006 and 2007 but by 10% between 2007 and 2008.\textsuperscript{15}

While the total antimicrobial consumption by adult inpatients within ADHB hospitals was comparable with the relatively low levels of consumption by adult inpatients in Scandinavian hospitals, the consumption of antimicrobials within each class differed significantly. These differences are clearly apparent with regard to penicillins, which comprised between $1/3$ and $1/2$ of the total adult inpatient antimicrobial consumption in the ADHB hospitals and in most European countries during 2008 (Figure 4).

Beta-lactamase sensitive penicillins (predominantly benzylpenicillin and phenoxymethylpenicillin) comprised a relatively small proportion of the total penicillin consumption within ADHB or Australian\textsuperscript{16} hospitals and a much greater proportion of total penicillin consumption in Scandinavian hospitals (Figure 5).\textsuperscript{13,15}
In contrast, beta-lactamase inhibitor combinations (such as amoxicillin/clavulanate) comprised a small component of total penicillin consumption in Scandinavian hospitals, a larger proportion of total penicillin consumption in ADHB and Australian hospitals and a very large proportion of total penicillin consumption in France, Belgium, and Greece.\textsuperscript{17}

**Figure 5.** Proportional consumption of different penicillin classes by adult inpatients in ADHB hospitals in 2009; Australian hospitals in 2009;\textsuperscript{16} Swedish hospitals in 2008;\textsuperscript{13} Norwegian hospitals in 2008;\textsuperscript{15} and in French, Belgian, and Greek hospitals in 2002\textsuperscript{17}

Note: Beta-lactamase sensitive penicillins include benzyl penicillin and phenoxymethylpenicillin; beta-lactamase resistant penicillins include flucloxacillin and dicloxacillin; extended spectrum penicillins include amoxicillin and ticarcillin; beta-lactamase inhibitor combinations include amoxicillin/clavulanate and ticarcillin/clavulanate.

A number of antimicrobial classes are regarded as “last-line” because there are few, if any, convenient alternative agents that can be used in the event of emergence of resistance to these classes. The ADHB hospitals have a relatively restrictive antimicrobial stewardship policy that is intended to constrain the consumption of fluoroquinolones (predominantly ciprofloxacin and norfloxacin), third and fourth generation cephalosporins (predominantly ceftriaxone and cefepime), carbapenems (predominantly meropenem and ertapenem), glycopeptides (predominantly vancomycin) and some other agents.

Figure 6 shows that the level of consumption of these agents by adult inpatients in ADHB hospitals is less than that in hospitals in Australia\textsuperscript{16} and generally comparable with that in hospitals in Sweden and Denmark.\textsuperscript{13,14}
The level of consumption of these “last-line” agents is of course determined, to some degree, by the prevalence of infection with organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA) and ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* that are resistant to most or all “first-line” antimicrobial agents.

Fortunately, the prevalence of infection with these multiresistant organisms is relatively low in inpatients in ADHB hospitals. For example, during 2009, 12% of blood culture isolates of *S. aureus* in ADHB hospitals were MRSA, 4.1% of *E. coli* and 16.4% of *K. pneumoniae* isolated from blood cultures were ESBL positive, and in recent years disease due to vancomycin resistant enterococci has been extremely rare.¹⁸

As the prevalence of infection with these multiresistant organisms rises we can expect that the level of consumption of these “last-line” antimicrobial agents will rise—hastening the emergence of pan-resistant organisms that are essentially untreatable.

**Figure 6. Antimicrobial consumption (DDD/100 inpatient days) for fluoroquinolones, third or fourth generation cephalosporins, carbapenems and glycopeptides by adult inpatients in ADHB hospitals during 2008 compared with consumption of agents within these antibiotic classes by adult inpatients in hospitals in Australia, Sweden and Denmark during 2008**¹³,¹⁴,¹⁶

*Note:* Data was not available on the level of consumption of third of fourth generation cephalosporins in Sweden during 2008.

We found that the total level of consumption of antimicrobials, and of restricted antimicrobial classes, was considerably higher in the DCCM, CVICU and the haematology ward than in the rest of the hospital (Figure 3).
The relatively high total levels of consumption in the DCCM (182 DDDs/100 inpatient days in 2009) and the CVICU (108 DDDs/100 inpatient days in 2009) were similar to those in 48 ICUs in Sweden in 2009 (median=135 DDDs/100 inpatient days, range=68-270)\(^{13}\) and 24 ICUs in Australia in 2009 (median=158 DDDs/100 inpatient days, range=118–222).\(^{16}\)

The total consumption of antimicrobials by inpatients in the haematology ward in 2009 (152 DDDs/100 inpatient days) was less than half that of the bone marrow transplant unit of the University Hospital in Zurich in 2006.\(^{19}\)

This audit has provided a comprehensive overview of the level of consumption of parenteral and oral antimicrobials by adult inpatients at Auckland City Hospital in recent years. To the best of our knowledge this is the first such audit of antimicrobial consumption in a New Zealand hospital.

To ensure comparability of our results with other reports we followed recently published guidelines on the measurement of the consumption of antimicrobials.\(^{19,20}\) Because the effective daily antimicrobial dose in paediatric patients may be very much less than the DDD, which is a consensus effective adult dose, and because there is a paucity of published data on inpatient consumption of antimicrobials by paediatric patients, we confined our analyses to antimicrobial consumption by adult inpatients.

Our results demonstrate that the current ADHB antimicrobial stewardship policy is, by and large, achieving its goal of constraining antimicrobial use in the expectation that this will slow the spread of antimicrobial resistance and prolong the utility of these essential medicines.\(^{21}\)

Other potential benefits of a prudent antimicrobial stewardship policy include reducing the incidence of adverse events, such as allergic reactions and *Clostridium difficile* colitis, that are a consequence of antimicrobial therapy, cost minimisation and limitation of environmental pollution by antimicrobials present in sewerage and wastewater discharged from the hospital.\(^{22}\) The audit has identified the potential for changes in the consumption of antimicrobial agents in the ADHB hospitals that might contribute to slowing the emergence of antimicrobial resistance in our community.

Such changes include reducing the use of broad spectrum antimicrobials (such as amoxicillin/clavulanate) and increasing the use of narrow spectrum antimicrobial agents (such as phenoxymethylpenicillin). We hope that our results help to encourage consistent, prudent use of antimicrobial agents by hospital-based clinicians at ADHB and throughout New Zealand.

**Competing interests:** None.

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Demographic variation in community-based MRSA skin and soft tissue infection in Auckland, New Zealand

Stephen R Ritchie, John D Fraser, Eric Libby, Arthur J Morris, Paul B Rainey, Mark G Thomas

Abstract

Aim To estimate the burden of skin and soft tissue infection caused by Staphylococcus aureus (S. aureus), and to determine the effects of ethnicity and age on the rate of skin and soft tissue due to MRSA in the Auckland community.

Materials and Methods We reviewed the culture and susceptibility results of all wound swabs processed by Auckland’s only community microbiology laboratory in 2007. Demographic data for a random sample of 1000 people who had a wound swab collected and for all people from whom a methicillin-resistant S. aureus (MRSA) strain was isolated were obtained and compared to demographic data for the total population of Auckland.

Results S. aureus was isolated from 23853/47047 (51%) wound swab cultures performed in 2007; the estimated annual incidence of S. aureus isolation from a wound swab was 1847/100,000 people; and the estimated annual incidence of MRSA isolation from a wound swab was 145/100,000 people. Māori and Pacific people had higher rates of non-multiresistant MRSA infection compared with New Zealand European and Asian people; elderly New Zealand European people had much higher rates of multiresistant MRSA infections compared with people from other ethnic groups.

Conclusion S. aureus is a very common cause of disease in the community and the incidence of infection with MRSA subtypes varies with ethnicity.

Staphylococcus aureus (S. aureus) is well known for its ability to cause serious, invasive disease. The very first edition of the New Zealand Medical Journal, in 1888, contains a case report of rapidly fulminant endocarditis with widespread embolism that is reminiscent of the S. aureus disease that is still encountered in our hospitals today.¹

The severe end of the spectrum of S. aureus disease in New Zealand has been reported.²–⁷ The other end of the spectrum, asymptomatic nasal carriage, has also been studied in New Zealand.⁸,⁹ The burden of less severe, but clinically overt, skin and soft tissue infection remains unknown.

Methicillin-resistant S. aureus (MRSA) infections were initially associated with acquisition within hospitals. However, rates of community-acquired MRSA infections have exploded in many parts of the world this decade; very large increases have occurred in Scandinavia.¹⁰,¹¹

The prevalence of MRSA in Auckland increased rapidly in the mid-1990s. The proportion of community-based isolates of S. aureus in Auckland that were MRSA
increased from 0.03% in 1988 to 5.9% in 1997, but the prevalence does not appear to have continued to rise as rapidly this decade.

In the late 1990s, the incidence of *S. aureus* bacteraemia was higher in Māori and Pacific people than in New Zealand (NZ) European people; Pacific people had an incidence that was four times higher than in NZ Europeans. The explanation for this is not known, but household crowding and social deprivation are likely to be important factors.

It is also possible that Pacific and Māori people are exposed to, and infected by strains of *S. aureus* that differ from those infecting NZ Europeans. This might seem an unlikely proposition until one considers that community-acquired infections caused by the Western Samoan phage pattern methicillin-resistant *S. aureus* (WSPP MRSA) are more common in Māori and Pacific people.

Between 1995 and early 1998 more than half of the cases of MRSA infection or colonisation at Middlemore Hospital, South Auckland were of Pacific ethnicity. While this was certainly a reflection of the hospital catchment, more than 90% of these MRSA infections were caused by WSPP MRSA. Higher rates of WSPP MRSA infections have also been reported among Pacific people living in Queensland, Hawaii and Alaska.

We aimed to estimate the burden of skin and soft tissue infection caused by *S. aureus* in the Auckland community. We further aimed to determine what proportion of this burden was caused by MRSA and whether MRSA-related skin and soft tissue infection was evenly distributed across all ethnic groups and ages. We reviewed the 2007 data from wound swab culture results at Auckland’s only community testing laboratory.

**Materials and Methods**

The culture results from all wound swabs processed by Diagnostic Medlab (DML) between 1 January and 31 December 2007 were reviewed. DML was the only community laboratory provider for the Auckland region in 2007. Superficial swabs from other sites (e.g. ear swabs) were not included in the survey; nor were swabs submitted for MRSA screening.

The identification of *S. aureus* and testing of isolates for susceptibility to β-lactam antibiotics, ciprofloxacin, erythromycin, cotrimoxazole, tetracycline, fusidic acid and mupirocin were performed according to CLSI methods and interpretive criteria. Non-multiresistant MRSA (nm-MRSA) were those isolates resistant to β-lactam antibiotics only; and multiresistant MRSA (mr-MRSA) were those resistant to β-lactam and one, or more, additional antibiotic(s).

We attempted to obtain demographic information (age, gender and ethnicity) for 1,000 patients randomly selected from the total dataset and for all patients from whom MRSA was isolated. Demographic data was only available for those patients whose National Health Index number (NHI) was available. Ethnicity data derived from the NHI has been utilised in a number of important publications regarding a range of topics, for example, mortality and cancer rates. The NHI might contain more than one ethnicity for each person, because people may self-report more than one ethnic group; thus, people were prioritised into five ethnic groups, in accordance with Ministry of Health categorisation.

These groups were Māori, NZ European, Pacific, Asian and “other”. We have assumed that the true ethnicities of people whose NHI numbers were not available (“unknown” ethnicity) reflect those of the total population of Auckland. Thus, we have not included results from people of “unknown” ethnicity in calculating the proportion of isolates of *S. aureus* and MRSA from each ethnic group.
The NZ European group contained people who identified as NZ European, European, and/or Pakeha. Only the first sample was included for those patients who had MRSA isolated from more than one swab.

Our central null hypothesis was that there would be no difference between ethnic groups in the proportion of wound infections from which *S. aureus*, MRSA, nm-MRSA and mr-MRSA were isolated. Data from 1000 randomly selected wound swabs were used to estimate the relative rates of collection of wound swabs and of isolation of *S. aureus* for each ethnic group.

Data from all of the wound swabs that cultured MRSA were used to estimate the relative rates of MRSA in each ethnic group. In order to estimate the incidence of MRSA infections in each ethnic group across different age groups we made the assumption that all people, irrespective of age and ethnicity, with skin and soft tissue infections were equally likely to seek medical help and have a wound swab performed.

Thus, the incidence of a positive culture of *S. aureus* was calculated from comparative demographic information for the total Auckland population obtained from the 2006 Census dataset, available from: (http://www.stats.govt.nz/Census/2006CensusHomePage.aspx). Age data were converted into incidence rates and expressed /100,000 people/year.

Ethical approval for this study was provided by the Northern Y ethics committee.

**Results**

**The incidence of *S. aureus* and MRSA skin and soft tissue infection in Auckland—** *S. aureus* was isolated from just over half (23853/47047; 51%) of the wound swab cultures performed in 2007; of which, 8% (1872/23853) were MRSA. Once duplicate swabs were excluded, specimens from 1794 people grew MRSA. If this rate of duplicate swabs (78/1872, 4%) was also found in those whose swabs grew *S. aureus* then approximately 22,900 Aucklanders suffered culture proven skin and soft tissue infection caused by *S. aureus* in 2007.

The overall incidence of isolation of *S. aureus* from a wound swab was 1847/100,000/year and the incidence of isolation of MRSA from a wound swab was approximately 145/100,000/year.

**S. aureus infection and ethnicity—** 855/1000 (85.5%) of the randomly selected wound swabs were obtained from people whose ethnicity was prioritised into one of four ethnic groups: Māori, Pacific, NZ European and Asian; in addition, 51 swabs were obtained from people of other ethnicities but the ethnicities of 94 people were not available.

The proportion of wound swabs that were obtained from Māori and NZ European people was not different to their proportion of the total population of Auckland, Table 1. The proportion of wound swabs obtained from Pacific people (239/906, 27%, 95%CI 24–29) was greater than expected, compared with the proportion of Pacific people in the total population of Auckland (14%, one sample t test, *p*<0.001).

The proportion of Asian people who had a wound swab performed (39/906, 4%, 95%CI 3-6) was lower than the proportion of Asian people in the total population (13%, one sample t test, *p*<0.001).

Table 1 also shows the proportion of wound swabs from which *S. aureus* was isolated for each ethnic group. The proportion of wound swabs that cultured *S. aureus* was highest in Pacific people (155/239, 65%, 95%CI 59–71) and lowest in Asian people (13/39, 33%, 95%CI 21–49; χ² test *p*<0.01).
Table 1. The proportion of wound swabs performed and the proportion of wound swabs that cultured *S. aureus* for each ethnic group derived from 1000 randomly selected wound swab cultures in 2007

<table>
<thead>
<tr>
<th>Variables</th>
<th>Māori</th>
<th>Pacific</th>
<th>NZ European</th>
<th>Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of the total population of Auckland¹</td>
<td>11%</td>
<td>14%</td>
<td>61%</td>
<td>13%</td>
</tr>
<tr>
<td>Proportion of 1000 randomly selected wound swabs (%, 95%CI)²</td>
<td>89 (10, 8–12)</td>
<td>239 (27, 24–29)</td>
<td>488 (54, 51–57)</td>
<td>39 (4, 3–6)³</td>
</tr>
<tr>
<td>Proportion of 1000 randomly selected wounds swabs from which <em>S. aureus</em> was isolated (%, 95%CI)⁴</td>
<td>50 (56, 46–66)</td>
<td>155 (65, 59–71)</td>
<td>230 (57, 43–52)</td>
<td>13 (33, 21–49)</td>
</tr>
</tbody>
</table>

¹ Census 2006 data
² 51 additional people belonged to other ethnic groups; the ethnicity of 94 people was not stated
³ one sample t-test versus proportion of the total population, *p*<0.01
⁴ observed versus expected; $\chi^2$ test *p*<0.01

**MRSA subtype and age**—The cumulative distribution of the ages of people from whom nm-MRSA was isolated differed from the cumulative distribution of the ages of people from whom mr-MRSA was isolated (Kolmogorov–Smirnov test, *p*=0.04), Figure 1. The rate of infection of mr-MRSA was constant until the age of 80 when the rate increased. In contrast, the rate of infection of nm-MRSA was higher in the first three decades of life and decreased with age (illustrated by the decreasingly positive slope in Figure 1).

**Figure 1. The cumulative distribution of nm-MRSA and mr-MRSA by age**
The difference in MRSA subtype by ethnic group—The proportion of isolates of MRSA that were obtained from wound swabs from patients of Pacific ethnicity (460/1153, 40%, 95%CI 37–43), Table 2, was significantly higher than the proportion of the total Auckland population that were of Pacific ethnicity (14%, one sample t test $p<0.001$).

The high proportion of MRSA isolates that came from patients of Pacific ethnicity is in part due to the higher rate of collection of wound swabs from Pacific people, Table 1. However, this does not appear to be the complete explanation as 40% of MRSA isolates came from Pacific people but only 27% (239/906, 95%CI 24–29) of wound swabs were collected from Pacific people.

The high rate of isolation of MRSA from Pacific people was largely due to an increase in nm-MRSA isolates; Pacific people were less likely to be infected with mr-MRSA. Māori people followed the same trend, except the proportion of wound swabs that were collected from Māori was not more than expected.

The proportion of isolates of MRSA that were cultured from NZ European people (411/1153, 36%, 95%CI 33–39) was less than the proportion of swabs collected from NZ European people (488/906, 54%, 95%CI 51–57) and this result remained significant after the swabs from Pacific people were removed from analysis ($\chi^2$ test, $p<0.001$). mr-MRSA was more likely to be isolated from NZ European people than expected; and they were less likely to be infected with nm-MRSA.

Asian people had low rates of MRSA and were less likely to have a wound swab cultured performed than expected [one sample t-test, $p<0.01$].

Table 2. The number of MRSA, nm-MRSA and mr-MRSA isolates by ethnic group

<table>
<thead>
<tr>
<th>Variables</th>
<th>Māori</th>
<th>Pacific</th>
<th>NZ European</th>
<th>Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of total Auckland population</td>
<td>11%</td>
<td>14%</td>
<td>61%</td>
<td>13%</td>
</tr>
<tr>
<td>Number of MRSA isolates (n=1153)$^1$</td>
<td>182 (16, 14–18)</td>
<td>460 (40, 37–43)$^4$</td>
<td>411 (36, 33–39)</td>
<td>18 (2, 1–3)</td>
</tr>
<tr>
<td>Number of nm-MRSA isolates (n=904)</td>
<td>173 (19, 17–24)</td>
<td>424 (47, 44–50)$^4$</td>
<td>220 (24, 22–27)</td>
<td>18 (2, 1–3)</td>
</tr>
<tr>
<td>Number of mr-MRSA isolates (n=249)</td>
<td>9 (4, 2–7)</td>
<td>36 (14, 11–19)</td>
<td>191 (77, 71–82)$^7$</td>
<td>0 (0, 0–2)</td>
</tr>
</tbody>
</table>

$^1$ 82 MRSA isolates were obtained from people of “other” ethnicity; 641 MRSA isolates were from people whose ethnicity was not available

$^2$ Proportion of MRSA isolates greater than expected from the proportion who had a wound swab performed, $\chi^2$ test, $p<0.001$

The highest incidence of culture of either subtype of MRSA from wound swabs was 627/100000 observed in mr-MRSA in NZ European over the age of 80 years. At ages less than 70 years mr-MRSA infections were rare and were not different between NZ
European, Māori and Pacific people (Figure 2A). In contrast, infection of nm-MRSA was more common in Māori and Pacific people than NZ European people until old age (Figure 2B).

Figure 2. The annual incidence/100,000 people of (A) culture of mr-MRSA from a wound swab and (B) culture of nm-MRSA from a wound swab for Māori, Pacific and NZ European people by age.
Resistance to other antimicrobials amongst mr-MRSA—Over half of the MRSA isolates (979/1794, 55%) were nm-MRSA. Of the 815 mr-MRSA, resistance to erythromycin was encountered most often, Table 3.

Table 3. Resistance to six antimicrobials in 815 MRSA isolated from wound swabs in Auckland in 2007

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>ERY (Total)</th>
<th>CIP</th>
<th>TET</th>
<th>COT</th>
<th>FUS</th>
<th>MUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (%)</td>
<td>419 (51)</td>
<td>330 (41)</td>
<td>65 (8)</td>
<td>20 (2)</td>
<td>325 (40)</td>
<td>179 (22)</td>
</tr>
</tbody>
</table>

ERY=erythromycin, CIP=ciprofloxacin, TET=tetracycline, COT=cotrimoxazole, FUS=fusidic acid, MUP=mupirocin.

Discussion

Our analysis of raw laboratory data indicates that *S. aureus* causes a huge burden of skin and soft tissue disease in NZ. Approximately two percent of Auckland’s population had *S. aureus* isolated from a wound swab during 2007. Not all of these infections required treatment, but this number probably underestimates the true burden of disease.

Some people with skin and soft tissue infections caused by *S. aureus* would not have seen a healthcare practitioner; many who did would not have had a swab performed; some would have attended a hospital emergency department and had cultures performed in hospital laboratories; and some swabs may have failed to grow *S. aureus* due to inadequate sampling or concomitant antibiotic treatment.

The number of wound swab cultures performed is conditional on the true incidence of disease and on societal factors such as access to healthcare. Our estimate of the incidence of *S. aureus* skin and soft tissue infection was reliant on the assumption that all members of society with a skin and soft tissue infection were equally likely to seek medical help and have a wound swab performed. However, this was not the case; we found a large discrepancy in the proportion of wound swab cultures performed in people of different ethnic groups.

Compared to their proportion of the Auckland population, Pacific people were more likely to have a wound swab performed, and Asian people were less likely to have a wound swab performed.

It is important to take the rates of performing a wound swab into account when interpreting the microbiology laboratory data. If rates of performing wound swab cultures were high among Pacific people for reasons other than an increased incidence of skin and soft tissue infection, then the incidence of *S. aureus* and MRSA infection that we have estimated might be artificially elevated.

Even after taking this into consideration, there were important differences in nm-MRSA or mr-MRSA rates in different ethnic groups. Māori and Pacific people had higher rates of nm-MRSA than NZ European people across almost all age groups; yet NZ European had higher rates of mr-MRSA in old age.
The very low proportion of Asian people that had wound swabs performed goes some way towards explaining their very low prevalence of MRSA infection. The current study was not able to explore the reasons for this, but it is possible that Asian people in Auckland have reduced access to healthcare, or seek alternative healthcare when unwell. It is also possible that Asian people living in Auckland are less likely to develop skin and soft tissue infections, or have lower rates of *S. aureus* carriage, a state known to predispose to *S. aureus* infection.

Likewise, we can only speculate about the reasons why Pacific people had a higher number of wound swabs performed than expected; although, this finding does suggest adequate access to healthcare. Higher rates of infection with nm-MRSA were evident from a young age; this raises the possibility that the incidence of skin and soft tissue infections, such as impetigo, is not equal among the four ethnic groups.²²

It could also represent good practice among healthcare practitioners, who might be aware of previous reports regarding ethnic variation in the prevalence of MRSA infection.¹²,¹⁴ Healthcare practitioners might be more likely to obtain a wound swab for antimicrobial susceptibility testing from Pacific people compared with people of other ethnicities.

We used an unconventional definition of nm-MRSA (resistant to β-lactam antibiotics only) to correlate antimicrobial susceptibility with strain designation; in particular to identify WSPP MRSA strains. WSPP MRSA strains are typically susceptible to all non-β-lactams and are the dominant MRSA strain in the community in NZ; in 2008, over three-quarters of the WSPP MRSA isolates came from community laboratories.²³

Thus, our results suggest that Māori and Pacific people are more likely to be infected with WSPP MRSA than NZ European and Asian people living in Auckland. The AK3 MRSA strain is also common in the Auckland community, and a proportion of these have lost their typical resistance to mupirocin. Some AK3 MRSA strains would have been classified nm-MRSA by the definition that we chose.

The association between nm-MRSA and younger age in Pacific people is likely to reflect acquisition in the community. The association between advancing age and mr-MRSA in elderly NZ European is likely to reflect healthcare acquisition, particularly in long-term residential care facilities.²⁴

No research to date has explored the reason why Māori and Pacific people might be infected with different strains of MRSA compared to other ethnic groups. This finding demands further investigation, particularly when the higher incidence of bloodstream infection found in Māori and Pacific people compared to other ethnic groups is taken into account.⁶

Some of the increased burden of diseases caused by *S. aureus* reported in Pacific people could be attributed to exposure to different strains of *S. aureus*.⁶, ⁷, ²², ²⁵ Infection with a particular strain of *S. aureus* might even be related to acquisition in other Pacific countries rather than acquisition in Auckland.

The current study has raised several questions that warrant further research. The high burden and severity of disease caused by *S. aureus* make this a high priority. Of major concern is the finding that Māori and Pacific people are more likely to develop community-acquired infection with nm-MRSA and at a young age. It is fortunate that,
for now, these strains of MRSA remain susceptible to all other commonly used anti-
staphylococcal antibiotics.

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**Acknowledgement:** Stephen Ritchie is a Clinical Training Fellow of the Health Research Council of New Zealand whom we thank.

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**References:**

Nasal carriage of *Staphylococcus aureus* in healthy Aucklanders

Nicola Best, John D Fraser, Paul B Rainey, Sally A Roberts, Mark G Thomas, Stephen R Ritchie

**Abstract**

**Background** Studies have reported higher rates of diseases caused by *Staphylococcus aureus* (*S. aureus*) amongst Māori and Pacific people, compared with people of other ethnicities.

**Aim** We aimed to estimate the prevalence of nasal carriage and to explore demographic differences between *S. aureus* carriers and non-carriers in Auckland, New Zealand.

**Materials and Methods** Nasal swab specimens were obtained from healthy population volunteers, who did not have recent healthcare contact. Each participant completed a short questionnaire.

**Results** 78/424 (18%; 95% CI, 15–22) *S. aureus* carriers were identified. Female participants were less likely to be *S. aureus* carriers than males; but there were no differences in the ages or ethnic groups between *S. aureus* carriers and non-carriers. Socioeconomic deprivation, recent non-hospital healthcare contact and past history of *S. aureus* infection were not associated with *S. aureus* carriage.

**Conclusion** Ethnic variation in the prevalence of *S. aureus* nasal carriage does not contribute to an increased risk of disease caused by *S. aureus*.

*Staphylococcus aureus* (*S. aureus*) causes many serious infections in New Zealand every year. *S. aureus* is a common cause of skin and soft tissue infection, bone and joint infection, endocarditis and healthcare associated infection. *S. aureus* colonisation can be defined as the presence of *S. aureus* at any of a number of anatomical sites in healthy and asymptomatic people.

The rates of colonisation vary with study methodology and the population under study; but the prevalence of nasal colonisation is generally between 20% and 37% of the healthy population. Most studies of *S. aureus* carriage have involved nasal carriers; and the anterior nares are the site most frequently colonised by *S. aureus*. Asymptomatic nasal colonisation (*S. aureus* carriage) is a risk factor for the development of *S. aureus* disease. Nosocomial *S. aureus* bacteraemia is more common in carriers, and there is evidence that treatment to resolve colonisation can reduce the incidence of subsequent surgical wound infection. Thus, a simple model of infection with *S. aureus* is one of exposure via direct or indirect contact followed by a period of asymptomatic colonisation prior to tissue invasion or contamination of damaged tissue and/or a medical device leading to the development of disease.

In New Zealand the incidence of *S. aureus* bacteraemia is higher in Māori and Pacific people, compared with people of other ethnicities. Ethnic variation in *S. aureus*...
 carriage has not been studied in New Zealand; but variation in either the overall prevalence of colonisation, or the prevalence of colonisation by particular strains of *S. aureus*, could contribute to the ethnic variation in the incidence of invasive disease in New Zealand.

In Queensland, Australia, Aboriginal people had lower rates of *S. aureus* colonisation than European people; and the prevalence of *S. aureus* carriage was lower in people from a socially deprived area of Queensland compared to the prevalence in people living in an affluent area. In a study of *S. aureus* carriage performed on a large national sample of over 9000 non-institutionalised individuals in USA, African Americans were less likely than Hispanic or white Americans to be carriers of *S. aureus*, and deprivation was not associated with carriage of *S. aureus*.

We performed the current study of nasal carriage of *S. aureus* in healthy population volunteers to investigate the prevalence of *S. aureus* carriage and to explore demographic differences between *S. aureus* carriers and non-carriers in New Zealand.

In this study we aimed to investigate whether ethnic variation in the prevalence of *S. aureus* bacteraemia is associated with higher rates of nasal carriage.

**Materials and Methods**

Ethical approval was provided by the Northern Y ethics committee of the New Zealand Ministry of Health.

Participants were recruited in public places in Central and South Auckland. Participants who had hospital contact in the previous three months, which might have influenced the prevalence of carriage, were excluded from the study. Recruitment took place between May 2008 and December 2008. After informed consent was obtained, a nasal swab was performed. One swab was inserted into both nostrils, being careful to sample the mucosa on the nasal septum adjacent to the nasal ostium, the preferred habitat of *S. aureus*. Participants completed a brief questionnaire about demographic factors, home address, household size, access to healthcare, and prior *S. aureus* infection.

Nasal swab specimens were transported at ambient temperature in sterile Amie’s media (Fort Richard, Otahuhu, Auckland, NZ) and were swabbed onto mannitol salt agar (MSA, Fort Richard) within 4 hours of collection. Following overnight incubation at 37°C presumptive *S. aureus* colonies were identified using the Staphyloslide™ Latex test kit (BD, Sparks, Maryland, USA). MSA plates that did not display growth of *S. aureus* were incubated for a further 24 hours. The identity of positive isolates was confirmed by the production of coagulase and staphylococcal DNase. Antimicrobial susceptibility was tested using a combination of agar breakpoint dilution (oxacillin, erythromycin, cotrimoxazole, doxycycline and gentamicin) and disc diffusion methods (penicillin) according to Clinical and Laboratory Standards Institute performance and interpretive criteria.

Information from the study population was compared with population data from the 2006 Census. Ethnicity was self-reported by participants who selected their ethnic group(s) from a list; the same list used in the 2006 New Zealand Census. Ethnicity was prioritised using the method advised by the Ministry of Health. To allow comparison with 2006 Census data, the ethnicity data collected was grouped according to level 1 classification. The NZ European ethnic group also contained people who identified as European and/or Pakeha.

The NZ index of deprivation (NZDep2006), an ordinal score of 1 to 10 derived for small residential blocks using data obtained from the 2006 Census, was used to estimate the deprivation score of the neighbourhood of each participant. The home address of each participant was used to determine their residential block and the NZDep2006 score for each residential block was obtained from published values. A bedroom occupancy rate was calculated from the ratio of the number of household occupants, resident on at least three nights per week, to the number of bedrooms.

Statistical analysis was performed using SPSS v16.0 software (Chicago, USA). 95% confidence intervals were calculated using the modified Wald method. Fisher’s exact test was used to test the
Results

424 subjects participated in the study, their median age was 22 (interquartile range 19–32) and 255/426 (60%) were female. When compared to the total population, people between the ages of 15 and 34 years were over represented in the sample, and there were no young children included in the study (Figure 1).

Figure 1. The age distribution of the 424 study participants in relation to that of the total population and the proportion of participants who were *S. aureus* carriers in each age group

The ethnicity of the 424 participants is shown in Table 1. Māori, Pacific and NZ European people were under-represented in the sample when compared to their proportions in the total population of Auckland; Asian people were over-represented (one sample T test *p*<0.01).
Table 1. The proportion of *S. aureus* carriers by ethnicity in 424 participants; and the proportion of each ethnic group in the total population of Auckland

<table>
<thead>
<tr>
<th>Ethnic group</th>
<th>Number (% , 95%CI)</th>
<th>Proportion of the total population¹</th>
<th><em>S. aureus</em> carriage (% , 95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Māori</td>
<td>29 (7%, 5–10)</td>
<td>11%</td>
<td>6 (21%, 10–39)</td>
</tr>
<tr>
<td>Pacific</td>
<td>44 (10%, 8–14)</td>
<td>14%</td>
<td>8 (18%, 9–32)</td>
</tr>
<tr>
<td>NZ European</td>
<td>159 (38%, 33–42)</td>
<td>61%</td>
<td>33 (21%, 15–28)</td>
</tr>
<tr>
<td>Asian</td>
<td>146 (34%, 30–39)</td>
<td>13%</td>
<td>26 (18%, 12–25)</td>
</tr>
<tr>
<td>Other²</td>
<td>46 (11%, 8–14)</td>
<td>1%</td>
<td>5 (11%, 4–24)</td>
</tr>
</tbody>
</table>

¹ The proportion of each ethnic group in the sample differed from their proportion in the total population, one sample T test, *p*<0.01.
² African (22/424, 5%); Middle Eastern (14/424, 3%); North American (8/424, 2%); and South American (2/424, <1%).

78/424 (18%; 95%CI, 15–22) *S. aureus* carriers were identified. The median age of *S. aureus* carriers (22 years, interquartile range 19–33) was not different from the median age of non-carriers (22 years, interquartile range 19–32). There were no significant differences in the rates of *S. aureus* carriage between different age groups. 35/78 (45%, 34–56) of *S. aureus* carriers were female, less than the proportion of females in the study population (258/424, 61%, 56–65, Fisher’s exact test, *p*=0.002).

There was no significant difference in the prevalence of *S. aureus* carriage between ethnic groups. Only 1/78 (1%) of the *S. aureus* isolates was methicillin-resistant (MRSA). This strain was isolated from a 32-year-old Indian male, who had lived in New Zealand for 7 years, and who did not report any healthcare contact.

The proportion of *S. aureus* carriers who held a current community services card (25/78, 32%, 23–43) was not different to the proportion of non-carriers (124/346, 36%, 31–41). Likewise, the proportion of participants who held private health insurance was not different between *S. aureus* carriers (29/78, 37%, 27–48) and non-carriers (134/346, 39%, 34–44); neither was the proportion of participants who were registered with a general practice (*S. aureus* carriers, 60/78, 77%, 66–85; non-carriers, 251/346, 73%, 68–77).

396/424 (93%) participants provided their home address, and the NZDep2006 scores of their neighbourhoods were able to be determined. The median NZDep2006 score of the *S. aureus* carriers (5, interquartile range 3–8) was lower than the non-carriers (6, interquartile range 3–8, Wilcoxon signed ranks test, *Z*=−7.154, *p*<0.01). This difference did not persist when the NZDep2006 scores were placed into three groups from least deprived (NZDep2006 score 1–3) to the most deprived (NZDep2006 score 7–10) (Figure 2). The mean bedroom occupancy rate did not differ between *S. aureus* carriers (1.14, SD 0.41) and non-carriers (1.15, SD 0.39).
Recent healthcare contact was not associated with an increased risk of *S. aureus* carriage. There was no significant difference in the proportion of *S. aureus* carriers who had been admitted to hospital in the previous 12 months (3/78, 4%, 1–11) compared to non-carriers (33/346, 10%, 7–13); and there was no significant difference in the proportion of people who reported a prior infection caused by *S. aureus* (*S. aureus* carriers, 3/78, 4%, 1–11; non-carriers 11/346, 3%, 2–6). 12/78 (15%, 19–25) *S. aureus* carriers had seen their general practitioner in the previous month compared with 92/346 (27%, 22–32) non-carriers (Fisher’s exact test, *p*=0.04).

**Discussion**

No previous studies of *S. aureus* carriage in the healthy population in New Zealand have been reported. Based on the results of the current study, over 230,000 healthy population members in Auckland are currently carriers of *S. aureus*. The prevalence of *S. aureus* carriage in Auckland, 18%, was at the lower end of the range of prevalence rates found in other populations.3 A large study conducted in the USA in 2006, found the prevalence of nasal carriage to be 32%;13 in Queensland in 2005/2006 the prevalence was 28%.11 The lower rate found in the current study was not likely to be a result of the nasal swab sampling strategy. The recovery of *S. aureus* from nasal swab specimens used the same microbiological method of similar studies;13,19 and a medical practitioner performed
all of the nasal swabs. It is also unlikely that the sampling strategy provided estimates of the prevalence of *S. aureus* carriage that were not representative of the total population.

The prevalence of *S. aureus* carriage did not differ between different age groups in the current study. The highest prevalence of *S. aureus* carriage occurs in the first few months of life but then declines over 6–12 months to rates that are similar to the adult population.\(^\text{19,20}\) Despite an increase in the incidence of disease caused by *S. aureus* in old age, *S. aureus* carriage is less common in adults over the age of 60.\(^\text{13}\) Thus, the age distribution of the sample in the current study is likely to provide a reliable estimate of the prevalence of *S. aureus* carriage in the population.

In the current study, females were less likely to be colonised with *S. aureus* than males. This finding is consistent with other international studies;\(^\text{11,13}\) even in the first year of life, males are more likely to be *S. aureus* carriers than females.\(^\text{20}\) The reason for the difference in colonisation between males and females is not known, but this difference might contribute to the lower incidence of *S. aureus* bacteraemia reported in females.\(^\text{21-23}\)

Social deprivation does not appear to play an important part in the development of *S. aureus* carriage in Auckland. We did not find any relationship between *S. aureus* carriage and holding a Community Services card, having private health insurance or the bedroom occupancy rate. When the home addresses of the participants were used to estimate the NZDep2006 scores of each participant’s neighbourhood, the level of deprivation was similar for *S. aureus* carriers and non-carriers. This finding was consistent with a previous study in Queensland, which found lower rates of *S. aureus* colonisation in people living in socially deprived areas compared to affluent areas.\(^\text{11}\)

In India, indicators of deprivation such as family income, household crowding and residence in a slum were not different between *S. aureus* carriers and non-carriers.\(^\text{24}\) In a large cohort of Dutch infants, maternal education level, maternal smoking, and breastfeeding did not influence the development of nasal carriage in the first year of life.\(^\text{20}\)

Only one carrier of MRSA (1/424, 0.2%) was identified in the current study, which was lower than expected from the prevalence of clinically significant MRSA infections. Contemporary studies have also found low rates of MRSA colonisation; in Queensland in 2005, the prevalence of MRSA colonisation was 0.7%;\(^\text{11}\) in the USA between 2000 and 2002, the prevalence of MRSA carriage was 0.8%.\(^\text{13}\) It is likely that the rate of MRSA carriage is increasing in parallel with community-acquired MRSA infections, yet the disparity between the prevalence of MRSA carriage and the frequency of MRSA isolation from clinical specimens suggests that diseases caused by *S. aureus* may not be a simple reflection of the prevalence of *S. aureus* carriage. It is also possible that MRSA strains are more virulent and more likely to progress from carriage to disease.

The current study has several strengths and weaknesses. A large number of people with diverse demographic characteristics were included in the sample, and the sample consisted entirely of healthy population members. As a result, the study population demographics were not well matched with the total population of Auckland. For example, no young children and very few people over the age of 65 years were
included in the study. Most of the study participants were young adults between the ages of 15 and 34.

The other major difference between the study sample and the total population of Auckland relate to the ethnicity of the participants. New Zealand European people were significantly under-represented and Asian people were over-represented. It is possible that the low proportion of NZ European people in the sample contributed to lower rates of \textit{S. aureus} carriage than expected.

In Queensland, the prevalence of \textit{S. aureus} carriage was highest in Europeans (32%) and lowest in Aboriginal people (18%).\textsuperscript{11} It is unlikely that the high proportion of Asian people in the sample contributed to the low prevalence; studies from India (52%) and China (33% and 18%) have found prevalence rates of \textit{S. aureus} carriage similar to, or higher than, the prevalence in the current study.\textsuperscript{24–26}

The current study does not provide an explanation for the ethnic variation in invasive \textit{S. aureus} disease in New Zealand. The simple model of \textit{S. aureus} disease arising from the huge number of people who are colonised with \textit{S. aureus} is not consistent with the absence of differences between \textit{S. aureus} carriers and non-carriers identified in this study.

Furthermore, the prevalence of MRSA carriage is lower than the rate predicted from the prevalence of MRSA skin and soft tissue infection in Auckland. Improved understanding of the differences between the \textit{S. aureus} strains that cause nasal carriage and those that cause disease is crucial to determining how an organism that predominantly causes asymptomatic colonisation causes serious illness.

\textbf{Competing interests:} None.

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\textbf{Acknowledgements:} Stephen Ritchie is a Clinical Training Fellow of the Health Research Council of New Zealand. We also thank Ron King, Auckland Regional Public Health Service for assistance with geocoding participants’ addresses.

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\textbf{References:}

\begin{enumerate}
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Impact of universal hepatitis B vaccination on antenatal hepatitis B prevalence in the Midlands region of the North Island, New Zealand

Michael Addidle

Abstract

Aim Universal hepatitis B vaccination has now been in place in New Zealand for 22 years. A retrospective laboratory data study has been carried out to give objective evidence of the impact that this is having on hepatitis B prevalence in the antenatal population.

Method A retrospective data search was performed of all antenatal hepatitis B surface antigen (HepBsAg) tests carried out at Pathlab Laboratories between 1997 and 2009.

Results When the change in prevalence with time is examined, there is a clear downwards trend in antenatal hepatitis B prevalence rates from 1997 to 2009. Dividing the antenatal population into different age groups, the downward trend is most marked for those aged ≤20 years.

Conclusions The prevalence of hepatitis B infection in the antenatal population in the Midlands region of New Zealand is now declining and is likely to be as a result of the introduction of the hepatitis B vaccine onto the universal schedule throughout New Zealand in 1988. This would also explain why the decrease is most marked in antenatal women below the age of 20.

Universal hepatitis B vaccination was introduced in New Zealand in 1988 along with a catch-up programme for preschool children\(^1\). It is hypothesised that this universal vaccination programme will be starting to impact on the hepatitis B prevalence in antenatal women, particularly amongst the younger age groups presenting for antenatal testing.

New Zealand has historically one of the higher rates of hepatitis B prevalence in the developed world, particularly in certain ethnic groupings such as those of Māori and Pacific Island origin.\(^2,3\) Apart from a small study carried out in 1984\(^4\), there is a paucity of published data looking specifically at hepatitis B prevalence in the New Zealand antenatal population. This retrospective study addresses this issue and also assesses the impact that universal hepatitis B vaccination is beginning to have on antenatal prevalence.

As is the case with HIV, prevalence studies for Hepatitis B infection using the antenatal population is useful in providing a sample cohort of the population that is not subject to potential sources of bias that may be seen in other studies.

Method

A retrospective data search was performed of all antenatal Hepatitis B surface antigen (HepBsAg) tests carried out at Pathlab Laboratories between 1997 and 2009. The data covered the Bay of Plenty.
Eastern Bay of Plenty, the Waikato region and Rotorua. Note that for the Waikato region, due to laboratory contracts, only a third of the total potential antenatal data was available until 2008. However as percentage prevalence rates were being calculated, it is not believed that this unduly impacted upon or biased the results. Hepatitis B prevalence rates were then calculated on a year by year basis.

For the purposes of calculating prevalence, the numerator was defined as the number of positive HepBsAg results obtained from requests coded as “antenatal booking visit”. The denominator was the total number of HepBsAg requests from antenatal booking bloods. Duplicate results were excluded. The data was then subdivided into age groups (<21yrs, 21–25 yrs, 26–30 yrs, 31–35 yrs, >35yrs) to specifically examine the differential impact of universal vaccination on these age groups.

Results

Between 1997 and 2009 inclusive, 103,294 antenatal HepBsAg tests were performed, with 1491 positive results. This gives an overall prevalence rate of 1.81%.

When the change in prevalence with time is examined, there is a clear downwards trend in antenatal hepatitis B prevalence from 1997 to 2009 (see Figure 1). The total antenatal hepatitis B prevalence for 2009 was 0.95%.

Figure 1. Overall antenatal hepatitis B prevalence in the Midlands region of New Zealand

Dividing the antenatal population into different age groups, the downward trend is most marked for those aged ≤20 years. However a decrease is seen across all age groupings in the antenatal population (see Figure 2). Note that in 2009, only 4/2473 (0.16%) of antenatal requests in the age group aged 20 or under were positive for HepBsAg.
Discussion

The prevalence of Hepatitis B infection in the antenatal population in the Midlands area of New Zealand is now declining. This is highly likely to be the case throughout the rest of New Zealand, although further study would be required to confirm this.

The decrease is most likely to be as a result of the introduction of the Hepatitis B vaccine onto the universal schedule throughout New Zealand in 1988. This would also explain why the decrease is most marked in antenatal women below the age of 20, of whom the vast majority should have received the Hepatitis B vaccine through the universal schedule. Hepatitis B vaccine at birth along with Hepatitis B immunoglobulin for babies of Hepatitis B surface antigen positive mothers may also have contributed to the decrease.

Note that the decrease occurs across all age groups. Even allowing for the catch up programme in 1988 for preschool children, all antenatal mothers presenting in 2009 aged 26 or over would not have received Hepatitis B vaccination routinely as part of the universal schedule. This indicates that a degree of herd immunity is also playing a role in decreasing prevalence.

The results provide objective evidence that the universal Hepatitis B vaccination campaign in New Zealand is having a significant impact. The study will also allow epidemiologists to model Hepatitis B prevalence rates within New Zealand in future decades. The results found in this study are consistent with other studies.
internationally, which have looked at prevalence rates in age groups who should have received universal vaccination.

Further evidence of the impact of vaccination is demonstrated in the National Sero-survey of Vaccine Preventable Diseases in 2009. Between 2005–2007, 1 out of 466 patients between 6–10 years and 0 out of 587 patients between 11–15 years were positive for HepBsAg (note these were patients having serum taken for numerous other diagnostic reasons). All of these patients would have been eligible for Hepatitis B vaccination under the universal schedule.

Currently only acute hepatitis B infection is notifiable to the Public Health authorities in New Zealand. There is a strong argument for compulsory Public Health notification of all positive Hepatitis B surface antigen results in antenatal women, whether they represent acute infection or the more likely scenario, chronic infection. Such a policy would clearly facilitate efforts to reduce vertical transmission in this cohort.

Despite universal vaccination there is still a small percentage of the younger antenatal population who remain Hepatitis B surface antigen positive with the consequent risk of ongoing transmission, both horizontal and vertical. There are various possible explanations for the existence of this population. These include failure to receive the vaccine in childhood, acquisition of hepatitis B before vaccination given and vaccine non-response. Further study of this population and the epidemiology of their Hepatitis B acquisition is important in the ultimate goal of eradicating Hepatitis B infection within New Zealand.

One limitation of this study is that it does not look at the impact of vaccination on different ethnicities. Our laboratories do not collect ethnicity data routinely. Although the presentation of some data by ethnicity may potentially have been achievable through the national NHI database this would have been difficult to perform retrospectively for over 100,000 samples. However this may offer the potential for a further study.

Competing interests: None.

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References:


Molecular epidemiology and susceptibility profiles of *Clostridium difficile* in New Zealand, 2009

Sally Roberts, Helen Heffernan, Nadia Al Anbuky, Christopher Pope, Susan Paviour, Tracey Camp, Terri Swager

**Abstract**

**Aim** The aim of this study was to provide baseline information on the molecular epidemiology and the antimicrobial susceptibility of *Clostridium difficile* (*C. difficile*) clinical isolates from patients throughout New Zealand.

**Methods** Faecal specimens that were *C. difficile*-toxin positive by EIA assay were cultured for *C. difficile*. Antimicrobial susceptibility testing was carried out using the agar dilution minimum inhibitory concentration method. The following antibiotics were tested: penicillin, piperacillin/tazobactam, vancomycin, ciprofloxacin, moxifloxacin, clindamycin, clarithromycin, meropenem and metronidazole. Molecular typing by PCR-ribotyping was performed on all isolates.

**Results** *C. difficile* was isolated from 108 of 159 submitted faecal specimens. After excluding the repeats, there were 101 isolates from 97 patients. Most isolates were fully susceptible to the range of antibiotics tested. Thirty-two PCR-ribotypes were identified among the 101 isolates. The most common ribotypes were 014 (18 isolates), 002 (11) and 005 (10). No PCR-ribotype 027 isolates were identified, but one isolate of another hypervirulent strain, PCR-ribotype 078, was identified.

**Conclusion** There is a wide range of *C. difficile* PCR-ribotypes circulating in New Zealand and antimicrobial resistance is uncommon. Ongoing surveillance for hypervirulent strains of *C. difficile* is essential to prevent the dissemination of these strains within New Zealand hospitals.

*Clostridium difficile* (*C. difficile*) is the most common cause of diarrhoea in hospitalised patients. Up to 20% of hospitalised patients are colonised with *C. difficile*, but only the minority experience symptomatic disease. Almost all antibiotics can cause *C. difficile*-associated diarrhoea (CDAD). Contaminated environmental surfaces, other patients with CDAD and healthcare workers’ hands all contribute to the spread of *C. difficile* in healthcare settings.

The incidence and severity of CDAD have increased since 2003 in North America and parts of Europe. These increases have in part been due to the emergence of an epidemic, hypervirulent strain: PCR-ribotype 027 or NAP1 (North American pulsotype 1). This strain produces high levels of toxins A and B due to partial deletions in the *tcdC* regulator gene. The *tcdC* gene is a putative down-regulator of toxin A and B production. The strain also produces a binary toxin, for which the role in the pathogenesis of CDAD is unclear. The third important feature of the strain is its resistance to fluoroquinolones.
Little is known about the *C. difficile* strains that are currently circulating in New Zealand or whether the hypervirulent strain, PCR-ribotype 027/NAP1, occurs in this country. There have been two recent reports of patients infected with *C. difficile* PCR-ribotype 027 in Australia.7,8 We undertook this study to provide baseline information on the molecular epidemiology and the antimicrobial susceptibility of *C. difficile* clinical isolates from patients throughout New Zealand.

**Methods**

Eight laboratories from five regions participated in the survey. These laboratories were asked to refer consecutive nonduplicate faecal specimens that were *C. difficile*-toxin positive by EIA assay to the Anaerobe Section of the Department of Microbiology, LabPlus weekly. Limited, non-identifiable demographic data was collected on the patients: gender, age and geographic location.

The faecal specimens were stored at 4°C until processed. The specimens were cultured onto CCF agar [cycloserine, cefoxitin, fructose agar (Fort Richard, Auckland New Zealand)] and incubated anaerobically for 48–72 hours. Isolates were identified by their colonial appearance, ability to fluoresce chartreuse under UV light and typical biochemical profile using the Rapid ID 32A kit (bioMérieux, Marcy-L’Etoile, France).

Susceptibility testing was carried out using the agar dilution minimum inhibitory concentration (MIC) method.9 Antibiotics were incorporated into Brucella agar supplemented with 5 µg/mL haemin, 1 µg/mL vitamin K1 and 5% (v/v) laked sheep blood. An inoculum with turbidity equal to a 0.5 McFarland standard was used. Plates were incubated anaerobically at 35°C for 48 hours. The following antibiotics were tested: penicillin, piperacillin/tazobactam, vancomycin, ciprofloxacin, moxifloxacin, clindamycin, clarithromycin, meropenem and metronidazole. MIC50 and MIC90 values are reported. Where available, CLSI interpretive criteria were applied.

Isolates were then sent to the Nosocomial Infections Laboratory, ESR, for PCR-ribotyping, which was performed according to the method used by the Anaerobe Reference Unit, National Public Health Service, Cardiff, Wales.10 Reference strains of PCR-ribotypes 001, 017, 027 and 106 were included. Images of the ribotyping profiles that did not match any of the reference strains were submitted to the Cardiff Laboratory for identification of the ribotype. Where a definitive identification could not be made from the images, representative isolates were sent to the Cardiff laboratory for ribotyping.

PCR for the A, B and binary toxin genes was performed as previously described.11 Truncating mutations and deletions in the *tcdC* gene were detected as previously described.12

**Results**

Between 1 February 2009 and 2 June 2009, *C. difficile* was isolated from 108 of 159 submitted faecal specimens. Repeat isolates of the same ribotype were obtained from four patients and another four patients each had two distinct *C. difficile* strains. After excluding the repeats, there were 101 isolates from 97 patients. Fifty-nine (61%) of the patients were female and the mean ± SD age was 64 ± 24 years. The geographical distribution of the 101 isolates was as follows: metropolitan Auckland (48 isolates), Waikato (26), Bay of Plenty (6), Wellington (8) and Otago (13).

Susceptibility rates, MIC ranges, and MIC50 and MIC90 values are shown in Table 1. All isolates were susceptible to metronidazole, vancomycin, meropenem and piperacillin/tazobactam, and resistant to penicillin. There are no interpretive criteria for ciprofloxacin, but only three (3.0%) isolates had MICs ≥32 mg/L. Two of these three isolates were resistant to moxifloxacin with MICs of 8 and 16 mg/L, respectively.

The breakpoint for susceptibility to clindamycin is ≤2 mg/L; only 39% of isolates were susceptible to clindamycin. However, among the clindamycin non-susceptible
isolates, only five had clindamycin MICs $\geq$32 mg/L. Nine isolates had raised MICs to one or more of the antimicrobial agents tested: clindamycin (MIC $\geq$32 mg/L) and clarithromycin (MIC $>$128 mg/L) (5 isolates), clarithromycin only (1), and ciprofloxacin (MIC $\geq$32 mg/L) (3). No isolates were resistant to both ciprofloxacin and clindamycin.

Table 1. Antimicrobial susceptibility among 101 *C. difficile* isolates

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>MIC (mg/L)</th>
<th>Range</th>
<th>Percent susceptible</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MIC$_{50}$</td>
<td>MIC$_{90}$</td>
<td></td>
</tr>
<tr>
<td>Penicillin</td>
<td>1</td>
<td>2</td>
<td>1–4</td>
</tr>
<tr>
<td>Piperacillin/tazobactam</td>
<td>8</td>
<td>8</td>
<td>8–16</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>0.5</td>
<td>1</td>
<td>0.5–2</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>8</td>
<td>16</td>
<td>8–128</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>2</td>
<td>2</td>
<td>1–16</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>8</td>
<td>8</td>
<td>1–128</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>1</td>
<td>1</td>
<td>1–128</td>
</tr>
<tr>
<td>Meropenem</td>
<td>2</td>
<td>2</td>
<td>1–4</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>0.25</td>
<td>0.5</td>
<td>0.25–0.5</td>
</tr>
</tbody>
</table>

* Interpretive criteria are not available for ciprofloxacin.

Thirty-two PCR-ribotypes were identified among the 101 isolates (Table 2). The most common ribotypes were 014 (18 isolates), 002 (11) and 005 (10). Three novel PCR-ribotypes, 295, 296 and 298, were identified. No PCR-ribotype 027 isolates were identified, but one isolate of another hypervirulent strain, PCR-ribotype 078, was identified.

Subsequent testing of this isolate showed it to have the genes for the A, B and binary toxins, and a truncating mutation and 39 bp deletion in the *tcdC* regulatory gene which are associated with the hypervirulence phenotype. The only clustering of ribotypes evident was in the Wellington area where seven of the total eight isolates were ribotype 014 (Table 2).

Table 2. PCR-ribotypes among 101 *C. difficile* isolates by geographic source

<table>
<thead>
<tr>
<th>Laboratory</th>
<th>Number of isolates</th>
<th>PCR-ribotype*</th>
</tr>
</thead>
<tbody>
<tr>
<td>North Shore Hospital Laboratory, Waitemata DHB</td>
<td>20</td>
<td>001, 002, 005, 014, 018, 020, 044, 070, 090, 150, 153, 159, 220, 295, 298</td>
</tr>
<tr>
<td>LabPlus, Auckland DHB</td>
<td>21</td>
<td>002, 005, 011, 014, 015, 018, 046, 056, 096, 150, 177, 207, 216</td>
</tr>
<tr>
<td>Diagnostic Medlab, Auckland</td>
<td>6</td>
<td>005, 103, 153, 220</td>
</tr>
<tr>
<td>Middlemore Hospital Laboratory, Counties Manukau DHB</td>
<td>1</td>
<td>153</td>
</tr>
<tr>
<td>Waikato Hospital Laboratory, Waikato DHB</td>
<td>26</td>
<td>001, 002, 003, 005, 014, 015, 018, 020, 054, 150, 153, 159, 220, 296</td>
</tr>
<tr>
<td>Pathlab Bay of Plenty, Bay of Plenty DHB</td>
<td>6</td>
<td>011, 014, 015, 053, 054, 159</td>
</tr>
<tr>
<td>Wellington Hospital Laboratory, Capital and Coast DHB</td>
<td>8</td>
<td>002, 014*</td>
</tr>
<tr>
<td>Southern Community Laboratories, Otago DHB</td>
<td>13</td>
<td>002, 006, 014, 044, 046, 054, 078, 104, 190</td>
</tr>
</tbody>
</table>

* Ribotypes in boldface indicate that there were $\geq$2 isolates of this ribotype from same laboratory;
* Seven of the eight isolates recovered from specimens from this laboratory were ribotype 014.
Discussion

There is a wide range of *C. difficile* PCR-ribotypes circulating in New Zealand, but the epidemic, hypervirulent strain, PCR-ribotype 027/NAP1, does not appear to be present. Although PCR-ribotype 027 was not identified, one isolate of another hypervirulent strain, PCR-ribotype 078, was.

The PCR-ribotype 078 strain has been associated with severe disease in younger-aged patients and with community-associated disease in The Netherlands. Over a 3-year period the incidence of this PCR-ribotype among isolates from patients with *C. difficile* infection in The Netherlands increased from 3% to 13%. Although this strain remains uncommon in Canada, similar to the Dutch experience, the incidence rates have tripled from 0.5% in 2004 to 1.6% in 2008 (p=0.22).

More recently this strain was reported as the second most frequently encountered ribotype in an Irish hospital outbreak. PCR-ribotype 078 strain was the predominant strain in swine and cattle in the United States and has been recognised as an emerging strain in piglets in The Netherlands.

Antimicrobial resistance is uncommon among *C. difficile* in New Zealand. All isolates were susceptible to metronidazole and vancomycin; the two agents used to treat *C. difficile* infection. The majority of the isolates were susceptible to all antimicrobial agents tested except penicillin and clindamycin. Relatively infrequent resistance to macrolides and fluoroquinolones was identified. Isolates of *C. difficile* PCR-ribotype 027 are reported to usually have clindamycin MICs ≥32 mg/L.

Only five isolates in this study had clindamycin MICs ≥32 mg/L and the MIC90 for all the isolates was 8 mg/L. There have been a number of studies of the antimicrobial susceptibility of clinical isolates of *C. difficile* prior to the emergence of the hypervirulent strain PCR-ribotype 027. Although different methodologies were used in these studies, in general resistance was uncommon.

Cross resistance between clindamycin and macrolides is well described and was observed with five of the isolates in this study. This cross resistance is most likely due to the presence of erythromycin ribosomal methylase B (ermB) genes. The five clindamycin- and clarithromycin-resistant isolates belonged to four PCR-ribotypes. Two were PCR-ribotype 159, but were from patients in different geographical regions. The other three isolates were PCR-ribotypes 014, 053 and 207.

The hypervirulent strain, PCR-ribotype 027, is associated with resistance to fluoroquinolones (ciprofloxacin MIC90 >128 mg/L and moxifloxacin MIC90 64 mg/L) and resistance to clindamycin (MIC90 >128 mg/L). None of the New Zealand isolates were resistant to both fluoroquinolones and clindamycin. Other PCR-ribotypes, 001, 002, 005, 014, 015 and 106, have been associated with resistance to imipenem, macrolides, fluoroquinolones and clindamycin in the United Kingdom.

Whilst some of these PCR-ribotypes were present in New Zealand, only two of the 18 PCR-ribotype 014 isolates identified in this study were associated with resistance; one isolate was resistant to both clindamycin and clarithromycin and the other to ciprofloxacin only. No resistance to meropenem was identified.
With the arrival of the hypervirulent PCR-ribotype 027 strain in Australia we need to increase our surveillance activities to detect the “silent” arrival of this virulent organism into the New Zealand healthcare setting. New Zealanders, and visitors to New Zealand, who have been hospitalised in overseas hospitals, including Australian hospitals, have the potential to become colonised with hypervirulent strains of C. difficile and act as vectors for the introduction to our hospitals.23

Laboratory-based surveillance needs to be undertaken, either continuously, or at regular intervals, as with methicillin-resistant Staphylococcus aureus, to characterise the molecular epidemiology of C. difficile isolates circulating in New Zealand. In addition, for patients presenting with severe disease, attempts should be made to culture C. difficile from the faeces and to test the isolate’s susceptibility to fluoroquinolones, ciprofloxacin and moxifloxacin, and clindamycin, to give an early indication of the likelihood that the patient is infected with a hypervirulent strain.

We know little of the epidemiology of C. difficile strains circulating in animals in New Zealand. Whilst it is unclear whether C. difficile is associated with zoonotic transmission or not, consideration should be given to undertaking surveillance in pigs in New Zealand to determine the prevalence of PCR-ribotype 078 in these animals.

Rigorous infection control measures are required to prevent the spread of C. difficile in the healthcare setting. The increased morbidity and mortality associated with infection caused by hypervirulent strains is a cause for concern and multiple strategies will be needed to prevent the establishment of these strains locally. These strategies include improved adherence to hand hygiene, implementation of appropriate isolation precautions, diligent environmental decontamination and active laboratory-based surveillance strategies.

Competing interests: None.

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Pertussis (whooping cough) epidemiology in Waikato, New Zealand: 2000–2009

Richard Wall, Anita Bell, Jason Theobald

Abstract

Aim To describe the epidemiology of pertussis in the Waikato region of New Zealand between 2000 and 2009, and to identify any differences in case characteristics between epidemic and non-epidemic periods.

Method Waikato pertussis notification data for the period 1 January 2000 to 31 December 2009 was analysed to identify any trends in the rates and distribution of key variables. Characteristics of case notifications were compared between an identified epidemic and non-epidemic period.

Results Pertussis notification rates in the Waikato region were higher than national rates but followed a similar yearly pattern. Epidemics were identified in the years 2000 and 2004. The age distribution of pertussis cases changed over the decade with an increasing percentage in older age groups. Notification rates were higher in Europeans than Māori and in the least deprived NZDep group compared to the most deprived. In contrast, hospitalisation rates were higher in Māori than Europeans and in the most deprived NZDep groups. No clear differences in case characteristics were identified between an epidemic and non-epidemic period.

Conclusion The epidemiology of pertussis in Waikato is similar to that reported elsewhere in New Zealand. Further studies are required to clearly identify whether there are differences in case characteristics between epidemic and non-epidemic periods.

Pertussis, also known as whooping cough, is caused by the bacteria *Bordetella pertussis*. Pertussis is highly infectious and can lead to severe complications, particularly in young infants.\(^1\) Seven out of 10 infants with pertussis aged less than 6 months of age, require hospitalisation and 1 in 7 of these either die or develop brain or lung damage.\(^2\)

There are 20 to 40 million cases of pertussis worldwide each year.\(^3\) The incidence of pertussis in New Zealand is high compared to other developed countries.\(^4\) In 1991, during a pertussis epidemic in New Zealand, the incidence was six times that of the epidemic occurring concurrently in the United Kingdom and seven times higher than the incidence of an epidemic in the United States in 1993.\(^4,5\)

Following the introduction of *Pertussis* vaccine into the immunisation schedule in 1960, the pertussis hospital admission rate decreased during the following decade.\(^4\) In 2000 the acellular pertussis vaccine replaced the whole cell vaccine, because of adverse events associated with the whole cell vaccine.

Both vaccine types have similar efficacy.\(^2\) The New Zealand Immunisation Schedule currently recommends pertussis vaccine at 6 weeks, 3 months and 5 months of age.
Booster dose at 15 months of age was added to the schedule in 1996\textsuperscript{1,6} and another booster dose was added at 4 years of age in February 2002.

In 2006 the 15-month booster was replaced by a booster of an adult dose of vaccine at 11 years of age.\textsuperscript{1} The vaccine gives protection against clinical disease in approximately 85\% of people,\textsuperscript{7} but neither natural infection nor vaccination leads to permanent immunity.\textsuperscript{7}

Despite the introduction of the pertussis vaccine to the immunisation schedule epidemics of pertussis in New Zealand have continued to occur approximately every 4 years and hospital admission rates have increased in each decade from 1970 to 2000.\textsuperscript{2,5}

Characteristics of pertussis cases have been reported elsewhere,\textsuperscript{2,3,5,8} but it is not known whether these characteristics differ between an epidemic and non-epidemic period. The identification of any differences in case characteristics between these two such periods may assist in the prevention of future epidemics.

Pertussis has been a notifiable disease in New Zealand since 1996.\textsuperscript{4} Direct laboratory notifications of the disease became mandatory in December 2007.\textsuperscript{9} Notification data for pertussis is therefore available for all of the last decade. Notifications are defined as confirmed if there is a clinically compatible illness that is laboratory confirmed or that is epidemiologically linked to a confirmed case.

Probable cases are defined as having a cough lasting longer than 2 weeks, for which there is no known cause and which is either paroxysmal, ends in vomiting or apnoea, or has an inspiratory whoop. In Waikato, cases with supportive serology but without culture or PCR confirmation are classified as probable.

We aimed to utilise notification data in order to describe the epidemiology of pertussis in the Waikato region of New Zealand, from 2000 to 2009. In particular we sought to determine whether there are differences in case characteristics between an epidemic and non-epidemic period.

**Method**

Waikato and New Zealand pertussis notification data for the period 1 January 2000 to 31 December 2009 was obtained from the EpiSurv database, the national notifiable disease surveillance system. All notified cases were included in the analyses, regardless of whether reported as confirmed, probable, suspected or under investigation.

Demographic variables, hospitalisation and vaccination status of Waikato pertussis cases were described for the 10-year period. Data from the years 2004 and 2005, an epidemic period, were combined and compared with the combined data from 2007 and 2008, a non-epidemic period. Comparisons were made of the distribution of gender, age group, ethnicity, deprivation quintile, hospitalisations for all and of the vaccination status of those aged under 5 years within each of these time periods.

Incidence rates were calculated using denominator values derived from New Zealand census usually resident population data. Annual population estimates were calculated from knowledge of 2001 and 2006 usually resident census populations and assumed that annual population changes followed a linear pattern. Incidence rates for the total 10 year period were calculated using the 2006 Census population. All incidence rates were calculated per 100,000 people per year.

The New Zealand Index of Deprivation 2006 (NZDep2006) was used as an area measure of deprivation. NZDep2006, based on data from the 2006 Census, reflects the degree of deprivation of the population. During analysis deprivation quintiles were utilised, each including two NZDep2006 scores...
and ranging from 1 (least deprived) to 5 (most deprived). Rates were calculated using denominator populations for each quintile obtained from the University of Otago Social Indicators website.\textsuperscript{10} Data was analysed using Microsoft Excel®, Epi Info Stat Calc® and STATA® computer software. P values were calculated using the Chi-squared test. A p value of less than 0.05 was considered statistically significant. Multivariate logistic regression analysis was performed to determine variables that influence hospitalisation of notified pertussis cases while controlling for possible confounding factors. Gender, deprivation quintile, ethnic group and age were included in the analysis.

**Results**

There were 2421 cases of pertussis notified in the Waikato region during the period 2000 to 2009. Approximately 34% of the cases were classified as confirmed, 64% as probable and 2% as suspected, under investigation or unknown. There was yearly variation in the percentage of confirmed cases ranging from 7% to 72%, but the percentage of suspected, under investigation or unknown cases was consistently low.

High rates of disease in Waikato, generally defined as epidemics, were observed during 2000 (162.4 per 100,000 people) and 2004 (143.1 per 100,000 people) continuing throughout 2005 and 2006 (Figure 1).

An increase in the rate occurred in 2009 (66.2 per 100,000 people), but was not as high as seen in previous epidemic years. The pattern of notifications over the decade is similar to that seen nationally, although rates were significantly higher within Waikato during most years.

The average annual notification rate over the 10-year period was 71.4 cases per 100,000 people in Waikato and 40.1 cases per 100,000 people nationally.

**Figure 1. Pertussis notification rates for Waikato and New Zealand, 2000 to 2009**

The rate in those aged less than one year (293.2 cases per 100,000 people per year), was at least double that in other age groups. The age distribution of pertussis
notifications changed over the period, with a gradual increase in the percentage of notifications in older age groups, peaking in 2007 (Figure 2). In 2007, 86% of cases were aged over 25 years, although this declined to 57% in 2009.

Figure 2. Age distribution of Waikato pertussis notifications, 2000 to 2009

Fifty-eight percent of all cases were female, but the rate was only significantly higher in females than males in the 15 to 64 year age groups. The rate was 1.3 to 2 times higher in females than males during 2000, 2003, 2004, 2005 and 2006. Although the difference was not significant in later years, this trend appeared to continue.

The rate of notified pertussis in Europeans was almost twice that of Māori and almost three times that of Pacific and Asian populations during the studied decade (Table 1). No yearly change in this trend was observed.

During the first 4 years of the decade there was no significant difference in notification rates between deprivation quintiles. This changed in the latter part of the decade, with significantly higher rates observed in the least deprived quintile compared to the most deprived quintile in 2004, 2005 and 2008. Combined data from all years studied showed a higher notification rate in the least deprived two deprivation quintiles compared to the most deprived quintile (Table 1).

Approximately 5% of cases were hospitalised over the 10-year period. The hospitalisation rate was highest in the year 2000. There were no hospitalisations for pertussis in 2007 (Figure 3).
Table 1. Waikato pertussis notifications and hospitalisations (2000 to 2009) by key variables

<table>
<thead>
<tr>
<th>Variables</th>
<th>No. of cases**</th>
<th>Rate*</th>
<th>CI</th>
<th>Hosp**</th>
<th>Hosp rate*</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>1811 (75)</td>
<td>79.6</td>
<td>75.9–83.2</td>
<td>54 (51)</td>
<td>2.4</td>
<td>1.8–3.0</td>
</tr>
<tr>
<td>Māori</td>
<td>310 (13)</td>
<td>45.9</td>
<td>40.8–51.1</td>
<td>39 (36)</td>
<td>5.8</td>
<td>4.0–7.6</td>
</tr>
<tr>
<td>Asian Pacific</td>
<td>53 (2)</td>
<td>30.8</td>
<td>22.5–39</td>
<td>1 (0.9)</td>
<td>0.6</td>
<td>-0.6–1.8</td>
</tr>
<tr>
<td>Pacific</td>
<td>27 (1)</td>
<td>25.4</td>
<td>15.8–35</td>
<td>1 (0)</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>Other</td>
<td>18 (0.7)</td>
<td>4.6</td>
<td>2.5–6.7</td>
<td>2 (2)</td>
<td>0.5</td>
<td>-0.2–1.2</td>
</tr>
<tr>
<td>Unknown</td>
<td>202 (8)</td>
<td>–</td>
<td>–</td>
<td>11 (10)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td><strong>Deprivation quintile</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>378 (16)</td>
<td>74.3</td>
<td>66.8–81.8</td>
<td>7 (7)</td>
<td>1.4</td>
<td>0.4–2.4</td>
</tr>
<tr>
<td>2</td>
<td>445 (18)</td>
<td>69.9</td>
<td>63.4–76.4</td>
<td>8 (8)</td>
<td>1.3</td>
<td>0.4–2.2</td>
</tr>
<tr>
<td>3</td>
<td>391 (16)</td>
<td>56.5</td>
<td>50.9–62.1</td>
<td>13 (12)</td>
<td>1.9</td>
<td>0.9–2.9</td>
</tr>
<tr>
<td>4</td>
<td>489 (20)</td>
<td>66.6</td>
<td>60.7–72.5</td>
<td>26 (24)</td>
<td>3.5</td>
<td>2.2–4.8</td>
</tr>
<tr>
<td>5</td>
<td>429 (18)</td>
<td>52.5</td>
<td>47.5–57.4</td>
<td>36 (34)</td>
<td>4.4</td>
<td>3.0–5.8</td>
</tr>
<tr>
<td>Unknown</td>
<td>289 (12)</td>
<td>–</td>
<td>–</td>
<td>17 (16)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>993 (41)</td>
<td>59.8</td>
<td>56.1–63.5</td>
<td>45 (42)</td>
<td>2.7</td>
<td>1.9–3.5</td>
</tr>
<tr>
<td>Female</td>
<td>1407 (58)</td>
<td>81.3</td>
<td>77.0–85.5</td>
<td>62 (58)</td>
<td>3.6</td>
<td>2.7–4.5</td>
</tr>
<tr>
<td>Unknown</td>
<td>21 (0.9)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td><strong>Age group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>146 (6)</td>
<td>293.2</td>
<td>245.6–340.7</td>
<td>71 (66)</td>
<td>142.6</td>
<td>109.4–175.8</td>
</tr>
<tr>
<td>1–4</td>
<td>232 (10)</td>
<td>119.6</td>
<td>104.2–134.9</td>
<td>15 (14)</td>
<td>7.7</td>
<td>3.8–11.6</td>
</tr>
<tr>
<td>5–14</td>
<td>601 (25)</td>
<td>113.5</td>
<td>104.4–122.5</td>
<td>6 (6)</td>
<td>1.1</td>
<td>0.2–2.0</td>
</tr>
<tr>
<td>15–24</td>
<td>273 (11)</td>
<td>55.8</td>
<td>49.2–62.4</td>
<td>0 (0)</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>25–44</td>
<td>528 (22)</td>
<td>58.6</td>
<td>53.6–63.6</td>
<td>7 (7)</td>
<td>0.8</td>
<td>0.2–1.4</td>
</tr>
<tr>
<td>45–64</td>
<td>472 (20)</td>
<td>59.0</td>
<td>53.7–64.3</td>
<td>2 (2)</td>
<td>0.2</td>
<td>-0.1–0.5</td>
</tr>
<tr>
<td>65 plus</td>
<td>167 (7)</td>
<td>39.1</td>
<td>33.2–45.0</td>
<td>6 (6)</td>
<td>1.4</td>
<td>0.3–2.5</td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (0.1)</td>
<td>–</td>
<td>–</td>
<td>0 (0)</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

CI=95% confidence interval; Hosp=number of cases hospitalised; Hosp rate=hospitalisation rate; * Per 100,000 people per year; ** Percentages in brackets.

The demographic distribution of hospitalised cases differed from that of notified cases (Table 1). Two-thirds of hospitalised cases were aged less than 1 year. Almost 50% of all notified cases aged less than 1 year were hospitalised. There was no significant difference in the gender of hospitalised cases.

Māori had a significantly higher hospitalisation rate than all other ethnic groups, being more than double that of Europeans over the decade (5.8 compared to 2.4 per 100,000). There were no hospital admissions for Pacific people during the studied decade. The hospitalisation rate was higher in those living in the most deprived deprivation quintile compared to the least deprived deprivation quintile.

A logistic regression model for hospitalisation of pertussis cases found that a young age, Māori ethnicity and living in the most deprived deprivation quintile all increased the odds of hospitalisation, but that gender had no effect.
Figure 3. Waikato pertussis hospitalisation rate

![Waikato pertussis hospitalisation rate chart]

Table 2. Waikato pertussis cases during an epidemic and non-epidemic period, by key variables

<table>
<thead>
<tr>
<th>Variables</th>
<th>Epidemic period</th>
<th>Non-epidemic period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number*</td>
<td>Rate**</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>340 (39)</td>
<td>104.2</td>
</tr>
<tr>
<td>Female</td>
<td>527 (60)</td>
<td>155.3</td>
</tr>
<tr>
<td>Unknown</td>
<td>9</td>
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</tr>
<tr>
<td>Deprivation quintile</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>164 (19)</td>
<td>161.1</td>
</tr>
<tr>
<td>2</td>
<td>159 (18)</td>
<td>124.9</td>
</tr>
<tr>
<td>3</td>
<td>152 (17)</td>
<td>109.7</td>
</tr>
<tr>
<td>4</td>
<td>196 (22)</td>
<td>133.5</td>
</tr>
<tr>
<td>5</td>
<td>142 (16)</td>
<td>86.8</td>
</tr>
<tr>
<td>Unknown</td>
<td>63</td>
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</tr>
<tr>
<td>Ethnic group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>715 (82)</td>
<td>152.6</td>
</tr>
<tr>
<td>Māori</td>
<td>88 (10)</td>
<td>66.2</td>
</tr>
<tr>
<td>Pacific</td>
<td>10 (1)</td>
<td>48.5</td>
</tr>
<tr>
<td>Asian</td>
<td>20 (2)</td>
<td>64.7</td>
</tr>
<tr>
<td>Other</td>
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<td>17.9</td>
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<tr>
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</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
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<td>273.8</td>
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<tr>
<td>1–4</td>
<td>51 (6)</td>
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<td>5–14</td>
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<td>15–24</td>
<td>102 (12)</td>
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<td>25–44</td>
<td>215 (25)</td>
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<tr>
<td>45–64</td>
<td>184 (21)</td>
<td>120.0</td>
</tr>
<tr>
<td>65+</td>
<td>80 (9)</td>
<td>97.0</td>
</tr>
</tbody>
</table>

CI = 95% confidence interval; * Percentages in brackets; ** Rate per 100,000 people per year.
During the epidemic period of 2004 and 2005, 876 cases of pertussis were notified in the Waikato region. In comparison only 156 cases were notified during the non-epidemic period of 2007 to 2008. The distribution of cases by age group differed between the epidemic and non-epidemic period (Table 2).

The proportion of cases in the 45 years and older age groups was higher during the non-epidemic period. In contrast the epidemic period had a higher proportion of cases aged 5 to 14 years. There were no obvious observed differences in the distribution of cases between the epidemic and non-epidemic period for gender, ethnicity, deprivation quintile, hospitalisations and vaccination status (Table 2 and Table 3).

Table 3. Number of Waikato pertussis cases during an epidemic and non-epidemic period, by hospitalisation and vaccination status

<table>
<thead>
<tr>
<th>Variables</th>
<th>Epidemic case numbers*</th>
<th>Non-epidemic case numbers*</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalisation status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>27 (3)</td>
<td>3 (2)</td>
<td>0.61</td>
</tr>
<tr>
<td>No</td>
<td>838 (97)</td>
<td>146 (98)</td>
<td></td>
</tr>
<tr>
<td>Vaccination status**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>40 (53)</td>
<td>2 (29)</td>
<td>0.26</td>
</tr>
<tr>
<td>No</td>
<td>35 (47)</td>
<td>5 (71)</td>
<td></td>
</tr>
</tbody>
</table>

* Percentages provided in brackets; ** Vaccination status in cases less than 5 years of age.

Discussion

This study describes 10 years of notification and hospitalisation data for pertussis in the Waikato region. No clear differences in Waikato case characteristics were identified between an epidemic and non-epidemic period during this time.

Over the studied period Waikato pertussis rates have followed a similar pattern to national rates, with epidemics identified in 2000 and 2004 and with a significant but smaller rate increase in 2009.

Surveillance over future years will be required to determine whether this latest increase reaches previous epidemic levels, but early indications in 2010 suggest that the rate is declining. This pattern over the past decade matches previous descriptions of epidemics occurring both globally and nationally on an approximately two to five yearly cycle.4, 5, 11, 12

Epidemics continue to occur in vaccinated populations because the vaccine derived immunity wanes over time, allowing infection of adults who may then infect unvaccinated children.11

This study identified higher pertussis rates in Waikato than nationally. Pertussis rates during epidemic periods in the last decade were higher than those seen nationally during the 1996 pertussis epidemic.8

Differences in vaccination coverage could explain this finding, as small differences in vaccination coverage potentially result in large reductions in disease prevalence.13 In
2005, in which there was a significantly higher pertussis rate in Waikato than nationally, Waikato pertussis vaccination coverage at 2 years of age was 75% compared to 79% coverage nationally. However other factors are likely to be involved, which may include differences in local public health messages, physician awareness, in laboratory diagnosis method or in the management of cases.

A higher percentage of cases were found in older age groups during the non-epidemic compared to the epidemic period. This difference is however unlikely to have been related to whether or not an epidemic occurred.

The study identified an increasing trend in the percentage of adult cases over time, which has also been reported in other developed countries of the world. This trend may relate to increased clinician awareness of the disease in older age groups or improved laboratory diagnosis. PCR gives a significant increase in diagnostic yield compared to culture. However the use of PCR has only occurred recently in Waikato, particularly in primary care, and so is unlikely to be associated with the observed trend.

Countries with higher vaccine coverage have a higher proportion of older cases than those countries with lower coverage. Increased vaccine coverage in younger age groups could therefore contribute to the trend of an increase in the percentage of older cases.

In New Zealand the introduction of a vaccine booster at age 11 in 2006 may also have contributed to this trend, by reducing the percentage of cases in the five to fourteen year age group. However a reducing percentage of notifications within this age group had been occurring over several years prior to the vaccine’s introduction.

Despite the increased rate of notifications within adults in later years, the hospitalisation rate remained low within these age groups, indicating that the most severe cases occur in the young, particularly in babies less than one year of age.

Pertussis rates were higher in females than males during some years of the last decade. This finding was only significant in the 15 to 64 year age groups, supporting previous literature in which the disease was found to be more frequent in females than males except during the first year of life. The gender differences observed in this study may relate to adult males being less likely than adult females to present to primary care when unwell.

The average annual notification rate was higher in Europeans than Māori during the studied period. In contrast hospitalisation rates were higher for Māori than Europeans. This finding has been reported elsewhere. Similarly notification rates were higher in the least deprived quintile compared to the most deprived quintile, but hospitalisation rates were higher in the most deprived quintile compared to the least deprived group. One possible cause of these findings is that there is poor or delayed access to primary and secondary care in Māori compared to Europeans, and in deprived populations.

There is a known relationship between high deprivation and Māori ethnicity. Logistic regression analysis in this study however, suggests that the high rate of pertussis hospitalisation for Māori is related to factors additional to socio-economic deprivation.
There was marked yearly variation in the percentage of cases that were classified as confirmed during the studied decade. This is likely to have occurred due to changes in the use of diagnostic tests over the period. PCR became the standard test for pertussis at the Waikato Hospital in 2006, but the use of PCR in Waikato primary care has only recently begun to increase, with widespread use of serology tests being common.

Serology evidence is not classified as being confirmed within Waikato. Both probable and confirmed cases were therefore included in the study to insure that all pertussis cases were captured. Other classifications of pertussis were included as they made up only a small percentage of the total notifications and so were unlikely to significantly influence the overall results.

There are several limitations to this study. A lack of case numbers in non-epidemic periods and a lack of recorded data regarding case vaccination status limited the power of this study in some areas. Identification of this issue has now led locally to new procedures to improve recording of vaccination status.

Ethnicity data obtained from the EpiSurv database is unlikely to have been self reported in all cases. This could have resulted in misclassification of cases within the study. While notification data can provide an estimate of the incidence of the disease, the true incidence of pertussis is likely to be much higher than identified in this study. Notifications are likely to underestimate the true incidence because many do not present to health care, clinicians may not consider pertussis in adults and the sensitivity of testing is limited, particularly beyond two to three weeks.

Pertussis notification rates in the Waikato are high in comparison to national rates but follow a similar yearly pattern. The age distribution of pertussis notifications has changed over this decade, with increasing rates in older adult age groups. No clear differences between epidemic and non-epidemic periods were identified. Further studies, which include greater case numbers and which examine a range of epidemic and non-epidemic periods, are necessary to determine whether case characteristics differ between such periods.

Competing interests: None.

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References:
Interactions between gastric and enteric infections: clues to the pathogenesis of inflammatory bowel disease?

Jacqueline I Keenan, Hazel M Mitchell, Andrew S Day

Abstract
Whereas the worldwide incidence of Crohn’s disease (CD) continues to rise, Māori and Pacific Islanders living in New Zealand remain largely unaffected. The reason for this is currently unknown but may be linked to emerging evidence suggesting a role for Campylobacter spp in the aetiology of CD. Rates of campylobacteriosis are notably lower among Māori and Pacific Islanders and while this may reflect poorer access to primary care and diagnostic services, resulting in lower rates of notified disease, we consider it may also reflect a level of protective immunity in Māori and Pacific Islanders as a result of chronic infection from an early age with the closely related gastric pathogen Helicobacter pylori. Understanding the interactions between these antigenically-related bacteria may provide us with clues that ultimately help unravel the complex aetiology of CD.

Crohn’s disease (CD), one of the inflammatory bowel diseases (IBD), is an incurable debilitating disease characterised by diarrhoea, rectal bleeding and abdominal pain that leads to significant nutritional impact, patient morbidity and health utilisation. Although most often diagnosed in young people (15–30 years of age), CD, however, can present at any age from infancy onwards. Upon development of disease, individuals with CD typically have lifelong relapsing symptoms.

Over the last five decades, the incidence of CD has risen exponentially in many countries throughout the world, with the highest rate worldwide reported in Canterbury, New Zealand. In 2004, 715 of a projected population of 460,680 people in this region were identified with this disease.1 The ethnicity of 707 (98.9%) of the patients was described as “other” and included more than 90% of the Canterbury population that are of European descent as well as people of other ethnicities, particularly those from Asia.

In contrast, only 8 (1.1%) of the 715 patients were of Māori descent, whilst no Pacific Islanders were identified in the disease cohort.1 One could argue that this finding is hardly surprising, given the relatively low numbers of Māori (7.2%) and Pacific Islanders (1.8%) who live in the Canterbury region. However, other epidemiologic studies of CD that include areas of New Zealand where these ethnic groups are better represented report similar findings.2–4 Moreover, a recent study failed to identify any Māori or Pacific Islander children among 52 cases of paediatric IBD.5

This apparent unchanging rate of disease over a single generation may indicate genetic factors that protect Māori and Pacific Islanders from CD. However, compelling evidence of a role for gut bacteria in the pathogenesis of CD6,7 raises the possibility that variations in the intestinal microflora of these peoples contributes to their low incidence of CD.
Campylobacter species are the predominant cause of food-borne gastroenteritis in the industrialised world. In recent years, C. jejuni has become the predominant pathogen in developed countries. Infection with C. jejuni manifests as acute gastroenteritis presenting with fever, diarrhoea and abdominal pain with some individuals going on to develop extra intestinal infections.

A 2007 report showed that rates of campylobacteriosis in New Zealand are amongst the highest in the developed world, with the incidence of reported cases increasing steadily since this disease first became notifiable in 1980. In the years since 2007, however, rates appear to have fallen (unpublished data, NZ Public Health Observatory).

We have recently shown that Campylobacter spp. may have a role in the aetiology of CD. A high prevalence of C. concisus DNA as well as immunoglobulin (Ig) G antibodies to C. concisus was found in children with CD. C. concisus is one of a number of emerging Campylobacter spp. that, in addition to the more commonly reported C. jejuni, C. coli and C. fetus strains, are associated with human gastroenteritis. While this study does not prove a causative role for C. concisus in CD, it does add weight to the hypothesis that acute Campylobacter infection may increase the risk or precipitate the onset of CD in genetically-susceptible individuals, as illustrated with C. jejuni.

Consistent with our hypothesis that Campylobacter spp may have a role in CD aetiology is a growing body of evidence that these bacteria have the potential to compromise the gut epithelial barrier. This barrier consists of a single layer of epithelial cells that serves to create a physical barrier to gut pathogens. Tight junctions seal the intercellular space between adjacent cells and also establish a semi-permeable barrier that restricts the entry of pathogens between the cells (paracellular translocation). However, during periods of inflammatory stress, gut barrier function can be compromised. Whereas this loss of function may be transient, it still provides the opportunity for gut bacteria to cross this normally impermeable barrier and initiate an inflammatory response that subsequently develops into IBD in a subset of individuals.

Until recently, changes in intestinal permeability resulting in a leaky gut were thought to be required for bacterial translocation across this barrier, regardless of its own invasiveness, has also been shown to promote the translocation of non-invasive bacteria across the intestinal epithelium. However, there is now compelling evidence that significant bacterial translocation can occur without overt leakiness. Specifically, a recent study has shown that C. jejuni can translocate through the epithelium in the absence of any disruption to intercellular tight junctions. Moreover, C. concisus also has the potential to damage epithelial integrity.

In New Zealand, the rates of campylobacteriosis are highest in children and young adults, males and Europeans (329.0/100,000) whereas notification rates are notably lower in Māori (93.5/100,000) and Pacific Islanders (70.2/100,000). This difference in notification rates may not reflect lower rates of infection, but could simply represent lower disease notification due to poorer access to primary care and diagnostic services. There are no data of the seroprevalence of specific antibodies in these populations.
These ethnic differences are unlikely to be a reflection of decreased gastric pH, exposure to contaminated foodstuffs or drinking water that are known to predispose to Campylobacter infection. Instead, we consider that this observation may reflect a level of protective immunity in Māori and Pacific Islanders as a result of chronic infection with the closely related gastric pathogen *Helicobacter pylori* from an early age or perhaps be consequent to prior acute Campylobacter infection in childhood.

In New Zealand, we have limited epidemiological data of the extent of *H. pylori* infection but it is clear that the incidence of infection is considerably lower in New Zealanders of European descent than age-matched Māori and Pacific Islanders. Two unrelated studies which report very low levels of *H. pylori* colonisation in young adults living along the east coast of the South Island again reflects the predominantly European ethnicity in this part of New Zealand.

In multicultural Auckland, Fraser et al showed that the seroprevalence of *H. pylori* increased with age in Europeans, from 7% in 11–12 year olds to 35.8% in a workforce survey. However, age-matched Māori and Pacific Islander children living in the same community already had seropositivity rates of 21% and 48%, respectively, indicating very high rates of childhood colonisation in these ethnic groups.

It is not clear why ethnicity is linked with *H. pylori* infection in New Zealand. Possible risk factors include socioeconomic status and overcrowding, particularly in childhood when acquisition of *H. pylori* is most likely to occur. Indeed, data from Canada over recent years suggests interesting parallels. *H. pylori* infection is more frequently seen in Canadian First Nation and Inuit populations than in predominantly Caucasian populations in southern Canada. Furthermore, rates of both CD and UC were greater in non-Aboriginal populations in a large population-based study from the province of Manitoba, Canada.

If our hypothesis is correct and the increased prevalence of *H. pylori* infection in Māori and Pacific people does provide a level of protective immunity against *Campylobacter* infection, it suggests that the current practice of eradicating *H. pylori* infection may further increase the incidence of *Campylobacter* enteritis. This may in turn increase the risk of CD in previously protected individuals. In support of these putative links are an increasing number of studies demonstrating lower rates of *H. pylori* infection in individuals with IBD.

In the first of these reports, El-Omar and colleagues compared the *H. pylori* IgG status of 110 patients with IBD with that of 100 age- and sex-matched controls. Twenty-two of the patients with IBD were seropositive for *H. pylori*-specific antibody, in contrast to 52% of controls. Another report, delineated that seropositivity to *H. pylori*-specific antibodies was associated with lower rates of IBD in patients from Finland and also that seronegative individuals had early disease onset than those who were seropositive. These studies were included in a recent systematic review and meta-analysis.

The authors identified 369 articles on this topic: after exclusion due to poor study design or inadequate data, just 23 studies fitting the authors’ inclusion criteria were reviewed in detail. An inverse correlation between *H. pylori* infection and IBD was seen in 13 of these 23 studies. Overall the authors concluded that *H. pylori* infection
may potentially be protective against the development of IBD (especially CD). Further definitive studies are required to confirm these interrelationships.

The likely mechanism by which H. pylori could protect against IBD is unclear. Most H. pylori-infected individuals (including children) produce antibodies against the bacterium that provide a serological marker for infection that usually persists for life in the human stomach unless treated with specific anti-microbials. Whereas H. pylori-specific antibodies play no role in eradicating this bacterium, they may however confer a degree of protective immunity from subsequent Campylobacter infection, given evidence of antigenic cross-reactivity between these two species of bacteria and the indication that immunity can protect individuals from campylobacteriosis.

Recent studies suggest that regulatory T cells may also play a role. Given that adoptive transfer of regulatory T cells is able to prevent or treat colitis in a range of animal models, it is feasible that these cells produced in response to H. pylori infection contribute to the prevention of IBD in the human setting. Further detailed studies are required to confirm this role, or to delineate other ways that H. pylori colonisation may protect against IBD.

In conclusion, there are intriguing data from various studies, demonstrating higher rates of H. pylori infection, lower rates of Campylobacter infection and much lower rates of IBD in Māori and Pacific Islanders in NZ. These observations may be related, suggesting a protective effect of H. pylori colonisation in these settings. Understanding the interactions between these antigenically-related bacteria may provide us with clues that ultimately help unravel the complex aetiology of CD.

Competing interests: None.

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World Salt Awareness Week: more action needed in New Zealand

Rachael M McLean, Jim I Mann, Janet Hoek

World Salt Awareness Week ran from 21 to 27 March 2011. Increasing attention to the detrimental health effects of a high dietary salt intake has led to substantial public health campaigns in the United Kingdom, New York, Finland, Japan, and Canada. Indeed, recent modelling indicates that salt reduction is likely to be one of the most cost-effective population public health interventions for chronic disease reduction available.

US estimates suggest reducing Americans’ salt intake by as little as 3 grams per day could reduce annual deaths by 44,000 and save between $10 billion and $24 billion in annual healthcare costs. The benefits with respect to cardiovascular disease outcomes for the US are estimated to be similar to population tobacco or obesity reduction strategies. Similarly, estimates suggest that among low and middle income countries salt reduction would be at least as effective as tobacco control for reducing deaths from cardiovascular disease.

Modelling work undertaken New Zealand in 2003 estimated that a population reduction of salt intake of 2.5 grams per day would lead to an overall decrease of 1.0 mmHg in the mean population systolic blood pressure (producing a 4-6 mmHg decrease in systolic blood pressure in adults ≥65 years of age), and would result in a total reduction of 282 deaths and 2613 years of life lost per year from heart disease and stroke.

Health consequences of a high salt intake

There is now a compelling body of evidence that demonstrates a linear dose response relationship between dietary salt intake and blood pressure. Large epidemiological observational studies such as INTERSALT (a cross-sectional study which examined the association between 24-hour urinary sodium excretion and blood pressure in 32 countries around the world) showed that populations such as the Yanomamo of Brazil with very low dietary salt intake demonstrated significantly lower blood pressure than populations with higher dietary salt intakes. These ‘low-salt’ populations also showed no increase in blood pressure with age, thereby challenging the view that increasing blood pressure is an inevitable consequence of ageing.

A Cochrane Collaboration systematic review and meta-analysis of randomised trials demonstrated that for adults, a reduction of sodium intake by at least 40 mmol (or 2.3 grams salt per day) would lead to an average reduction in blood pressure of 5/3 mmHg for hypertensive and 2/1 mmHg for normotensive adults. Furthermore, the authors estimated that if these changes were to be achieved at a population level this would reduce stroke deaths by approximately 14% and ischaemic heart disease deaths by 9% in adults with hypertension, and 6% and 4% respectively in those with normal blood pressure.
A meta-analysis of controlled trials investigating salt intake and blood pressure in children and adolescents (≤18 years) showed that a modest reduction in sodium intake would significantly reduce blood pressure. While there is some evidence that some individuals and population groups (such as African Americans and obese adults) are more ‘salt sensitive’ than others, the overwhelming evidence shows that the vast majority of both normotensive and hypertensive people will respond to a reduction in dietary sodium intake with a small reduction in blood pressure.

There is little evidence to support the notion that only the few ‘salt sensitive’ individuals need to monitor their dietary sodium intake. The combination of a diet high in potassium and low in sodium such as the Dietary Approaches to Stop Hypertension or DASH diet (a diet high in fruits, vegetables and low-fat dairy products, and low in saturated and total fat) is particularly effective in reducing blood pressure in adults with hypertension.

Evidence also links dietary salt intake directly with adverse cardiovascular outcomes. A systematic review and meta-analysis of prospective studies published 1966–2008 showed that a diet high in salt is associated with significantly increased risk of stroke and total cardiovascular disease.

While much of this effect is likely to be mediated by elevated blood pressure, increasingly, dietary salt intake is recognised as having direct adverse cardiovascular effects such as impaired endothelial function and arterial vascular tone. In addition to cardiovascular effects, a high dietary salt intake is also associated with increased risk of gastric cancer, kidney disease and osteoporosis.

**Nutrient reference values**

New Zealand and Australia have jointly determined nutrient reference values for sodium with the recommended upper level of intake (UL) for adults set at 2300mg/day (equivalent to 5.8 grams salt per day). For children and adolescents the UL has been extrapolated at a lower level based on proportional energy intake.

The New Zealand guidelines state that for some people (older or overweight people and those with existing hypertension) a lower ‘suggested dietary target’ of 1600 mg sodium per day or 4 grams salt per day would be beneficial. US dietary guidelines released early 2011 now recommend a population upper level of intake of 1500 milligrams per day of sodium or 3.75 grams salt.

‘Salt’ and ‘sodium’

Since the majority (around 90%) of dietary sodium is in the form of sodium chloride or salt, many public health initiatives refer to ‘salt’ rather than ‘sodium’. The use of the word ‘sodium’ on food labels however can cause some confusion, especially since, to convert sodium to salt, consumers must multiply the amount of sodium by approximately 2.5 (so that 1 gram of sodium converts to approximately 2.5 grams of salt).

Consequently many consumers have difficulty understanding the relationship between ‘sodium’ and ‘salt’. For instance, a study of 226 New Zealand shoppers in 2006 showed that only 10% were able to correctly identify the value for the sodium UL when expressed as salt. Although 67% of participants reported that they monitored
their salt intake, only 2% were able to correctly identify the amount of salt in a can of baked beans, based on information on sodium content in the Nutrition Information Panel. The majority of participants believed that the terms ‘salt’ and ‘sodium’ were interchangeable.\textsuperscript{15}

**Estimates of salt intake**

New Zealanders have an estimated salt intake of around 9 grams per day, which is consistent with similar countries around the world. This estimate is based on 24 hour urine sodium measurements from adults 16 years and older in Milton in the 1970s and 1980s,\textsuperscript{16} and further 24 hour urinary samples from a range of participants in Dunedin, Waikato and Taranaki from 1993–1998.\textsuperscript{17}

Estimates of salt intake for minority population groups such as Māori and Pacific people within New Zealand are lacking. Alarmingly, population estimates in many Asian countries are substantially higher than 9 grams, raising the possibility that Asian populations within New Zealand may also have particularly high salt intakes. Recent estimates suggest a mean population dietary salt intake of 11 grams per day in Japan, 12 grams per day in China, 8.5 grams per day in an urban south Indian population, and 11–13 grams per day in the Republic of Korea.\textsuperscript{18–20}

While a 24 hour urinary sodium is considered the ‘gold standard’ estimate of dietary salt intake,\textsuperscript{21} dietary surveys are useful to indicate the key sources of sodium in the diet. In Western countries it is generally accepted that around 75% of dietary sodium intake comes from processed foods, 10–15% from sodium naturally inherent in foods, 10% is discretionary added in cooking and at the table, and around 1% comes from drinking water.\textsuperscript{14,22}

Other populations show different patterns of sodium intake. In China, it is estimated that around 78% of sodium intake is added during cooking, and in Japan the main sources of sodium include soy sauce, fish and soups with around 10% as added salt during cooking.\textsuperscript{18,23}

New Zealand research shows that for all age groups, bread is the leading source of salt intake from processed foods, with processed meats (such as bacon and sausages) sauces, breakfast cereals, instant meals (including meat pies and instant noodles) and baked and dairy products also contributing substantially to dietary salt intake.\textsuperscript{3,24,25}

**Uses of salt in processed food**

In modern food processing, salt performs three main functions: taste enhancement, preservation, and processing functions. Salting is one of the earliest methods of food preservation. Salt slows microbial growth by reducing water activity at particular concentrations. The use of salt as a preservative is particularly important in meat and meat products, pickled vegetables, fermented products (e.g. soy sauce), sauces, and chilled foods.\textsuperscript{26}

In baked products such as bread and cakes, salt delays mould formation thereby extending shelf life. In processing, salt is reported to improve texture and succulence by its ability to retain water in products such as sausages.\textsuperscript{26} It also allows producers to add weight (and therefore value) to meat products, while maintaining that a product is
In bread and other baked products, salt helps to control the rate of yeast fermentation, influencing texture.  

Although risks to microbiological food safety are a potential barrier to salt reduction in some processed foods, surveys show that sodium content in similar foods varies greatly, so it should be feasible to reduce salt content in several foods without compromising food safety, providing the lowest level of salt already in use remains inhibitory.

Modern processing and refrigeration also contribute to preservation and processing functions thereby enabling further salt reduction. In addition to providing a salty taste, salt blocks unpleasant tastes such as bitterness and flavours related to food spoilage, and it enhances the effect of other more palatable flavours such as meaty flavours.

Salt moderates the sweetness of sugars used in breakfast cereals and confectionary. Humans have a natural preference for salty tastes, thought to be mediated by specific salt receptors on the tongue, however preference for salty foods is related to salt intake over the previous 8–12 weeks, and humans adjust their salt preferences to either a high salt or low salt diet accordingly.

A gradual reduction in salt concentration is therefore unlikely to be noticed by consumers, making this a sensible way of achieving population wide gains in salt reduction.

**Salt reduction strategies:**

Since around three-quarters of dietary salt intake comes from that already in processed foods interventions with the greatest impact would change food composition, and thus consumers’ food supply. Reduction of discretionary salt used at home in cooking and at the table has limited potential to result in significant overall reductions in salt intake, and risks lowering dietary iodine intake because much of the salt used at home is iodised.

Reducing the amount of salt in processed food would have a greater impact in terms of population salt reduction, and would probably not substantially reduce New Zealanders’ iodine intake. This is because apart from bread, which has contained iodised salt since 2009, most of the salt in processed foods non-iodised. However, monitoring of population iodine status, particularly in childhood, will need to be maintained.

If iodine status is threatened by salt reduction a number of alternatives could be considered such as:

- Increasing the concentration of iodine in iodised salt
- Mandating the use of iodised salt in all processed foods, not just bread
- Making iodisation of other staple foods such as oil, bread, drinking water, sugar and animal feeds mandatory.

Since 2003 the UK Food Standards Agency (FSA) has undertaken a salt reduction strategy that can be seen as a model for the rest of the world. It appears to have been a success with a 10% reduction in mean population salt intake from an average of 9.5 grams/day salt in 2000–2001 to 8.6 grams/day in 2008.
Key elements of the FSA strategy include setting a population salt intake target of an average of 6 grams per day, working with the food industry to reformulate processed food to contain less salt, making improvements to food labelling which include introduction of a traffic light labelling scheme, and conducting a public awareness campaign. New Zealand would benefit greatly from a co-ordinated government-led population salt reduction strategy, similar to that undertaken in the United Kingdom. Based on the available international evidence the following strategies should be implemented:

- Reformulation of processed foods can reduce dietary salt intake for the whole population without requiring people to alter their dietary habits, thereby achieving maximum population impact. If done gradually consumers are unlikely to notice any difference in taste.

In New Zealand, the National Heart Foundation has worked with the food industry in this area for several years, first with the award winning Project Target 450 which has reduced the amount of sodium in many low-cost and high-volume breads to 450 milligrams sodium per 100 grams, and more recently with project HeartSAFE. However, more could be achieved by setting sodium concentration targets across a wide range of foods, as has been done in the United Kingdom. Modelling has shown that the setting of a wide range of targets relating to specific foods is the most effective and cost-effective method of population dietary salt reduction.

- Raising consumer awareness has been an important part of many successful salt reduction strategies. Dietary advice on its own is unlikely to be either effective or cost-effective, and indeed has largely failed to reduce sodium intake on a population level in the past. However as part of a comprehensive salt reduction programme raising public awareness of the need for dietary salt reduction has a number of potential benefits. Food industry representatives have in the past cited lack of consumer demand for low salt products as barriers to reformulation, pointing out that “public tastes continue to dictate the marketplace”. Increased consumer demand for lower salt products is likely to encourage industry to produce and promote low salt options, as well as reformulate mainstream products. An evaluation of the UK FSA public awareness programme indicated changes to self-reported behaviour from consumers such as cutting down on their salt intake and increased attention to food labels for sodium/salt levels. Although it is unclear to what extent these self reported changes have translated to altered purchasing and eating behaviours, population surveys show a reduction in dietary sodium intake of around 10% over the period of the salt reduction strategy as a whole.

Healthcare professionals have an ideal opportunity to promote salt reduction, especially when engaging patients in discussions about cardiovascular risk and blood pressure.

- Labelling of processed food needs to be improved in order to help consumers identify the amount of salt in foods. Nutrition labelling has been mandatory in New Zealand since 2002, and includes reference to sodium content. More
recently, several food manufacturers have voluntarily introduced front of pack Percent Daily Intake (PDI) labels to complement the mandatory Nutrition Information Panels. However, the PDI for sodium is based on upper level of daily sodium intake for adults of 2300 milligrams/day rather than the suggested dietary target of 1600 milligrams per day. The adult reference values are used in calculating the PDI for all foods, even those which are marketed to children, despite the upper limit for children under 14 years of age being lower than the recommended adult levels. This is potentially misleading for consumers, particularly those shopping for children.

- In 2007, the UK FSA introduced a voluntary front of pack labelling scheme that uses multiple traffic lights (MTL) to communicate fat, saturated fat, salt and sugar levels of a food. The MTL uses the word ‘salt’ rather than ‘sodium’ and there are set criteria for salt level in foods. International research suggests that visual devices such as the MTL, which enable consumers to assess nutritional composition without the need to process detailed numerical information, may enable consumers to better differentiate between high and low sodium foods. Nutrition claims such as ‘light’, ‘reduced salt’, ‘low salt’ may also enhance understanding of sodium content. In New Zealand a product can be labelled ‘low salt’ if it contains less than 120mg/100g of sodium, and labelled ‘reduced salt’ if the food has at least 25% less sodium than the comparative reference food.

Current New Zealand legislation prohibits health claims relating to disease prevention (other than for folate). However, Food Standards Australia New Zealand (FSANZ) is developing a Nutrition, Health and Related Claims Standard (Proposal P293) that will outline requirements for nutritional content claims, general level health claims and high-level health claims. It is important to investigate how health claims could influence consumer purchasing behaviour with respect to claims regarding sodium and salt prior to their implementation in New Zealand.

- Although further research specific to New Zealand context is pending we should not delay implementation. Further research could then form the basis of monitoring and evaluation of dietary salt intake in the future.

Many multinational food companies are developing and implementing sodium reduction strategies in response to public health initiatives overseas. Now is the ideal time for New Zealand maximise the opportunities presented by these international salt reduction activities. International evidence shows that a comprehensive public health programme to reduce population dietary salt intake is one of the most effective and cost-effective public health interventions available.

A co-ordinated, government-led salt reduction programme should include: setting sodium concentration targets across a wide range of foods; raising public awareness of the health consequences of a high salt intake and how to reduce their own salt intake; and improvements to food labelling. Ongoing monitoring of New Zealanders’ salt intake and salt content in foods should support this. Cardiovascular disease remains one of the leading causes of death and disability in New Zealand. An
An effective salt reduction strategy could reduce morbidity from heart disease and stroke, reduce healthcare costs, and save hundreds of lives a year.

**Competing interests:** None.

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Beta agonist use during asthma exacerbations: how much is too much?

Mitesh Patel, Kyle Perrin, Richard Beasley

Abstract

Overuse of inhaled beta agonist therapy is associated with risk in adult asthmatics. We report on a case of excessive short-acting and long-acting beta agonist use in the setting of a severe exacerbation of asthma, which highlights some important good practice points.

There is ongoing debate regarding the safety of long-acting beta agonist (LABA) therapy in asthma. Combination inhaled corticosteroid (ICS)/LABA therapy is considered the preferred therapeutic approach, as it ensures that LABAs cannot be taken as monotherapy.

Currently, patients on combination ICS/LABA therapy have a variety of options for reliever medication use in the setting of worsening asthma, including the “as-required” use of short-acting beta agonists (SABA) such as salbutamol, or further doses of their combination ICS/LABA inhaler, in accordance with the SMART (single maintenance and reliever therapy) regime. We present a case of excessive use of inhaled short- and long-acting beta agonist therapy in the setting of worsening asthma, highlighting the potential risks for patients and the need for written self-management plans.

Case report

A 37-year-old woman was admitted to hospital with severe asthma following 3 days of worsening symptoms at home. She had been diagnosed with asthma in childhood, with the requirement for frequent hospital admissions and at least one Intensive Care Unit (ICU) admission. Eight months prior to the admission, in response to poor asthma control, she was changed from fluticasone propionate and salmeterol as separate inhalers to a combination ICS/LABA inhaler (Vannair® – 200 mcg budesonide/6 mcg eformoterol per actuation, 120 puffs per inhaler).

She was instructed to take the Vannair 2 actuations twice a day and as required for the relief of symptoms, “like a Ventolin inhaler”, in accordance with the SMART regime. She also had access to a nebuliser at home; she did not have a written self-management plan.

In the month prior to the onset of the severe asthma exacerbation she used three Vannair inhalers. Three days prior to admission (in response to worsening asthma symptoms) she obtained a new Vannair inhaler from her pharmacy and used it frequently over the next 24 hours such that it was empty the following day. She also used her nebuliser to administer salbutamol and ipratropium bromide on three occasions during this 24-hour period.
Two days prior to hospital admission, she attended an after-hours centre where she received a medical assessment, two salbutamol/ipratropium bromide nebulisers, a prescription for fluticasone, salmeterol and salbutamol inhalers in place of her Vannair and course of prednisone and antibiotics.

She was instructed to use her nebuliser at home every 4 hours and as a result she continued to use her nebuliser frequently during the next 2 days, initially salbutamol and ipratropium bromide and then salbutamol alone when the supply of ipratropium bromide ran out. She also took 10 actuations of her salbutamol inhaler via a spacer three times on the morning of her admission.

The patient’s total exposure to beta agonist in the 3 days prior to admission was 120 doses of eformoterol (720 mcg), 14 doses of salbutamol via nebuliser (70 mg), and 30 doses of salbutamol via spacer (3 mg) (Figure 1).

Figure 1. Beta agonist use prior to hospital admission

* Prednisone commenced

**Discussion**

This case highlights at least three important points. Firstly, it illustrates the potential for overuse of combination ICS/LABA therapy when taken in accordance with the SMART regime. The patient took 120 actuations of her Vannair inhaler within a 24-hour period, resulting in the self-administration of 720 mcg of formoterol and 24,000 mcg of budesonide. These doses are untested and potentially associated with significant risk. Formoterol is a potent beta agonist with high intrinsic activity resulting in greater adverse effects than salbutamol when used repeatedly in high doses.

Secondly, this case illustrates the potential for excessive beta agonist use by various methods of delivery, when self-administered by the patient both independently and following advice from health professionals.
There needs to be a greater awareness of the potential risks of excessive beta agonist use, and both patients and health professionals need to recognise that frequent beta agonist use is a marker of risk of a life threatening attack. Other markers of risk of mortality in her case included a hospital admission in the previous 12 months and the prior ICU admission. 4

Thirdly, the case illustrates the importance of an asthma self-management plan in which the patient can be guided when to start prednisone and to seek medical help in the situation of a severe attack of asthma.

Asthma management plans based on ICS and SABA therapy have been shown to reduce morbidity and risk of mortality, 5 and are well established in clinical practice. For ICS/LABA therapy, AstraZeneca has recently promoted a novel self-management plan incorporating the SMART regime, in which it is recommended that the patient seeks review by a doctor on the same day if >12 actuations of Symbicort® are taken on any one day, or if >6 reliever actuations per day are taken over several days. 6,7 A recent review of the SMART regime has generated active debate about its role in asthma therapy. 8

We suggest that healthcare professionals advise patients of the risks of overuse of short and long acting beta agonist therapy and provide written guidelines in the form of an asthma self-management plan on when to seek medical review in severe exacerbations.

Competing interests: The authors are undertaking clinical research investigating single inhaler therapy in adult asthma.

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References:


A young male with sudden onset quadriplegia

Sumit Chatterjee, Susmita Chatterjee, Partha Sarathi Karmakar

Case history

A 35-year-old male presented in our Department of Medicine with sudden onset of weakness of all four limbs after a minor injury to his neck while doing household work. This was associated with loss of sensations to all the modalities in similar distribution, and retention of urine and constipation. There was no history of fever or any other major illness in the past.

On examination, higher mental functions, spine, cranium and cranial nerves were normal. Fundoscopy examination was normal. Sensations were diminished in all four limbs and trunk, however no sensory level could be delineated. Hypertonia was present in all four limbs, deep tendon reflexes were exaggerated, and plantar was bilaterally extensor. Lhermitte’s sign was present.

Complete haemogram, serum electrolytes, liver and renal function test were normal. Family history was not a contributing factor. Patient had no history of smoking or alcohol abuse, nor was he diabetic, however he had hypertension which was controlled with medications. His X-ray cervical spine revealed the following.

Figure 1. Plain X-ray lateral view of neck showing os odontoideum (white arrow). The dens is small and the posterior arch of C1 is displaced anteriorly.
Subsequently a MRI cervical spine was done, which revealed the following.

Figure 2. MRI cervical spine T1 weighted image showing the presence of os odontoideum (light arrow) and subsequent spinal cord compression with myelopathy in cervical region (weighted arrow)

What is the diagnosis?
Answer—*Os odontoideum causing quadriparesis on minor neck injury.*

**Discussion**

The os odontoideum (Greek for ‘tooth like’) is a rare congenital anomaly of the 2nd cervical vertebra (C2). It is a small accessory ossicle of variable size and shape with smooth, well-corticated borders that is separated from the base of a shortened odontoid process and there is no bony connection to the body of the axis.¹

This biologic abnormality first described from postmortem studies by Giacomini in 1886, weakens the atlantoaxial joint stability and can lead to spinal cord compression. To evaluate the instability in os odontoideum it is important to check the sagittal plane rotation angle and the instability index. A sagittal plane rotation angle of more than 20 degrees or an instability index of more than 40% predisposes the patient to develop myelopathy.²

Although traditionally it is believed that this defect is congenital, there is now emerging consensus on the traumatic aetiology of os odontoideum rather than a congenital source. However, the aetiology does not play a major role in its diagnosis or management.¹

Os odontoideum has been classified into two anatomic types, orthotopic and dystopic. Orthotopic describes an ossicle that moves with the anterior arch of C1, whereas dystopic defines an ossicle that is functionally fused to the basion.³

The initial diagnosis of os odontoideum can be made with plain cervical spine X-rays, but magnetic resonance imaging and computed tomography are advisable for detailed evaluation and preoperative planning. Radiologically and clinically, this defect frequently mimics acute fracture of the odontoid, however, in an acute fracture or non-union of the odontoid the gap between the os odontoideum and the odontoid process is narrow and irregular and extends into the body of the axis below the level of the superior facet where, as in an os odontoideum, the gap extends to above the superior articular facet of the atlanto-axial joint.⁴

Patients with this condition can be asymptomatic or present with a wide range of neurological dysfunctions. In a study featuring the clinical manifestations of various cranio cervical abnormalities, the incidence of spastic quadriparesis in os odontoideum was found to be 80%.⁵ There is, however, insufficient evidence to support treatment standards and guidelines. Patients with os odontoideum, either with or without C1–C2 instability, who have neither symptoms nor neurological signs, may be managed with clinical and radiographic surveillance.

On the other hand, surgery has a definite role in symptomatic cases. The main method of surgical treatment today is posterior decompression after reduction and fusion via independent C1 and C2 instrumentation. In experienced surgical hands an irreducible, persistent anterior compression from os odontoideum can be approached by a transoral route with good results.¹³

In this case the patient was referred to the Neurosurgery Department for further examination. He underwent posterior C1, C2 internal fixation and fusion and was discharged in a stable condition. Till now he is doing well and has been neurologically asymptomatic.
The incidental detection of an os odontoideum should not be neglected but should be referred for appropriate spinal evaluation and surveillance. This condition may have special relevance in children and athletes whose sporting activities may have to be restricted due to minor trauma.

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**References:**

Synthetic cannabinoid analogues—not repeating past mistakes

Presently there is a global concern about the increasing use of synthetic cannabinoid analogues. In some countries, the marketing, sale and consumption of these designer analogues can be achieved legally, bypassing laws prohibiting cannabis use.

In New Zealand, there is presently no legislation banning the use of these analogues and consequently there has been an alarming increase in their availability and consumption. Indeed, the National Poisons Centre has received an increasing number of calls this year concerning the toxicity of these analogues following their recreational use.

There is a public health concern that these analogues will have a similar impact upon society as benzylpiperazine (BZP) had after its introduction in early 2000. Corner shops sold this amphetamine-like drug, and although their sale was prohibited to those less than 18 years of age, minors still readily used it. In addition, despite growing evidence of its adverse clinical effects, attitudes in some sectors of society changed, leading to a normalising of drug behaviour. By 2005, it was estimated that 20 million tablets had been sold, and for a small population of 4 million, per capita this represented a substantial number of tablets. It was finally scheduled in 2008.

The use of cannabis is widespread throughout the world; indeed, the United Nations Office on Drugs and Crime has recognised it as the most prevalent drug of abuse. Its use in New Zealand, for example, is widespread, especially amongst the youth. Research has shown the detrimental effects it has upon young users - for some leading to increased risks of cognitive impairment and mental disorders.

The synthetic cannabinoid analogues describe a large number of chemicals with unrelated structures, which bind to CB1 and CB2 cannabinoid neural receptors and mimic the effect of ∆9-tetrahydrocannabinol (THC), though with greater efficacy. Although little is known about the clinical effects of these analogues, signs and symptoms are anticipated to be similar to those associated with THC. Indeed, accidental overdosing may lead to more significant toxicity than would be expected with THC, which is only a partial cannabinoid agonist.

Adverse effects on the cardiovascular and nervous systems have been reported. Recent reports describe the exacerbation and reoccurrence of psychotic symptoms following use of these cannabinoids. To the knowledge of the authors, there are no published reports on the long-term effects following chronic abuse.

Given the consequences of chronic cannabinoid misuse, especially amongst the young, the failure to control the abuse of these analogues increases the risk of recreating the social impact that occurred following the liberalisation of BZP. These analogues need to be stringently regulated and the legislation covering novel psychoactive substances must be enacted to protect the public.
The safety of any novel substance intended for human consumption should be established by the manufacturer and a regulatory body before public sale—as with any food or drug.

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References:

Call for doctors not to practice homeopathy or refer to homeopaths

The Medical Council of New Zealand (MCNZ) released their Statement on Complementary and Alternative Medicine (CAM) in March 2011, in order to inform doctors of the standards of practice that are expected of them if they have patients who use CAM.1

The key principle is that the Council does not oppose CAM use if it has "...demonstrated benefits for the patient...and patients have made an informed choice". The Council state that they endorse comments made in a Medical Practitioners Disciplinary Tribunal decision that "there is an onus on the practitioner to inform the patient not only of the nature of the alternative treatment offered but also the extent to which it is consistent with conventional theories of medicine and has, or does not have, the support of the majority of practitioners...". Further, the Council statement says that patients "must be aware of the likely effectiveness of a given therapy according to recognized peer-reviewed medical publications, notwithstanding your individual beliefs".

Some CAM therapies have been shown to be safe and effective, and others are scientifically plausible but only have weak evidence to support their use. However, there is no grey area with respect to homeopathy, a practice which involves diluting substances to such a degree that not a single molecule remains. An example of a homeopathic product is "Berlin Wall", which consists of dust from the Berlin Wall, diluted until none remains, sold to people to help them stop feeling repressed. It is not hard to see why the British Medical Association recently described homeopathy as witchcraft.2

A 2006 survey found that around 15% of New Zealand GPs will either administer homeopathy or refer patients to a homeopath,3 but this would appear not to be compatible with the Medical Council statement.

In terms of demonstrated benefits, there are none other than placebo effects.4 A US $1 million prize remains unclaimed for anyone who can demonstrate any in-vitro or in-vivo effects of any homeopathic product. Therefore the "likely effectiveness... according to recognized peer-reviewed medical publications" is that there will be no benefits beyond those of a placebo.

With respect to "the extent to which it is consistent with conventional theories of medicine", this is also clear—homeopathy is biologically implausible and completely inconsistent with our understanding of medicine, biology, pharmacology and pathology.

Homeopathy does not have the support of the majority of medical practitioners, as demonstrated by the British Medical Association statement above and the 2006 New Zealand survey which found that most GPs say that it does not have benefits.2,3
Therefore in order for informed consent to occur according to the MCNZ statement, a doctor would have to say that:

- Homeopathy has no demonstrated benefits for patients other than placebo, and so recommending it is contrary to the MCNZ guidelines.
- The vast majority of doctors are opposed to homeopathy, often vehemently.
- There is no active ingredient in homeopathic products—it has all been diluted away.
- It is based on two false premises, that "like cures like" and that the more dilute a product, the more powerful it is.
- It is biologically implausible and completely inconsistent with our understanding of medicine, biology, pharmacology and pathology.

The authors of this letter consider that practicing homeopathy, or endorsing it by referring patients, is not consistent with the ethical or regulatory requirements of practicing medicine, and call for doctors to do neither.

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References:
2. [http://www.telegraph.co.uk/health/alternativemedicine/7728281/Homeopathy-is-witchcraft-say-doctors.html](http://www.telegraph.co.uk/health/alternativemedicine/7728281/Homeopathy-is-witchcraft-say-doctors.html) accessed on 24/3/11
Good smokefree law compliance in rural pubs in New Zealand: results from fine particulate (PM$_{2.5}$) air sampling

Background—There is extensive evidence that smokefree laws in New Zealand have been effective in reducing exposure to secondhand smoke (SHS). This applies to the law passed in 1990 and for the more recent revision of the law that became operational in 2004 (i.e., covering all of bars, pubs and restaurants). Other work suggests high compliance with the law for schools and early childhood centres. There are also survey data indicating majority public (and sometimes majority smoker) support for various new forms of smokefree laws.

Despite the evaluation work to date, there may still be concerns about the level of smokefree compliance in rural pubs in New Zealand. Internationally, living in a rural area may increase the risk of exposure to SHS. In a 2005 survey of New Zealand bar managers, the proportion supporting smoking bans in enclosed areas of pubs 11 months after a smokefree bar law was put in place, was stronger among managers of urban bars (65%) than for rural bars (49%).

Managers of rural bars were also more likely to view the legislation as having had a negative economic impact on their venue (73% compared with 44%; p<0.01), and they were more likely to agree that they would ignore the law if they could get away with it (35% compared with 19%; p<0.01). Some data from 2006 suggested good compliance in rural pubs, though this was based on only a small sample in two districts (see last row of Table 1).

So because rural bars appear to be one of the public settings most likely to still have smoking, we aimed to collect new data in such settings using an established approach to fine particulate sampling.

Methods—We took a convenience sample of 10 pubs in 6 North Island districts between November 2010 and March 2011 (see Table 1 for details). Most were in towns with populations of hundreds to a few thousand, with the largest town having a population of just under 10,000. In towns where there was a choice of pubs, we purposefully selected the most “traditional” style of pub (i.e. pubs focused more on serving alcohol and not a mix of meals and alcohol). The use of the air quality monitor followed a protocol modified from one developed for a global air quality monitoring project and which has been used in other New Zealand studies by the authors.

In the sampling, fine particulates were measured (PM$_{2.5}$, i.e. particulate matter ≤2.5 µm in diameter) using a portable real-time airborne particle monitor (i.e. the TSI SidePak AM510 Personal Aerosol Monitor, TSI Inc, St Paul, USA). The air monitor was carried hidden in a bag on the back of one of the investigators or placed on a seat or table wherever possible to sample the ambient air close to the breathing zone. A position near the centre of the main room of the pub was adopted for at least 30 minutes in each venue. To avoid affecting occupants’ behaviour, the investigators...
behaved discretely and as normal customers (i.e. purchased drinks and food) and were often with friends (i.e. total group sizes from 2 to 5).

A calibration factor (0.32) for SHS based on empirical validation studies with the *SidePak* monitor\(^\text{16}\) was applied (i.e. adjusted in the monitor’s internal settings). The monitor was zero-calibrated prior to each day of field work, was fitted with a 2.5 µm impactor, had an air flow rate of 1.7 L/min and had a logging period of 30 seconds. A length of Tygon™ tubing was attached to the inlet of the monitor, with the other end left protruding slightly outside the bag it was carried in.

In all the settings we discretely looked for evidence of smoking behaviour (actual observable smoking, the presence of ash trays and discarded cigarette butts). We also counted the number of customers in the pub and in any attached gaming area.

Ethical approval was obtained through the University of Otago (Category B ethics approval process) and the investigators were cognisant of the ethical issues involved in this type of research.\(^\text{17}\)

**Results**—The results indicate low values for fine particulate (PM\(_{2.5}\)) levels in the pubs with a time-weighted mean value of 8 µg/m\(^3\) and a range of maximum values of: 5–50 µg/m\(^3\) (Table 1). The highest mean level and the highest maximal level was in one of the two pubs where the investigators smelt tobacco smoke indoors (“Pub J”, see Table 1). In both these pubs there were open windows facing either the outdoor smoking area or the footpath where customers smoked (i.e., for “Pub I” that had no outdoor smoking area with seating).

In terms of observational data, in all the pubs surveyed there was no illegal indoor smoking observed and no other evidence of ash trays or discarded butts in indoor areas. Smoking was commonly observed in the outdoor smoking areas, and all but one pub had such an area (with at least some seating). One smoking area appeared to be extremely enclosed with walls on three sides, a roof and even a pool table.

**Discussion**—This study found no evidence of illegal indoor smoking and generally good air quality as indicated by measuring fine particulates (PM\(_{2.5}\)). These results are consistent with a 2006 study that included a survey of rural pubs,\(^\text{4}\) and suggests that compliance with the upgraded smokefree law has remained high 6 years after the implementation. The mean level of PM\(_{2.5}\) was very similar to that in a sample of traditional pubs and “sports bars” in Wellington (bottom row of Table 1).
Table 1. Results of air quality monitoring (fine particulates, PM$_{2.5}$) in 10 rural pubs in 6 North Island districts (November 2010 to March 2011)

<table>
<thead>
<tr>
<th>Setting</th>
<th>Mean PM$_{2.5}$ (µg/m$^3$)</th>
<th>Minimum PM$_{2.5}$ (µg/m$^3$)</th>
<th>Maximum PM$_{2.5}$ (µg/m$^3$)</th>
<th>Sampling time per venue (minutes)</th>
<th>Number of customers (mid-point of sample period)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pub A, Carterton District, Saturday, November 2010*</td>
<td>8</td>
<td>4</td>
<td>23</td>
<td>55</td>
<td>20</td>
</tr>
<tr>
<td>Pub B, South Wairarapa District, Saturday, November 2010</td>
<td>8</td>
<td>3</td>
<td>37</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Pub C, South Wairarapa District, Saturday, November 2010</td>
<td>9</td>
<td>5</td>
<td>40</td>
<td>146</td>
<td>45</td>
</tr>
<tr>
<td>Pub D, Waikato District, Sunday, December 2010</td>
<td>2</td>
<td>1</td>
<td>5</td>
<td>44</td>
<td>8</td>
</tr>
<tr>
<td>Pub E, Otorohanga District, Monday, December 2010</td>
<td>5</td>
<td>4</td>
<td>10</td>
<td>79</td>
<td>8</td>
</tr>
<tr>
<td>Pub F, Wairoa District, Saturday, March 2011</td>
<td>10</td>
<td>2</td>
<td>20</td>
<td>48</td>
<td>24</td>
</tr>
<tr>
<td>Pub G, Wairoa District, Saturday, March 2011</td>
<td>5</td>
<td>4</td>
<td>17</td>
<td>40</td>
<td>3</td>
</tr>
<tr>
<td>Pub H, Wairoa District, Saturday, March 2011</td>
<td>6</td>
<td>3</td>
<td>15</td>
<td>35</td>
<td>13</td>
</tr>
<tr>
<td>Pubs where smoke was smelt indoors (drift through open windows from outdoor smoking areas)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pub I, Waipa District, Saturday, December 2010</td>
<td>10</td>
<td>5</td>
<td>23</td>
<td>31</td>
<td>7</td>
</tr>
<tr>
<td>Pub J, Wairoa District, Saturday, March 2011</td>
<td>13</td>
<td>3</td>
<td>50</td>
<td>32</td>
<td>14</td>
</tr>
<tr>
<td>All pubs</td>
<td>Time-weighted mean: 8</td>
<td>Range: 1–5</td>
<td>Range: 5–50</td>
<td>Median: 42</td>
<td>Median: 14</td>
</tr>
<tr>
<td>All of the above pubs (n=10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comparison data from former studies (same type of air monitor)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Traditional pubs and “sports bars” (n=10, purposeful sampling in Wellington on Friday and Saturday nights in August/September 2010)</td>
<td>Mean: 12</td>
<td>Range: 2–15</td>
<td>Range: 4–57</td>
<td>Median: 30</td>
<td>–</td>
</tr>
<tr>
<td>Traditional style rural pubs in the Wairarapa and Carterton Districts (n=8) in June 2006</td>
<td>Mean: 17</td>
<td>Range: 1–16</td>
<td>Range: 5–109**</td>
<td>All 30 minute samples</td>
<td>–</td>
</tr>
</tbody>
</table>

Notes:
* Pub A was the only afternoon sample, all other samples were in the evening after 1800h and up to midnight for “Pub C”.
** The high particulate levels in one of these pubs may have been due to a rubbish fire that was observed burning just outside this pub, as well as the presence of a lit open fire indoors.
This picture of good smokefree law compliance is also consistent with the small number of prosecutions nationwide for breaches of the law since it was implemented in 2004 (n=5 as of August 2010). It is also consistent with the drop off in public complaints about smoking in smokefree areas in a national database following implementation of the new law (see Figure 3 in: Edwards et al). Furthermore, none of the authors have ever observing smoking inside rural pubs or restaurants in other New Zealand towns over the past six years (despite regular visits to such areas, including very remote pubs on road cycling holidays).

However, the evidence of tobacco smoke drifting indoors from “outdoor smoking areas” (via open windows) may be a problem in some settings, as previously noted for urban pubs. Similarly, the occurrence of highly enclosed “outdoor” smoking areas is also problematic in terms of health risks for workers and customers (which has also been reported for NZ urban settings). Therefore we reiterate previous suggestions that policy makers consider upgrading smokefree laws to reduce SHS drift from outdoor smoking areas to indoor areas and to further reduce SHS pollution levels in the “outdoor” smoking areas at hospitality venues e.g., by limiting smoking to 50% of the area or completely banning such areas entirely.

Of note is that this study has various methodological limitations, particularly the convenience sample, the small sample size and the potential for measurements being affected by fine particulates from open fires or cooking in venues that also served hot food (as per other work using the same monitor). Future studies could be larger and better address residual problematic aspects of highly enclosed “outdoor” smoking areas and the associated drift of smoke indoors.

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Competing interests: Although we do not consider it a competing interest, for the sake of full transparency we note that all the authors have previously worked for health sector organisations working for tobacco control.

References:


The apprenticeship model in 1842

At the present time, some young doctors are signifying that they are willing to accept assistance with fees in return for an offer of a bond that will require them to work for a specified period, and for a specified salary, in unpopular areas. No details have yet been revealed.

For many years, all of our veterinarians were trained in Sydney. The training was heavily subsidised. Ten new students went from here to the School each year, and no young man could afford an education in Australia without assistance. They were all bonded by the Veterinary Services Council to work upon graduation with Veterinary Clubs situated in or near farming areas. The Council was controlled by the Meat Board, the Dairy Board, and the Wool Board.

The demand for rural veterinarians was intense, and the bond lasted for 5 years. It was a simple deal. The graduates were well treated on their return to New Zealand, and they got plenty of help with housing and motor vehicles. A typical starting salary in 1956 was £800, of which £100 was deducted as part-payment of the student loan.

Trained and employed in this way in the 1950s was my old friend Pat Cooper. Pat went to Rotorua for several years. He was a well-known veterinary surgeon who had, in addition to his routine work, a strong association with the horse-racing industry.

The medical and veterinary professions were in his family, and Pat has loaned me a form of Indenture drawn up and signed when his great-great-grandfather, John Hankins, took up an apprenticeship with a veterinary surgeon in Hereford in 1842. It reads as follows:

This Indenture Witnesseth that John Hankins, of the Parish of Bartestree in the County of Hereford doth put himself Apprentice to Joseph Hall of the City of Hereford Veterinary Surgeon, to learn his Art, and with him after the manner of an Apprentice to serve from the day of the date hereof unto the full end and term of two years from thence next following to be fully complete and ended during which term the said apprentice his master faithfully shall serve, his secrets keep, his lawful commands everywhere gladly do he shall no damage do to his said master nor see to be done to others but to his Power shall tell or forthwith give warning to his said master of the same he shall not waste the goods of his said master nor lend them unlawfully to any he shall not commit fornication nor contract matrimony within the said term he shall not play at Cards or Dice Tables or any other unlawful games whereby his said Master may have any loss with his own goods or others during the said Term without licence of his said master he shall neither buy nor sell he shall not haunt Taverns or Playhouses nor absent himself from his said master’s service day or night unlawfully.

But in all things as a faithful Apprentice he shall behave himself towards his said Master and all his [obscured] the said Term And the said Joseph Hall in consideration of the sum of ninety-eight pounds lawful money of the United
Kingdom of Great Britain and Ireland to him in hand well and truly paid by
the said John Hankins on or immediately before the execution of these
presents his said Apprentice in the Art of a Veterinary Surgeon which he useth
by the best means that he can shall teach and Instruct or cause to be taught and
instructed Finding unto the said Apprentice sufficient Meat Drink and Lodging
and all other necessaries during the said Term(wearing apparel and washing
excepted) and the said John Hankins hereby agrees at the expiration of the said
term not to practice the Art of a Veterinary Surgeon in the said City of
Hereford or within fifteen miles thereof without the consent in writing of the
said Joseph Hall first had and obtained And for the true performance of all and
every the said covenants and Agreements either of the said parties bindeth
himself unto the other by these Presents In Witness whereof the parties above
named to these Indentures interchangeably have put their Hands and Seals the
ninth day of April and in the fifth year of the Reign of our Sovereign Lady
Queen Victoria by the Grace of God of the united Kingdom of Great Britain
and Ireland QUEEN and Defender of the Faith and in the Year of our LORD
One Thousand Eight Hundred and Forty-two.”

Both John Hankins and Jos. Hall signed the document in an educated hand and
affixed a red wax seal that is still stuck to the paper in front of me. The bureaucracy
got its cut. Registration of this simple document cost 3 pounds—getting on for a
month’s wages for a ploughman.

John Hankins
Hankins was from a well-to-do family. The fee of £98-0-0 for the 2-year apprenticeship as a veterinary surgeon (with accommodation provided) would have been more than the total earnings of a labourer over the same 2-year period at that time. At that time, a field labourer would have been lucky to get half-a-crown a day. There were 784 half-crowns in £98-0-0.

Hankins emigrated to Canterbury in 1863 with his wife and 10 children. He was the first veterinary surgeon in Canterbury and he helped found the Canterbury Jockey Club. He died in 1911.

Roger M Ridley-Smith
Retired GP
Wellington
Epidemic strains of *Clostridium difficile* are present in Auckland, New Zealand

The emergence of highly virulent strains of *Clostridium difficile* in North America,\(^1\) Europe\(^2\) and more recently Australia\(^3\) is of concern. In particular, outbreaks of severe *C. difficile*-associated diarrhoea or disease (CDAD) have been caused by the epidemic, hypervirulent strain termed PCR-ribotype 027 or NAP-1.

This strain is associated with:

- The presence of a binary toxin (for which the role is not clear),
- Resistance to fluoroquinolones, and
- Increased toxin production.

Increased toxin production in PCR-ribotype 027 is putatively due to a mutation in the *tcdC* gene which regulates expression of the toxin genes themselves. Increased toxin production may help to explain the association between the PCR-ribotype 027 strain and both severe disease and increased mortality. Another strain, PCR-ribotype 078, found to be present in livestock, has also recently been associated with severe CDAD.\(^4-6\)

Until recently, little was known about the strains of *C. difficile* circulating in New Zealand.\(^7\) A survey in 2009 of 101 isolates from across New Zealand did not demonstrate the presence of PCR-ribotype 027. However, one year later, we describe two patients from Auckland hospitals confirmed to be infected with epidemic strains of *C. difficile* (see Table 1).

Notably, neither of the patients had a history of recent travel or hospitalisation overseas, raising the possibility that these strains have already become established within a reservoir of asymptomatic carriers in the Auckland area. The patient with PCR-ribotype 078 lived in a rural setting but did not have contact with farm animals.

A recent review identified a number of independent risk factors for disease due to *C. difficile* PCR-ribotype 027 including: age greater than 65 years, presence of comorbidities, current or previous admission to hospital and sharing an environment with other people infected with *C. difficile*.\(^8\)

In contrast, PCR-ribotype 078 appears to be associated with a younger age group and community-onset infections. Contact with animals may be a factor in acquisition of infection with this strain as it can cause colitis in piglets and calves.\(^4\)
In the preceding 1-month period, *TECHLAB® C. diff Quik Chek Complete™* rapid membrane enzyme immunoassay for simultaneous detection of *Clostridium difficile* glutamate dehydrogenase antigen and toxins A and B and *Cepheid Xpert™ C. difficile* PCR assay (Cepheid, Sunnyvale, CA, USA)

# CLSI methodology for MIC agar dilution determination

§ PCR-ribotyping and sequencing of the *tcdC* gene performed as previously described. Both isolates had the truncating mutations and deletions in the *tcdC* gene typically associated with each of the ribotypes.

Table 1. Characteristics of patients with epidemic strains of *C. difficile*

<table>
<thead>
<tr>
<th>Age (years) and Gender</th>
<th>Comorbidities</th>
<th>Recent antibiotic use*</th>
<th>Diagnostic test^</th>
<th>Minimum inhibitory concentration (mg/L)#</th>
<th>Strains§</th>
<th>Disease severity and outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>72 Female</td>
<td>Pancreatitis secondary to gallstones</td>
<td>Amoxicillin/ clavulanate</td>
<td>EIA and PCR</td>
<td>moxifloxacin &gt;32, clindamycin &gt;32</td>
<td>PCR-ribotype027</td>
<td>Diarrhoea resolved after treatment with metronidazole</td>
</tr>
<tr>
<td>24 Female</td>
<td>Chronic respiratory illness with bilateral lung transplant</td>
<td>Ciprofloxacin, co-trimoxazole and azithromycin</td>
<td>EIA</td>
<td>moxifloxacin 1.0, clindamycin 1.0</td>
<td>PCR-ribotype078</td>
<td>Recurrent diarrhoea, this episode resolved after treatment with metronidazole followed by vancomycin</td>
</tr>
</tbody>
</table>

* In the preceding 1-month period
^ *TECHLAB® C. diff Quik Chek Complete™* rapid membrane enzyme immunoassay for simultaneous detection of *Clostridium difficile* glutamate dehydrogenase antigen and toxins A and B and *Cepheid Xpert™ C. difficile* PCR assay (Cepheid, Sunnyvale, CA, USA)
# CLSI methodology for MIC agar dilution determination
§ PCR-ribotyping and sequencing of the *tcdC* gene performed as previously described. Both isolates had the truncating mutations and deletions in the *tcdC* gene typically associated with each of the ribotypes.
It is important for clinicians to be aware of the strengths and limitations of laboratory testing for *C. difficile*. A recent survey of both hospital and community laboratories across Australia and New Zealand showed that the majority of laboratories use methods with relatively low sensitivity for *C. difficile* infection. Widely used methods such as enzyme immunoassays (EIA) and immunochromatographic tests have the advantage of being rapid and easy to perform but only have a sensitivity of 70-80%.

These assays usually directly detect the toxin itself. A second antigenic target known as glutamate dehydrogenase (GDH) increases sensitivity but is present in both toxigenic and non-toxigenic (non-pathogenic) strains of *C. difficile*. Thus, whilst the sensitivity of EIA for detecting GDH is very high, their specificity is relatively poor. For this reason, detection of GDH without detectable toxin can be a difficult test result to interpret. To address this difficulty, a two-step testing algorithm has been suggested in a recent review.

This two-step testing algorithm was introduced at LabPlus in early 2010. Firstly an EIA on faecal specimens for simultaneous detection of GDH and toxins A and B (TECHLAB, Blacksburg, VA, USA) is used. Detection of GDH and toxins A and B is reported as positive.

Subsequently any GDH positive but toxin negative specimens are tested using the Xpert™ *C. difficile* polymerase chain reaction (PCR) assay (Cepheid, Sunnyvale, CA, USA). Although this latter assay is considerably more expensive than the EIA and for this reason is not used on all specimens submitted for *C. difficile* testing, it has markedly superior sensitivity to EIA based methods.

Finally, for epidemiological purposes, *C. difficile* is cultured from faecal specimens that test positive for toxin and referred to the Institute of Environmental Science and Research for PCR-ribotyping, detection of toxin genes, and sequencing of the tcdC gene to detect mutations associated with up-regulation of toxin production in PCR-ribotypes 027 and 078.

The identification of these epidemic *C. difficile* strains should prompt diagnostic laboratories in New Zealand to optimise their testing algorithms for *C. difficile* and a laboratory-based surveillance programme for *C. difficile* is required. At the clinical level, these findings should heighten awareness of *C. difficile* as a cause of diarrhoea and should prompt clinicians to become more aware of the strengths and weaknesses of laboratory testing for this organism.

CDAD should be tested for in patients with healthcare contact who develop diarrhoea either in hospital or after discharge and also in non-hospitalised patients with diarrhoea in whom other causes for infective gastroenteritis have been excluded.

Finally, further work needs to be done to establish the link between PCR-ribotype 078 and animals. Given the large nature of the agricultural sector, this association may be particularly relevant in New Zealand.

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Background prevalence of extended-spectrum β-lactamase-producing *Enterobacteriaceae* in the Auckland community

Over the past decade the isolation of extended-spectrum β-lactamase-producing *Enterobacteriaceae* (ESBLPE) has gone from being novel to uncomfortably common in Auckland’s three public hospitals. The Institute of Environmental Science and Research’s (ESR’s) 2009 survey of ESBLPE reported an annualised incidence rate of 431 people with ESBLPE per 100 000 population for the three Auckland district health boards (DHBs).\(^1\)

To determine the background prevalence of ESBLPE colonisation in the Auckland community we performed the following study. The local ethics committee approved this study and an education grant from Merck Sharp and Dohme covered the laboratory costs.

The first 75 faeces (equally distributed between four age groups: 0–15 y, 16–40 y, 41–65 y and >65 y) submitted to Diagnostic Medlab each month from February to July 2009 (inclusive) for diagnostic testing of any kind were also cultured for ESBLPE. A portion of faeces was incubated overnight in cefotaxime 2 mg/L MacConkey broth (Fort Richard) and sub-cultured onto chromogenic agar (ChromID ESBL, BioMérieux).

Oxidase-negative, non-fermentative, Gram-negative bacilli were tested for extended-spectrum β-lactamase (ESBL) production by combination disc diffusion tests using ceftazidime, cefotaxime and cefpirome with and without clavulanic acid. Any isolates with an ESBL phenotype were identified by the Vitek-2 GN card and susceptibilities performed using the AST GN-25 card (BioMérieux).

Growth of any enteric pathogens from the faeces was recorded in addition to the following patient demographic data: age, gender, hospital admission within the last 12 months, and long-term-care facility (LTCF) residency. Patients were counted only once, and where a patient had more than one specimen submitted, if at least one specimen grew ESBLPE, that patient was considered to be colonised.

During the six-month study period 1799 specimens were received from 1691 patients; 44.1% were male and 2.1% were residents of a LTCF. ESBLPE were identified from 92 (5.1%) of the specimens. *Escherichia coli* accounted for 76 (82.6%) of the 92 ESBLPE isolates, *Klebsiella pneumoniae* for 10 (10.9%) and *Enterobacter cloacae* for 6 (6.5%). Percentage antibiotic susceptibilities were as follows: gentamicin 52%, ciprofloxacin 38%, cotrimoxazole 18%, and nitrofurantoin 70% (83% of *E. coli* and 6% of *Enterobacter* and *Klebsiella* species). All ESBLPE were susceptible to amikacin and carbapenems.

To further characterise the ESBL types among these isolates, 38 available isolates underwent molecular analysis at ESR. Isolates were tested for CTX-M-type ESBL by PCR; negative isolates were then tested for SHV-type ESBL; isolates negative for both CTX-M and SHV ESBLs were tested for TEM-type ESBL. Thirty-five isolates were identified with CTX-M-type ESBLs (21 CTX-M-15, 9 CTX-M-14, 3 CTX-M-
The remaining three non-CTX-M-type ESBLs identified were all SHV-12.

Possible factors (age, DHB of domicile, gender, LTCF residency, concurrent isolation of enteric pathogen and hospital admission in the previous 12 months) impacting the likelihood of ESBLPE carriage were examined. A multiple regression model identified male gender (relative risk 3.0 [95% confidence interval 1.4–6.6]) and LTCF residency (19.8 [7.0–56.2]) as independently associated with ESBLPE. A trend to significance was seen with enteric pathogen isolation as a single factor (1.6 [0.9–3.0]). The finding that being a LTCF resident was highly associated with carriage is consistent with results of studies of community-acquired ESBLPE infection in Auckland and elsewhere. We did not find an association with hospital admission (to the three Auckland DHB hospitals) in the previous 12 months which is consistent with community spread independent of some traditional risks for multi-resistant organisms. The association with male gender is interesting; it has been found to be a risk factor in only some studies.

Isolation of an enteric pathogen was more common among ESBL-positive stools, although this was not statistically significant. The presence of an enteric pathogen suggests ingestion of contaminated food or water; this is a possible route of acquisition of ESBLPE in addition to the enteric pathogen. Symptomatic infection with an enteric pathogen may also facilitate spread of ESBLPE in the community, particularly among household members and LTCF residents. There is increasing evidence that the food chain may be an important source of ESBLPE.

We were not able to analyse ethnicity or travel data. However, there is evidence that ESBLPE in the Auckland community may be at least partly due to importation from overseas, in particular, the Indian subcontinent. Another postulated source is contact with animals.

This is the first study of ESBLPE colonisation in the Auckland community and it has identified the presence of ESBLPE colonisation in our community. The prevalence is relatively low compared with the rates reported elsewhere, particularly Spain, Asia and the Indian subcontinent. ESBLPE colonisation in the community is clinically significant for the empiric treatment of community-acquired *E. coli* urinary tract infection as well as infection control policy, especially in LTCF.

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Time for a rethink of vitamin B12 injections?

Vitamin-B12 (B12) deficiency is seen in two populations: those with food-bound B12 malabsorption and those with inadequate dietary B12 intake (common in populations with low or non-meat eating dietary practices).¹

In the first situation, traditional treatment has been high-dose intramuscular (IM) B12 injections² and in the second situation oral supplementation is a logical treatment. In practice, however, a number of these people are also being treated with IM B12 injections. Is this practice appropriate?

Vitamin B12 deficiency is important to treat, or ideally prevent, as it is associated with the risk of megaloblastic anaemia plus cognitive and neurological deficits.³,⁴ Even with borderline B12 deficiency, concentrations of the metabolite homocysteine, a documented risk factor for cardiovascular disease, are increased.⁵,⁶

B12 interacts with folate in critical metabolic pathways; they are co-factors in the ubiquitous one-carbon metabolism and the balance between these two co-factors is important.³,⁵ Elevated levels of folate can intensify the physiological effects of B12 deficiency more than if folate levels were normal and B12 levels low.³ Of particular concern are the effects of raised homocysteine concentrations and B12/folate imbalances on pregnancy outcomes such as early pregnancy loss, prematurity, low birth weight⁷ and neural tube defects.⁷,⁸

Clinicians are aware that folic acid supplementation in pregnancy is important to reduce the risk of birth defects, but it is not well recognised that if a woman has low B12 stores, giving folic acid augments the effects of low B12 on the foetus.⁶ Maternal B12 deficiency predicts increased abdominal adiposity, early signs of insulin resistance,⁹ and diminished cognitive performance in offspring.⁴ These effects are more pronounced with high maternal folate and low B12.⁹ In the opposite situation of relative B12 excess, it is not known if there are adverse effects. However, it would seem prudent to avoid increasing B12 concentrations much higher than is physiologically required.

In a current AUT University study (ANZCTR:ACTRN12610000262000) investigating the efficacy of oral B12 supplementation for Indian women of child-bearing age, 5 out of 63 women were withdrawn or excluded because they received out of protocol IM B12 injections by their general practitioner. Following administration of the IM injections, serum B12 measurements exceeded 1476 mcg (the maximum laboratory measurement limit and significantly above the 800 mcg upper limit of normal). One woman reported persistence of this elevated serum B12 measurement at 18 months after injections.

The recommended dietary intake for B12 is 2.4 mcg/day.¹⁰ In B12 deficiency due to inadequate intake, transport proteins for B12 absorption are increased and enterohepatic recycling of B12 is more efficient. B12 deficiency from inadequate intake is not as profound as deficiency secondary to B12 malabsorption.¹ When
gastrointestinal absorption of B12 is intact, increased dietary intake of B12 or low-dose oral B12 supplements are effective to increase serum B12.

In a 2009 study on oral B12 supplementation in India, daily doses of 2 mcg and 10 mcg over a 12-month period resulted in 64% and 119% increases respectively in serum B12 with a large reduction in homocysteine concentrations.6

Research evidence supports the therapeutic efficacy of oral B12 supplements (commonly cyanocobalamin) for treating deficiency, even in those with B12 malabsorption.2 Transport proteins, such as intrinsic factor, are required to absorb 95–99% of a physiological load of B12 (1.5–3 mcg), while the balance is absorbed by passive diffusion.1,2 Transport proteins for vitamin B12 are fully saturated at approximately 1.5–3 mcg, but the amount absorbed via passive diffusion increases with higher doses.1

Even with malabsorption, sufficient B12 can be absorbed orally via passive diffusion if the dose is high enough.2 Unlike food-derived B12 which is released from the food matrix by acid hydrolysis, cyanocobalamin exists as free B12. This is advantageous for people with low levels of gastric acid and food-bound B12 malabsorption (the commonest form of B12 malabsorption).1

Changing cultural demographics in New Zealand, trends towards vegetarian or vegan dietary preferences and the high costs of meat, fish and dairy products all exacerbate the population-risk of B12 deficiency secondary to inadequate intake. It is important to consider whether inadequate intake is the cause of B12 deficiency. If so, then low-dose oral supplements and dietary advice to increase B12 intake are more appropriate than high-dose B12 injections.

Issues such as low compliance with oral supplements or dietary advice, a preference for IM injections and the lack of a PHARMAC-funded oral B12 supplement need consideration. However, these are offset by a decrease in the discomfort and inconvenience associated with IM injections and greater autonomy for patients with being able to maintain a regular intake of B12 without the excessive serum B12 increases created by high-dose IM B12 injections.

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References:

The Plunket Nurse: part 2


Under the new system, the Plunket nurse becomes the family adviser, and illustrates and expounds the medical man's words. Which would you rather, Sir, the grandmother or a trained nurse to interpret and carry out your instructions?

If we as a profession take advantage of the services of the Society, there is a reasonable prospect of a stock of healthy children growing up in the dominion to take our places; and there is more than, a chance that summer diarrhoea, that dirt disease, fostered by the carelessness and ignorance of those who have charge of babies, may be chocked at its origin. It is not, so checked at present, in spite of the efforts of the profession; for it is a truism that the death-rate from this disease is somewhat of a reproach to us. Will not the medical profession, in accordance with the noble traditions it claims, assist in this national work, even if by so doing its own income lessens as the incidence of disease decreases?

Florence Nightingale, in her "Notes on Nursing for the labouring classes," said: "A really experienced, and observing nurse neither physics herself nor others. And to cultivate, in things pertaining to health, observation and experience, in women who are mothers, governesses or nurses, is just the way to do away with amateur physicing; and, if the doctors did but know it, to make the nurses obedient to them—helps to them instead of hindrances. Such education in women would indeed diminish the doctor's work—but no one really believes that doctors wish that there should be more illness, in order to have more work."

This was written half-a-century or so ago. It seems to me to apply to the case now under discussion, and to be worth more than a passing thought.

Holding as I do these views about the Society's work, you will understand, Sir, that I contend that the recent action of the Branch Council in endeavouring to force the Society to restrict its work to the needy, is hasty, ill-advised, and difficult to apply; amid this view I placed as strongly as I could before a recent special meeting of the South Canterbury Division. It appears to me to have been a hasty action, as the Divisions were not previously consulted as to that particular point. If my view of the Society's work, that it is educational, is correct, it is certainly very ill-advised to limit it to the needy.

The need for education in these matters does not necessarily diminish with increase of income, and it seems to me that if our better class patients express a wish to have the advantage of this education at the hands of the Plunket "nurse," our refusal to allow it will arouse considerable hostility. If the work of the "nurse" is helpful, why, logically, are such patients not to have her? Perhaps, in the future, there may be private nurses to be had with a similar training.
At present, in Timarn at least, I know of none. If the work of the "nurse" is harmful, we are neglecting our needy patients if we allow her to work evil among them. Logically, we must either declare that we refuse all help from her, or we must accept her help for all classes. Lastly, this action of the Council is difficult to apply, because not only is the definition of "needy" patient very difficult, but also it is difficult to see how those medical men who believe that it will be in the best interests of their patients to employ the Plunket "nurse" are to be coerced into acting contrary to their opinions.

I now wish to say that, though I wish to see the Society's work approved by the medical profession, find myself on different ground when we approach consideration of the district nursing scheme so ably advocated by Dr. Valentine. As I understand it, these nurses are to act not only as Plunket nurses, but are also to give ordinary nursing, and, on occasion, to attend confinements, for any, rich or poor, who contribute towards her salary. Here, indeed, we may find real menace to the nursing and medical profession:

It opens an easy path to the abuses we see described in the British Medical Journal with regard to the working of the Rural District Nursing Associations in England, where there apparently has been an extension of the lodge system of attendance by contract from the medical profession to the nursing profession. In some parts of England the doctor is called to a midwifery case only after the nurse has done her best, or her worst, and is expected then to shoulder the responsibility of the case.

The New Zealand scheme is described by its ingenious advocate, whose fixed salary has made him forgetful of the struggles to live the make up the lives of the private doctor and nurse, as back-blocks scheme.

Why, then, is it to be put into operation at Hastings? I understand Hastings to be no inconsiderable place. Certainly, it is not a back block. At least, it boasts eight doctors or so, I am told—who will soon be able to tell us how they appreciate nurses, subsidised by the Government (v. "Otago Daily Times," 31/8/10), independent of their criticise working among their patients, nursing, giving advice not only on the feeding and care of the baby, even attending midwifery cases. The prospect pleases, and I commend it to the scrutiny of two noble professions that have their living to make.—I am, etc.,

L. S. TALBOT, F.R.C.S., Eng.
Timaru,
1st September, 1910
Which long-acting bronchodilator is best for moderate/severe chronic obstructive airways disease (COPD)?

Treatment guidelines recommend the use of inhaled long-acting bronchodilators to alleviate symptoms and reduce the risk of exacerbations in patients with moderate to very severe COPD. This report concerns a randomised trial which compared the effect of treatment with 18µg of tiotropium inhaled once daily with that of 50µg of salmeterol inhaled twice daily.

Over 7000 patients were randomised to either the long-acting anticholinergic tiotropium or the long-acting β-agonist salmeterol. After 1 year, the tiotropium was found to be significantly better in preventing exacerbations. Serious adverse effects were similar with both drugs. The downside for NZ patients is that the tiotropium treatment is about 2.5 times more expensive and requires a Special Authority for subsidy.


Is there an interaction between amoxicillin/clavulanic acid (amoxiclav) and warfarin that could harm patients?

Several case reports and retrospective studies have suggested that amoxiclav may interact with warfarin and lead to an increased INR and bleeding. This prospective randomised study reviewed 12 patients who were anticoagulated with warfarin and had a stable INR between 2 and 3. Half were treated with a week’s course of amoxiclav and the other half a week’s placebo in addition to their usual warfarin. The INR was tested on days 0, 3, 5, 6, 7 and 10 and the warfarin plasma concentration was assessed on days 0 and 7. Amoxiclav was not found to modify either the INR or the plasma concentration of warfarin.


Aromatase inhibitors (AI) vs tamoxifen in the management of oestrogen receptor positive breast cancer

Both tamoxifen and the AI have been proven to be valuable in the management of oestrogen receptor positive breast cancer in the post menopausal patient. The third-generation aromatase inhibitors anastrozole, exemestane and letrozole have been shown to be superior to tamoxifen in terms of disease-free survival (delayed recurrence) but have not been shown to improve overall survival.

This paper and an accompanying editorial note that the AI have overtaken tamoxifen in Australia and review the implications. The adverse effects come into consideration — tamoxifen increases the risk for thrombostasis and endometrial cancer whereas the AI can cause arthralgia and increased risk of fractures due to a decrease in bone mineral density.
Tamoxifen is cheap, costing (in NZ) about $40 pa whereas the AI range between 8 and 50 times more expensive. The editorial writer points out that the cost of managing the adverse effects of the AIs would probably exceed the management costs of the tamoxifen adverse effects.


C-reactive protein concentration (CRP) and the vascular benefits of statin therapy

It is widely believed that an elevation of the serum CRP is associated with the risk of coronary heart disease, ischaemic stroke and vascular and non-vascular mortality. Conversely, some believe that statin therapy might be ineffective in people with low concentrations of both CRP and LDL cholesterol.

This study looks at data from the records of 20,536 men and women aged 40–80 years at high risk of vascular events randomly assigned to simvastatin 40mg daily versus matching placebo for a mean of 5.0 years. Benefits from the treatment were analysed with respect to the pretreatment CRP and LDL cholesterol levels.

Overall, the simvastatin-treated patients had a significant 24% proportional reduction in major vascular events compared with the placebo patients. In particular, there was clear evidence of benefit in those with both low LDL cholesterol and low CRP (27% reduction). The benefit was seen even in those whose CRP was <1.25mg/L (29% proportional reduction). So the CRP level is not very useful in these circumstances.


Is there a link between enterovirus infection and type 1 diabetes mellitus?

Observational studies suggest that this is possible and this systematic review tries to elucidate. The authors review 33 controlled studies, 9 in pre-diabetic subjects and 24 concerning patients with an established diagnosis. Proof of infection was obtained by measuring enterovirus RNA or viral protein in the blood, stool or tissue of the subjects.

They report a significant association between enterovirus infection and type 1 diabetes-related autoimmunity. So there is an association, but is the association causal or casual? Other factors, particularly genetic, would probably be involved. If the association is causal, should those at risk be immunised against the virus?

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Malcolm Bryce Gunn

20 December 1923 – 27 March 2011

Dr Malcolm Bryce Gunn (Bryce) spent the greater part of his professional life in Cambridge, Waikato. He was born in Christchurch, the oldest son of Harold (Joe) and Mafeking Baden Gunn (Mafie).

At the time birth, his father had been sent to Christchurch from Wellington where he was employed as a health administrator for the Department of Health. From Christchurch they eventually moved back to Wellington.

Bryce started at Wellington College in 1936 and was the youngest enrolled pupil and therefore ended up completing 7 years of secondary school. At Wellington College he played cricket and hockey and was in the First XI for both from the 5th form.

In his final year at school, Dad was both Head Prefect and the Captain of the Hockey First XI.

After his last year at school, he was conscripted into the army at Linton. There he learnt to use the anti aircraft guns and spent some time defending Rongotai Air Base (now Wellington Airport).

In 1944 he studied for the medical intermediate at Victoria University and then entered Otago Medical School in 1945. While at Otago he played hockey and golf for the university and gained a New Zealand University Blue in hockey. He finished at Otago in 1949 and graduated in 1950 being capped at Victoria as a graduate of Otago University. While at University he married Meredyth, a fellow medical student (Dr Meredyth Colston Gunn). In 1950 Bryce started his house officer years at Palmerston North and remained there completing 1 year as a medical registrar.

In 1953 they left Palmerston North and Bryce became the sole GP in Coromandel. At that time it was considered remote. The roads were unsealed and there were frequent washouts and slips and when it rained heavily the town was often cut off. There was a large rural Marae-based population and once-a-month Bryce would visit the settlements at Colville, Port Charles, Kennedy Bay and Fletcher Bay. There was a lot of obstetrics and he also delivered Whitianga. He was frequently the ambulance as well—as people needed transfer so they would be put in the car and bought back to the hospital in Coromandel. When they left Coromandel, Dad was thanked for supporting the establishment of the local ambulance service.
After 5 years in Coromandel they started a practice in Cambridge. At that time there were 4 doctors in town and as was the custom of the day the medical rooms were attached to the house. He eventually moved the practice into the house next door. He was the quintessential family doctor involved in all aspects of family health: deliveries, elder care and child health. He did not run an appointment system so patients turned up and waited.

Following the break-up of their marriage in 1973, Dad remained in Cambridge and a few years later married Dot Howarth and became stepfather to Rebecca. He remained in practice until the 1990s when computerisation was required. He remained the Medical Officer at the Cambridge Harness Racing Club until 2007.

He was actively involved in several sporting clubs in Cambridge. He was the President of the Cambridge Golf Club, the Patron of the Cambridge Cricket Club; in addition he was a member of the Cambridge Bowling Club and a life member of the Cambridge Harness Racing Club. He was also a councillor for one term and was involved with the St John’s Ambulance.

He had a number of chronic health problems over the past decade but his final illness was brief. He is survived by his wife Dorothy; four children, Graeme, Diana, David, and Cynthia (Cindy); and step daughter Rebecca.

Prof Cindy Farquhar (Postgraduate Professor of Obstetrics and Gynaecology, University of Auckland), his youngest daughter, wrote this obituary.
Alastair Fleet Burry

Dr Alastair Burry once wrote: "On the whole, I do not like myself very much". He confessed to being "hasty, arrogant, intolerant, opinionated and sarcastic".

Others would judge him more kindly as an endlessly interesting character. He then described his drift into old age, like a plea in mitigation.

"Irritability is common in old men. I am certainly irascible… I become almost incoherent with rage" (when advertisements interrupt quality television), he wrote.

Will Sky TV soon pause coverage of a rugby match, as the ball is to be thrown into a lineout, to make a plug for Viagra, he asked?

The Christchurch pathologist and controversialist died recently. He was 84. Burry was one of two sons of a Gallipoli veteran who introduced his family to camping, fishing and hiking. Both sons maintained these pursuits, but only one inherited athletic ability—younger brother Hugh, a 1960 All Black.

Raised in comfortable circumstances at Riccarton, Burry attended Fendalton Primary School and Christ's College. He felt burdened by his mother's ambition for him and "dreaded failure".

He hated taking orders from anyone, but abandoned his dream of being a journalist for a career in medicine—at her behest. Otherwise, his childhood and adolescence were idyllic. He fuelled his imagination with reading, enjoyed College, had many friends, loved holidays on his uncles’ farms and revelled in honest sweat on vacation jobs.

Passing his medical intermediate year at the University of Canterbury qualified him for entry to Otago Medical School in 1944. However, a prolonged bout of rheumatic fever forced him to take 2 years' leave. In the second year, he worked in the veterinary laboratory at Lincoln College. There he mastered skills he would use later as a pathologist.

Graduating from medical school was delayed by having to resit some exams. He was also criticised for his bedside manner and warned: "A non-clinical career might be advisable".

Burry remembered the warning when he completed his house surgeon year in Christchurch. He chose to pursue pathology. In the 10 years from 1952, he rose from registrar to junior specialist (on acceptance of his Doctor of Medicine thesis) to pathologist-in-charge at Princess Margaret Hospital.
These years included 9 months of study and work in London, during which he expanded his appreciation of music and drama. Back from this trip in 1958, he married pathology technologist Jill Leech, of Rangiora. Their first two children were born in Christchurch, and the next three in Brisbane, where Burry became anatomical pathologist at Princess Alexandra Hospital in 1963.

Appointment as director of pathology at Royal Brisbane Hospital in 1967 meant a three-month tour of hospitals in the United States, Sweden and Britain to inspect the latest equipment and organisational structures. He was elected a Fellow of the Royal College of Pathologists in 1964 and was Queensland's councillor on the Australasian college.

Frequent visits to New Zealand during their 13 years in Brisbane convinced the Burrys to move home to a lifestyle farm. They managed near self-sufficiency on a six-hectare block at Clarkville.

Burry served as anatomical pathologist at Christchurch Hospital from 1977 and worked part-time in private practice. He retired from the hospital in 1990 but continued in practice until 1994.

The Burrys' eldest son, Matthew, was killed in a climbing accident on Mt Rolleston in 1983. Soon after, the family moved to a smaller farmlet near Halswell. Burry immersed himself in extra-mural studies for an Arts Degree in English Literature and French. He and Jill enjoyed their large garden and orchard and trips around New Zealand in their campervan. But Jill died of cancer in 1997.

Burry moved into Christchurch in 1999. He was an enthusiastic golfer, but a hit in the eye by a golf ball forced him to give up playing. He wrote the history of the Christchurch Golf Club and took up bowls and bridge.

He also crafted letters to the editor of The Press on a wide range of subjects. His letters mostly reflected conservative values, expressed with barbed wit. They echoed the clarity of style evident in his many lectures, speeches, medical papers and chapters for text books.

Long ago, as a young doctor in Christchurch, Burry had delivered meals-on-wheels to the needy. At last, his health declining, he accepted a return of the favour.

Alastair Fleet Burry, born Christchurch, December 8, 1926; died Christchurch, March 21, 2011. Predeceased by wife Jill and son Matthew; survived by daughters Celia, Ruth and Kate, son Cameron and eight grandchildren.

Mike Crean of The Press wrote this obituary (9/4/11); we thank them for the reprint permission.
Soul Matters: the spiritual dimension within healthcare


‘Holistic’ is a term that is bandied about these days in regard to holistic health, holistic healthcare and even holistic lifestyles.

Mabel Aghadiuno is a general practitioner in London and through this book informs and challenges all healthcare professionals to consider the multifaceted needs of their patients. Here she majors on the spiritual dimension of health and illness.

She is widely read and weaves together sources as diverse as recent research and classical literature, patient narratives and her own clinical experience. In Chapter 1 Aghadiuno gives a broad picture of health and illness, arguing that we must consider much more than the physical dimension (the ‘biomechanical model’) but also the social, psychological, cultural and spiritual components.

From several sources Chapter 2 supports the case for the spiritual dimension in all of us. Then in ‘The neglected dimension of health’, the spiritual one is considered, the author challenging that it is not just important to the ‘palliative care team or the psychiatrist’.

Agadiuno also practices homeopathic medicine; this emphasises ‘every aspect of the patient is important’ and it sits well in this book—it is her book! I have questions as to its connection with the spiritual dimension.

‘Patient narratives’ (Chapter 4) can reveal key aspects of their spirituality in their suffering and how they cope with this. Obtaining stories is time-consuming but after all this is “history taking”. In this context the author acknowledges the role that the chaplain may fill in the healthcare team. Chapter 5, ‘Spiritual Distress’ may be important in a patient’s illness and may ‘generate symptoms’. Its recognition is important. In assessing this and the other dimensions of illness the healthcare worker must relate to their patient as a person, ‘never merely as a clinical case’.

The author concludes with extracts from Chiara M’s life story and journey through a chronic debilitating illness—illustrating the spiritual dimension and how vital it was to her. This book is a good read but not an easy read. It is a strong statement for person-centred care whether we agree or disagree that soul matters, matter.

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