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This Issue in the Journal

**Prevalence and risk factors for *Chlamydia trachomatis* infection in female New Zealand university students**

M Baker, J Ortega-Benito, N Garret, C Bromhead, K Leslie, J MacDonald, A McNicholas

*Chlamydia* is the most commonly diagnosed sexually transmitted infection in New Zealand. This research offered *Chlamydia* testing, using a urine specimen, to female students aged 18–25 years attending a university student health service in 2003. It found that 2.7% (19 out of 715) were infected with this bacteria without knowing it. It also found that a majority (60%) of students were willing to participate in this screening programme. This study provides more evidence that New Zealand needs an adequately resourced and evidence-based *Chlamydia* control strategy. This strategy should contain guidelines on screening in a range of settings, including universities, as well as approaches for preventing *Chlamydia* infection.

**Low birth weight and cardiovascular risk factors in Auckland adolescents: a retrospective cohort study**

B Daly, R Scragg, D Schaaf, P Metcalf

The proposal, that poor fetal development (such as low birth weight) is associated with increased cardiovascular disease risk later in life, was examined in 855 hospitals-born Auckland adolescents. We found that blood pressure, blood cholesterol, and blood glucose levels were unrelated to low birthweight but positively associated with current adolescent weight. These results indicate that prevention of cardiovascular risk factors in adolescence should focus on lowering current weight rather than trying to achieve higher births weights among at-risk populations.

**Coeliac disease diagnosed at Starship Children’s Hospital: 1999–2002**

E Westerbeek, S Mouat, A Wesley, S Chin

Coeliac disease is a condition caused by an inability to digest gluten, which often results in bowel symptoms, weight loss, or failure to gain weight. It is relatively common in New Zealand. Our study reviewed the clinical presentation and testing of children diagnosed with coeliac disease at Starship Children’s Hospital over a 4-year period between January 1999 and December 2002; 48 patients were studied (range 1.6 to 15.7 years). Older (>5 years) children mostly presented to hospital with abdominal pain, while younger children mostly presented with ‘failure to thrive’; children are mostly being first diagnosed at an older age. Anti-endomysial and tissue transglutaminase antibodies are reliable tests for coeliac disease. However, in younger patients or if there is a high clinical index of suspicion of coeliac disease, small bowel biopsy should be performed, even if the anti-endomysial and tissue transglutaminase antibody tests are negative.
Sore throat management in New Zealand general practice
M Kljakovic, P Crampton

Rheumatic fever is an important sequel of throat infections in some areas of New Zealand, particularly for at-risk Maori or Pacific Island children aged 5–14 years. This study found that sore throat remains one of the top-10 symptoms patients present to their GP over the last decade. It was encouraging that more at-risk patients attended their GP with sore throat than had been observed 10 years previously. The perceived urgency of visit to the GP was greatest in parents worried about their young children. However, a wait for over a week with a sore throat among the at-risk group of 5–14 years may influence the attack rate of rheumatic fever. Most GPs were certain of their diagnoses; however, fewer GPs explicitly stated viral causes of sore throat than might be expected given the higher prevalence of viral related sore throats in the community. 61% of sore throat patients were prescribed an antibiotic and 6.6% had a throat swab. Overall, GPs appeared to have different management policies for patients with sore throat who come from different ethnic backgrounds, as there was less swabbing of the throat and more prescribing of antibiotics for Maori and particularly Pacific Island patients compared to European patients.
Chlamydia—the problem that just won’t go away

Edward Coughlan, Sue Bagshaw

Last year in this Journal, Nicky Perkins from Auckland Sexual Health wrote an editorial calling for a screening programme in response to the rising prevalence of *Chlamydia* infection in New Zealand.¹ A year later, the prevalence has risen again² and there is still no screening programme, although a study of cost effectiveness is being undertaken in Wellington (personal communication, Hazel Lewis, 2005).

Most published studies pertaining to chlamydial prevalence in New Zealand have concentrated on selected populations. An early study³ reported on 2,034 attendees at a Christchurch family planning clinic between May 1984 and July 1985. The prevalence of infection in this group was 17.5%. In pregnant attendees aged 20 years or less, the prevalence was 23%. This study used an immunoenzyme assay known as ‘Chlamdiazyme’ which is known to be less sensitive than the newer nucleic acid amplification tests (NAATs).

The word then got out! Opportunistic screening for genital chlamydial infection began. This often accompanied screening for cervical pre-cancer. It was encouraged in sexually active young people under 25 years of age, especially those with more than 3–5 partners or a partner change in the previous 3–6 months. Ten years later (in 1995), at the same Christchurch family planning centre, the prevalence was again studied, this time involving 819 women who were tested using both Amplicor PCR and Chlamdiazyme EIA.⁴ In 10 years, the prevalence had dropped to 5.8% with a slightly higher estimate using the Amplicor PCR test (5.3% vs 4.2%).

Since then, Cole et al⁵ tested 200 asymptomatic male army recruits aged from 17 to 35 years—they found a 4% prevalence in this group. Furthermore, in a study involving secondary schools in Christchurch,⁶ a prevalence of 2% was found among the Year 12 and Year 13 students who had a mean age of 16.7 years. And a group in Wellington estimated both the rate of chlamydial testing and chlamydial prevalence among pregnant women who delivered between 1999 and 2002⁷—testing was done on 37.5% of these women with 4.8% being positive.

Testing rates and chlamydial positivity varied with age and ethnicity. In those younger than 25 years, the number tested was 61.7% and the chlamydial prevalence 12.2%. The highest chlamydial prevalence (in regards to ethnicity) was found in the Maori group (15.2 %), followed closely by those of Pacific Island origin (12.5%). Women presenting for termination of pregnancy at a fee-paying private clinic and a government-funded clinic were also studied.⁸ Overall, 7.7% were positive for chlamydia with higher rates in those aged under 25 years (11.2%). Again, ethnic differences were noted—rates in Pacific women were 18.6%, in Maori 12.9%, in Asian 7.3%, and in European women 4.4%.

The sexually transmitted infections (STI) surveillance team from the Institute of Environmental Science and Research Limited (ESR) report on data obtained from sexual health centres (SHCs), family planning clinics (FPCs), student youth health clinics (SYHCs), and laboratories. Using the total number of visits at a clinic as a
denominator (rather than number of tests done), SHCs had the highest rates (5.4%) from clinics in 2004, with FPCs 1.1% and SYHCs 0.3%. In 2004, laboratories in the Auckland area reported testing 114,530 specimens with 6.2% being positive for chlamydia, thus giving a rate for the region of 581 per 100,000. In the Waikato region, 23,399 specimens were tested with 9.7% being positive, thus yielding a rate of 712 per 100,000. The latest in this series of studies found published later in this issue of the *Journal* is of sexually active female university students using the Roche Amplicor CT/NG PCR test. This time, the prevalence was 2.7%.

A population group defined all these studies whether they were clinic attendees, army recruits or 16–18 year old secondary school students. There was a marked drop in the prevalence of *Chlamydia* in these communities that occurred at the beginning of opportunistic screening in the late 1980s. The prevalence seems to have been relatively constant since then, despite rises recorded by laboratory data in the last 2–3 years.

To reduce the incidence of this infection further, more drastic measures seem to be required. The infection carries with it expensive, well-recognised health consequences such as neonatal conjunctivitis and pneumonia, pelvic inflammatory disease (PID), infertility, and ectopic pregnancy. Testing is now more sensitive and specific than ever before so that sampling can be done using self-administered vaginal swabs or urine tests, which means that more flexible testing can take place. And treatment of a stat dose of two tablets of azithromycin could not be easier.

With all this going for us should we be able to reduce the prevalence, despite the fact that this is largely an asymptomatic infection? Chlamydial infection can be prevented by using public health campaigns, aimed at condom use and limiting numbers of partners. Prevention can also be achieved by screening and treatment. The question needs to be asked: might not a true community prevalence study using the flexible sampling methods now available, be a better way of measuring changing prevalence? This could be a much better audit of primary prevention. In addition, both public health campaigns and screening can be focused or universal.

There is debate as to whether screening should be limited to women. There are also questions about the role of older men who do not come forward for screening. A community prevalence study could help decide where to focus screening or health promotion. One thing is for sure, chlamydia isn’t going away, and unless we make more coordinated efforts (involving education, health promotion, and screening), it’s not going to go away in the near future.

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**References:**


Marketing communications and obesity: a view from the dark side

Janet Hoek

Recent papers (Quigley and Watts as well as Maher, Wilson, and Signal) have focussed attention on the role played by marketing communications in shaping young people’s eating behaviours. Quigley and Watts call for a more detailed analysis of the environmental factors thought to contribute to obesity, and highlight marketing as a key issue meriting closer scrutiny. This paper is a response to their suggestion.

Marketing communications are a ubiquitous part of our media environment, whether they appear on radio or television, on billboards or signage, or in sales promotions. Their purpose is clear. First, they shape behaviour so it aligns more closely with marketers’ objectives. Second, they reinforce existing behaviour patterns (where these are already favourable) so consumers continue to buy specific brands. These goals are not inherently problematic; however, where the promoted behaviours may contribute to health problems it becomes necessary to consider marketing’s role and regulation more closely.

Despite the claims sometimes made about them, marketing communications are rarely coercive—they do not typically make people behave in a particular way. However, they do maintain behaviour patterns, provide reassurance about these, and offer incentives likely to increase the rate at which the promoted behaviours are performed. The prevalence of particular marketing themes and the frequency with which these are repeated may also make people less receptive to alternative messages.

The effect of marketing communications on consumers’ behaviour raises important questions about how marketing may contribute to obesity. It is difficult to argue that advertising makes consumers buy food that is high in fat, salt, or sugar. Yet, because promotions for these foods appear so regularly, and are found in such a disparate range of media, they may foster the impression that products high in fat, salt, or sugar are consistent with a ‘normal’ diet.

This message would be of less concern if it only affected people who consume these foods infrequently, since their behaviour is unlikely to put them at risk. However, research suggests consumers notice promotions for the brands they use, since these are already salient to them. Consequently, marketing communications may have a disproportionate effect on people who consume high fat, salt, or sugar foods frequently.

By reminding people to consume ‘fast foods’ and providing extra incentives to do so, marketing communications may also increase consumption. Marketers have traditionally found it very difficult to change the rate at which consumers purchase a product (consumers can only use so much shampoo and wash their hair so many times a day). However, some fast food promotions seem likely to achieve this goal.

For instance, some promotions offer the opportunity to redeem a discount coupon several times within a limited period, while others feature competitions that require
several purchases to meet the entry criterion. These promotions link frequent consumption within a tightly defined time period with the opportunity to receive an immediate benefit (lower prices) or the promise of a future benefit (winning a prize).

The widespread use of loyalty programmes based on characters from children’s movies also aims to instil a regular purchase pattern and may increase the frequency with which consumers purchase particular menu items.\(^8\) As well as encouraging increased frequency of consumption, marketing campaigns encourage increased volume of consumption by fostering beliefs that ‘up-sizing’ is both sensible (it represents better value per unit) and normal (why else would super-value combos exist?).

Where behaviours are stimulated by special offers, rewarded by additional benefits, and maintained by advertising that ensures the salience of promoted brands remains high, those behaviours become routine and habitual.\(^9\) However, although the effects of advertising and sales promotions are more obvious, these are not the only marketing communications to affect consumers’ eating behaviours.

Sponsorship involves pairing an individual or team with a brand so that an association between that individual’s (or team’s) attributes and the brand develops. As the tobacco industry knew, sports sponsorship offered an unparalleled opportunity to associate an unhealthy product with individuals who epitomised sporting excellence and robust good health.

Similarly, manufacturers of foods high in fat, salt, or sugar have also developed relationships with individuals whose success and talent are indisputable—Hamish Carter (Olympic Triathalon Champion), Sarah Ulmer (Olympic Track Cycling Champion), and the Tall Blacks (New Zealand Basketball Team), to mention just three New Zealand examples. Promotions featuring top athletes suggest they endorse the brands that sponsor them, thus reinforcing the impression that these products are not inconsistent with a healthy diet. However, these promotions rarely, if ever, mention whether the sponsored athletes eat their sponsors’ products and, if so, the menu items they choose, and how frequently they consume these.

Because advertising, sales promotions, and sponsorships reassure consumers and provide additional reasons to purchase high fat, salt, and sugar foods; they clearly help maintain unhealthy behaviour patterns. This, in turn, reduces the likelihood that individuals will either recognise the behaviours as unhealthy or seek to change these. As Quigley and Watt\(^1\) noted, arguments that individuals must take greater responsibility for their own actions are illogical when the media environment encourages continuation of those very behaviours.

Although education and social marketing campaigns have been proposed as means of addressing obesity, they are unlikely to succeed in the current media environment.\(^10\) If individuals are to be empowered to make better choices, the marketing environment must be changed so it is conducive to messages promoting healthy food choices. Such a change seems most unlikely to come about through voluntary restraint on the part of advertisers or the media (as our experience with tobacco promotions demonstrates). However, politicians are curiously reluctant to regulate food promotions.

Their stance relies on two flawed arguments: the need for causality to be established and the complexity of the issue.\(^11\) The first argument claims the relationship between
marketing and obesity is unclear and that regulation in the absence of a direct causal relationship is unwarranted. This reasoning is familiar; for several decades, the tobacco industry disputed the causal relationship between smoking and a range of cancers in an effort to stave off regulation.

Causality is difficult to establish; even time-consuming and expensive longitudinal studies may not provide indisputable findings about the relationship between environmental variables and behaviour. For this reason, regulators need to place greater emphasis on what is known about marketing communications and their effects. Examination of theory reveals that, even if marketing communications do not cause behaviour, they nevertheless shape, encourage, and reinforce behaviour patterns linked to adverse health consequences.\textsuperscript{3,5,6,9} As a result, they cannot be viewed as merely providing information that creates greater choices for consumers; food marketing is neither a neutral nor an innocuous activity.

Opponents of government regulation have claimed that because obesity is a complex problem, attempts to single out and regulate marketing activities are both unfair and unlikely to succeed.\textsuperscript{12} However, identifying the precise role played by each of the factors known to contribute to obesity would be time-consuming and likely to be dominated by methodological disputes. Accepting this argument inevitably means deferring regulatory action, and risks sub-optimal allocation of resources to initiatives less likely to change behaviour.

Dispersing responsibility for obesity moves attention away from marketing’s contribution to this problem. More specifically, it overlooks the role of marketing in maintaining the salience of promoted brands—by supporting continued and increased consumption of these brands, marketing fosters the continuation of less healthy behaviours and militates against acceptance of alternative eating patterns.

Quigley and Watts are right to urge policy makers to turn their attention towards creating a regulatory environment that will support healthier food choices.\textsuperscript{1} Using policy to decrease the visibility of less healthy foods, while also making these more expensive or more difficult to access, will reduce the salience of these foods and discourage consumption. These initiatives are much more likely than education or social marketing to promote healthier eating habits—a fact that even marketing’s strongest proponents must surely know.

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Prevalence and risk factors for *Chlamydia trachomatis* infection in female New Zealand university students

Michael Baker, Jose Ortega-Benito, Nick Garret, Collette Bromhead, Kathryn Leslie, Jane MacDonald, Anne McNicholas

**Abstract**

**Aims.** To measure the prevalence of urogenital *Chlamydia trachomatis* infection in a sample of sexually active female university students, to identify risk factors associated with infection, and to measure the uptake of screening.

**Methods.** Female students aged 18–25 years, presenting to a university student health service from March to October 2003, were invited to participate. Information on demographic details and sexual behaviour was collected with a self-completed questionnaire. The students were tested for *Chlamydia* infection using the Roche Amplicor CT/NG PCR test of first void urine specimens.

**Results.** *Chlamydia* prevalence was 2.7% (19/715). Infection was associated with previous sexually transmitted infection (STI), non-European ethnicity, and irregular use of condoms. Most participants were not using condoms regularly despite the risk of STI. Screening was technically straightforward and the participation rate was 59.9% (718/1199).

**Conclusions.** New Zealand needs to develop and implement an adequately resourced and evidence-based *Chlamydia* control strategy. This strategy should contain national guidelines on screening in a range of settings, including universities, as well as strategies for primary prevention of *Chlamydia* and other STI. Clinicians treating university-aged students should consider opportunistic *Chlamydia* screening for all of those who are sexually active. Further research, preferably in conjunction with intervention studies, is essential to assess the prevalence of *Chlamydia* in other populations.

*Chlamydia trachomatis* infection is an important public health problem because of its high incidence, significant health impact on those infected, and potential preventability. Urogenital infection causes urethritis and cervicitis in women and urethritis in men. Long-term sequelae in women include pelvic inflammatory disease, ectopic pregnancy, and tubal infertility.\(^1\) In men, complications of untreated chlamydial infections include epididymitis which may lead to infertility. *Chlamydia* infections are asymptomatic in up 70–90% of women and a large percentage of men.\(^1\)

Asymptomatic chlamydial infections can persist for months or years, although the usual duration is still not known.\(^2\) Men and women with asymptomatic or undiagnosed *Chlamydia* act as important reservoirs of infection for their sexual contacts.

*Chlamydia* infection was diagnosed in 5.6% of patient visits at New Zealand sexual health clinics in 2003, making it the most commonly reported sexually transmitted infection (STI) in this population.\(^3\) In 2003, laboratory surveillance found an
incidence of 613 per 100 000 in Auckland, and 739 per 100 000 in the Waikato and Bay of Plenty regions. These rates are high by international standards, being almost six times higher than those reported in Australia. There is also evidence that the rate of infection is rising—with a 65.5% increase in cases presenting to sexual health clinics over the 5 years from 1999 to 2003 and a 25% increase in laboratory diagnosed cases from 2001 to 2003.

The true prevalence of Chlamydia infection is greater than that indicated by either clinic or laboratory data. The majority of such infections are asymptomatic, and New Zealand clinicians do not routinely screen for this disease. Recent New Zealand studies found a prevalence of 4.8% in pregnant women and 2.0% in sexually active high school students. A cohort study found a self-reported cumulative incidence of Chlamydia of 2.4% for males, and 9.0% for females by age 21.

Screening of asymptomatic patients is recognised as a key strategy for identifying and treating those with Chlamydia and decreasing the prevalence of infection and its sequelae. It has become more feasible since the introduction of highly sensitive nucleic acid amplification tests (NAAT). These methods allow screening using urine specimens which are less invasive than endocervical specimens collected from women and urethral specimens from men, which makes screening more acceptable to asymptomatic individuals. Treatment has also become simpler with single dose azithromycin.

Unlike many developed countries (such as England, Scotland, the United States, and some European countries), New Zealand does not have screening guidelines for Chlamydia. The aims of this research were to measure the prevalence of urogenital Chlamydia trachomatis infection in a sample of sexually active female university students; to identify risk factors associated with infection; and to assess the uptake of screening in this population.

Methods

Subject recruitment—Participants were female university students aged 18 to 25 years who attended a University Student Health clinic from March to October 2003. Excluded were attendees who were not sexually active; had been diagnosed and/or treated for Chlamydia infection in the previous 3 months; or whose English was insufficient for comprehension of the information sheet. The Wellington Ethics Committee approved the study design, questionnaire and information sheet. Depending on patient volumes and response rates, clinic receptionists approached a fixed proportion of attendees, ranging from every second to every third female appointment for the clinic. These potential participants were given an information sheet. Those who declined to participate were asked to record their age, ethnicity, and reason(s) for non-participation on a brief questionnaire.

Participant questionnaires—Participants were asked to complete a brief self-administered questionnaire. It included demographic details and questions on sexual behaviour, contraceptive use, history of STI, urogenital symptoms, and health service use. All of the questions used tick-boxes except for two that asked about age. Participants could record multiple ethnic groups.

Laboratory specimen collection and testing—Approximately 25 ml of first-void urine was obtained from consenting participants. Urine must not have been passed for 2 hours or, alternatively, an early morning specimen was collected the following day. An endocervical swab may also have been collected if a pelvic examination was carried out.

Specimens were transported to the laboratory within 48 hours and processed within 7 days of collection. The Roche Amplicor CT/NG microwell plate PCR test (Roche Molecular Systems Inc., Branchburg, NJ, USA) was used to detect the presence of Chlamydia trachomatis plasmid DNA in clinical specimens. The internal control (IC) was detected for all specimens. Positive specimens were defined as any yielding an OD₄₅₀ of ≥ 0.8 on two separate tests, regardless of the IC value.
Negative specimens were defined as any which had a valid IC value and an OD_{450} < 0.2. Any specimen having a signal of 0.2 ≤ OD_{450} < 0.8 was defined as equivocal, referred for further testing, and interpreted as negative for the purposes of the study. Persistently inhibited specimens (invalid IC) were re-tested to resolve the result.

Data entry and analysis—Each questionnaire and laboratory result was identifiable only by a unique study number. Data were double entered into an electronic database. SAS® software (SAS Institute Inc. Cary, NC, USA) was used to produced frequency tables of the study variables and calculate crude odds ratios and 95% confidence intervals for the risk factors under investigation. Confidence intervals for rates were calculated using the Wilson score method incorporating continuity correction. Variables that appeared important predictors of Chlamydia risk were then added to a multivariate model.

Follow-up of participants. The study coordinator advised all participants of their test results by telephone. Those with positive Chlamydia test results were requested to return for appropriate treatment, counselling, and contact tracing (following standard Wellington Sexual Health Clinic practices).

Results

Participation rate—The participation rate was 59.9% (718/1199). A total of 1397 female patients at Victoria University Student Clinic were approached to take part in this study. Of these; 10 were found not to be in the age range for the study, 184 were excluded because they had never been sexually active, and 4 were excluded as they had recently tested positive or were presently taking antibiotics for Chlamydia infection—thus leaving an eligible population of 1199.

Of this group, 377 declined to participate and a further 104 dropped out between agreement at initial consultation and data/specimen collection. This left 718 students who were interviewed and provided specimens. Three specimens could not be tested (2 did not arrive at the laboratory and 1 had insufficient volume).

Reasons for non-participation were given by 365 of the 377 eligible students who declined to participate. These (non-exclusive) reasons were: “not interested” (60.2%), “feel embarrassed” (6.9%), “don’t have the time” (6.1%), “offended at being asked” (1.6%), “recently tested negative” (1.0%), or “other reasons” (29.7%).

Demographic characteristics of participants and non-participants—The demographic characteristics of the participants and non-participants are presented in Table 1. These data show that the age group and ethnicity of participants and non-participants were similar. The participants were predominantly aged 18 to 21 years (68.4 %) and of European ethnicity (82.6%).

Sexual history—The majority (63.3%) of participants reported first sexual intercourse before the age of 18 years; 15.9% before the age of 16 years. Over the previous 12 months, the majority (95.2%) were exclusively heterosexual, with 2.2% reporting both male and female partners, and 2.5% female partners.

About half (53.7%) had a single sexual partner, 39.0% reported 2–4 partners, and 6.2% reported 5–8 partners. Half (50.5%) reported changing or having a new sexual partner in the previous 12 months and 15% having more than one sexual partner in the same time period.
Table 1. Demographic characteristics of study participants and those who declined to participate or were lost to follow-up

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Grouping</th>
<th>Declined to participate</th>
<th>Lost to follow-up</th>
<th>Participants</th>
<th>Total eligible</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>n</td>
<td>(%)</td>
<td>n</td>
<td>n</td>
<td>n</td>
</tr>
<tr>
<td>Age group (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–21</td>
<td>221</td>
<td>(71.5)</td>
<td>63</td>
<td>491</td>
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<td>22–25</td>
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<td>Ethnicity*</td>
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<td>European</td>
<td>298</td>
<td>(81.6)</td>
<td>86</td>
<td>590</td>
<td>974</td>
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<td>Maori</td>
<td>21</td>
<td>(5.8)</td>
<td>2</td>
<td>49</td>
<td>72</td>
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<td>Pacific Island</td>
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<td>(1.9)</td>
<td>3</td>
<td>16</td>
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<td>East Asian</td>
<td>22</td>
<td>(6.0)</td>
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<td>South Asian</td>
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<td>(3.3)</td>
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<td>Other</td>
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<td></td>
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<td>4</td>
<td>25</td>
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<tr>
<td>Non-European</td>
<td>67</td>
<td>(18.4)</td>
<td>9</td>
<td>124</td>
<td>200</td>
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<td></td>
<td><strong>Total</strong></td>
<td><strong>377</strong></td>
<td><strong>104</strong></td>
<td><strong>718†</strong></td>
<td><strong>1199</strong></td>
</tr>
</tbody>
</table>

*Prioritised ethnicity (Each participant is assigned one ethnicity. If multiple ethnicities are recorded, then the ethnicity is prioritised firstly for Maori, then for Pacific, then for Asian, then for European, and then for Other); †Three participants supplied an insufficient volume of urine for testing or their specimen was missing so were excluded from further analyses.

Table 2. Contraceptive methods used by participants in the previous 12 months

<table>
<thead>
<tr>
<th>Number of methods</th>
<th>Combinations of methods with 10 or more participants</th>
<th>Number</th>
<th>Chlamydia positives</th>
<th>Chlamydia rate % (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No contraceptive methods</td>
<td>8</td>
<td>0</td>
<td>0.0 (0.0–40.2)</td>
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<tr>
<td>1</td>
<td>Total</td>
<td>200</td>
<td>10</td>
<td>5.0 (2.6–9.3)</td>
</tr>
<tr>
<td></td>
<td>- Condom</td>
<td>107</td>
<td>5</td>
<td>4.7 (1.7–11.1)</td>
</tr>
<tr>
<td></td>
<td>- Pill</td>
<td>78</td>
<td>3</td>
<td>3.8 (1.0–11.6)</td>
</tr>
<tr>
<td></td>
<td>- Depo injection</td>
<td>13</td>
<td>2</td>
<td>15.4 (2.7–46.3)</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>451</td>
<td>7</td>
<td>1.6 (0.7–3.3)</td>
</tr>
<tr>
<td></td>
<td>- Condom / Pill</td>
<td>423</td>
<td>7</td>
<td>1.7 (0.7–3.5)</td>
</tr>
<tr>
<td></td>
<td>- Condom / Depo injection</td>
<td>16</td>
<td>0</td>
<td>0.0 (0.0–24.1)</td>
</tr>
<tr>
<td>3</td>
<td>Total</td>
<td>28</td>
<td>1</td>
<td>3.6 (0.2–20.2)</td>
</tr>
<tr>
<td></td>
<td>- Condom / Pill / Depo injection</td>
<td>15</td>
<td>1</td>
<td>6.7 (0.3–34.0)</td>
</tr>
<tr>
<td></td>
<td>Total*</td>
<td>687</td>
<td>18</td>
<td>2.6 (1.6–4.2)</td>
</tr>
</tbody>
</table>

*Based on 687 women who reported having one or more male sexual partners in the previous 12 months
**Contraceptive and condom use**—Participants were asked to record all of the contraceptive methods they had used in the last 12 months (Table 2). The majority had used more than one method during this period, with the combination of condom and pill being most common. The predominant barrier contraceptive method was the condom which had been used by 87.2% (599/687) of those who had been sexually active with a male partner in the past 12 months. Two women reported having used a diaphragm and one the female condom.

Participants were also asked about the regularity of condom use in the last 12 months. Of the women who responded (and who reported having one or more male sexual partners in the previous 12 months), 24.0% used a condom always, 43.4% sometimes, 23.3% occasionally, and 9.3% never. Among those with 2 or more male partners in the past 12 months, the proportion using condoms always was 21.3%. Among those who reported having been tested for a sexually transmitted disease it was 19.7%, and of those having tested positive for an STI it was 19.6%.

Participants were asked to record their reasons for not using a condom. Of the 522 sexually active participants who did not use a condom always, responses were recorded by 506. Reasons (non-exclusive) for not using a condom were: “used other form of contraception” (84.8%), “problem at time of use (e.g. fell off/broke)” (12.1%), “intoxicated” (7.7%), “partner doesn’t like using them” (9.3%), and “forgot” (5.3%).

**Sexually transmitted infections**—Sixty percent (431/718) of participants reported having been tested for an STI in the past. Of these, 21.8% (94/431) reported testing positive for an STI. These (non-exclusive) infections were listed as Chlamydia (40), genital warts (40), genital herpes (14), gonorrhoea (3), pubic lice (2), trichomonas (2), human papilloma virus [HPV] (2), and thrush (1).

**Result of Chlamydia testing**—The Chlamydia prevalence was 2.7% (95% CI: 1.7–4.2). The 696 negative test results included 4 that had been equivocal and 5 that had to be retested (4 with inhibited test results and 1 with insufficient specimen).

**Characteristics of those testing positive for Chlamydia**—The results of chlamydial testing are shown in Table 3. Individually, each of the following characteristics was associated with significantly elevated Chlamydia prevalence relative to other categories: having previously tested positive for a STI; having had a previous chlamydial infection; and having non-European ethnicity (odds ratios were elevated for all non-European ethnic groups—but these only reached statistical significance for Pacific Island and East Asian ethnic groups individually).

In addition, the risk of being infected with Chlamydia was inversely associated with the regularity of condom use. After putting these characteristics into a stepwise multivariate model, only previous chlamydial infection remained a risk factor (OR=4.89 95%CI=1.54–15.48). No other factors continued to be associated with significantly elevated Chlamydia prevalence.
Table 3. Characteristics of study participants, *Chlamydia* prevalence and odds ratios (calculated in relation to a defined reference value for each characteristics)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Grouping</th>
<th>Chlamydia rate (%)</th>
<th>OR</th>
<th>95%CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-21</td>
<td>2.7 (13/488)</td>
<td>1.00</td>
<td>–</td>
<td>(0.37–2.64)</td>
<td>0.99</td>
</tr>
<tr>
<td>22-25</td>
<td>2.6 (6/227)</td>
<td>0.99</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>1.9 (11/589)</td>
<td>1.00</td>
<td>–</td>
<td>(0.48–10.39)</td>
<td>0.30</td>
</tr>
<tr>
<td>Maori</td>
<td>4.1 (2/49)</td>
<td>2.24</td>
<td>(0.48–10.39)</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td>Pacific Island</td>
<td>13.3 (2/15)</td>
<td>8.76</td>
<td>(1.75–43.87)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>East Asian</td>
<td>8.8 (3/34)</td>
<td>5.09</td>
<td>(1.35–19.16)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>South Asian</td>
<td>5.9 (1/17)</td>
<td>3.28</td>
<td>(0.40–26.99)</td>
<td>0.27</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>0 (0/6)</td>
<td>-</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Non-European</td>
<td>6.6 (8/122)</td>
<td>3.69</td>
<td>(1.45–9.37)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Years since first sexual intercourse*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 1</td>
<td>4.4 (5/113)</td>
<td>1.00</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>&gt; 1</td>
<td>2.3 (14/600)</td>
<td>0.51</td>
<td>(0.18–1.46)</td>
<td>0.21</td>
<td></td>
</tr>
<tr>
<td>Number of sexual partners in last 12 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2.9 (11/383)</td>
<td>1.00</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>2–4</td>
<td>1.8 (5/278)</td>
<td>0.62</td>
<td>(0.21–1.80)</td>
<td>0.38</td>
<td></td>
</tr>
<tr>
<td>5–9</td>
<td>4.5 (2/44)</td>
<td>1.61</td>
<td>(0.35–7.51)</td>
<td>0.54</td>
<td></td>
</tr>
<tr>
<td>0 or Not stated</td>
<td>10.0 (1/10)</td>
<td>3.76</td>
<td>(0.44–32.30)</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td>Change or new sexual partner last 12 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3.1 (11/358)</td>
<td>1.00</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Yes</td>
<td>2.2 (8/357)</td>
<td>0.72</td>
<td>(0.29–1.82)</td>
<td>0.49</td>
<td></td>
</tr>
<tr>
<td>&gt;1 sexual partner at same time last 12 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>2.6 (16/608)</td>
<td>1.00</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Yes</td>
<td>2.8 (3/107)</td>
<td>1.07</td>
<td>(0.31–3.73)</td>
<td>0.92</td>
<td></td>
</tr>
<tr>
<td>Contraceptive or protective method used in the last 12 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barrier only</td>
<td>4.4 (5/113)</td>
<td>1.00</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Non-barrier Only</td>
<td>4.9 (5/102)</td>
<td>1.11</td>
<td>(0.31–3.96)</td>
<td>0.87</td>
<td></td>
</tr>
<tr>
<td>Both Barrier and Non-barrier</td>
<td>1.6 (8/486)</td>
<td>0.36</td>
<td>(0.12–1.13)</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>None or not stated</td>
<td>7.1 (1/14)</td>
<td>1.66</td>
<td>(0.18–15.34)</td>
<td>0.65</td>
<td></td>
</tr>
<tr>
<td>Regularity of condom use†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Always</td>
<td>1.2 (2/165)</td>
<td>1.00</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Sometimes</td>
<td>2.3 (7/298)</td>
<td>1.96</td>
<td>(0.40–9.55)</td>
<td>0.40</td>
<td></td>
</tr>
<tr>
<td>Occasionally</td>
<td>3.8 (6/160)</td>
<td>3.18</td>
<td>(0.63–15.97)</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>4.7 (3/64)</td>
<td>4.01</td>
<td>(0.65–24.57)</td>
<td>0.13</td>
<td></td>
</tr>
</tbody>
</table>

Chi-squared for trend (1 sided) 0.04
<table>
<thead>
<tr>
<th>Ever tested for STI</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.1</td>
<td>2.3</td>
</tr>
<tr>
<td></td>
<td>(9/286)</td>
<td>(10/429)</td>
</tr>
<tr>
<td></td>
<td>1.00</td>
<td>0.73</td>
</tr>
<tr>
<td></td>
<td>(0.29–1.83)</td>
<td>0.51</td>
</tr>
<tr>
<td>Ever tested positive for STI</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>2.1</td>
<td>6.4</td>
</tr>
<tr>
<td></td>
<td>(13/621)</td>
<td>(6/94)</td>
</tr>
<tr>
<td></td>
<td>1.00</td>
<td>3.19</td>
</tr>
<tr>
<td></td>
<td>(1.18–8.61)</td>
<td>0.02</td>
</tr>
<tr>
<td>Previous Chlamydia infection</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>2.2</td>
<td>10.0</td>
</tr>
<tr>
<td></td>
<td>(15/675)</td>
<td>(4/40)</td>
</tr>
<tr>
<td></td>
<td>1.00</td>
<td>4.89</td>
</tr>
<tr>
<td></td>
<td>(1.54–15.48)</td>
<td>0.01</td>
</tr>
<tr>
<td>Total</td>
<td>All</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>2.7</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>(19/715)</td>
<td>-</td>
</tr>
</tbody>
</table>

*Total is 713 as two participants did not state age at first intercourse; † This analysis is restricted to the 687 women who reported having one or more male sexual partners in the previous 12 months.

Table 4. Urogenital symptoms of study participants and their Chlamydia prevalence rates

<table>
<thead>
<tr>
<th>Symptom†</th>
<th>Prevalence of symptom†</th>
<th>Chlamydia positives</th>
<th>Chlamydia rate % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain during sexual intercourse</td>
<td>13.5 (95/704)</td>
<td>1/95</td>
<td>1.1 (0.1–6.6)</td>
</tr>
<tr>
<td>Pain on passing urine</td>
<td>4.3 (30/704)</td>
<td>0/30</td>
<td>0.0 (0.0–14.1)</td>
</tr>
<tr>
<td>Lower abdominal pain</td>
<td>12.6 (89/704)</td>
<td>0/89</td>
<td>0.0 (0.0–5.2)</td>
</tr>
<tr>
<td>Changes in usual vaginal discharge</td>
<td>7.7 (54/704)</td>
<td>3/54</td>
<td>5.6 (1.4–16.3)</td>
</tr>
<tr>
<td>Bleeding in between periods</td>
<td>9.2 (65/704)</td>
<td>2/65</td>
<td>3.1 (0.5–11.6)</td>
</tr>
<tr>
<td>Any of the above</td>
<td>32.5 (229/704)</td>
<td>5/229</td>
<td>2.2 (0.8–5.3)</td>
</tr>
<tr>
<td>None of the above</td>
<td>67.5 (475/704)</td>
<td>14/475</td>
<td>2.9 (1.7–5.0)</td>
</tr>
<tr>
<td>Not stated</td>
<td>11</td>
<td>0/11</td>
<td>0.0 (0.0–32.1)</td>
</tr>
<tr>
<td>Total</td>
<td><strong>715</strong></td>
<td><strong>19/715</strong></td>
<td><strong>2.7 (1.7–4.2)</strong></td>
</tr>
</tbody>
</table>

†Individual may indicate more than one; †† Calculated from 704 subjects who responded
**Urogenital symptoms**—The majority (67.5%) of participants were asymptomatic (Table 4). The remainder indicated a range of symptoms (Table 4). The asymptomatic group had a slightly higher (2.9%) *Chlamydia* prevalence than the symptomatic group (2.2%). No single reported symptom was significantly associated with chlamydial infection, although those reporting changes in usual vaginal discharge did have a higher rate of infection than other participants.

**Health-seeking behaviour**—Participants were asked to indicate where they would go if they were concerned about or suspected that they had an STI. The majority indicated student health clinic (584), followed by family planning association (171), sexual health clinic (118), their own GP (108), ‘Other GP’ (16), or ‘Youth clinic’ (9).

**Discussion**

This study found a urogenital *Chlamydia trachomatis* infection prevalence of 2.7% in 18 to 25-year-old female students attending a university health clinic. *Chlamydia* infection was associated with non-European ethnicity, irregular use of condoms, and previous STI. Screening was technically straightforward, with an uptake of about 60%. These findings help to define the burden of *Chlamydia* in New Zealand and how it can be managed.

The *Chlamydia* prevalence found in this study suggests approximately 5,400 undiagnosed infections among the 200,000 female New Zealanders aged 18 to 25 years. University students are, however, unlikely to be representative of young woman more generally. Other New Zealand prevalence data suggest that this finding may in fact be an under-estimate. *Chlamydia* prevalence was 12.2% in pregnant women <25 years of age tested in the Wellington region from 1999 to 2002 and 2.3% among sexually active female Christchurch high school students (predominantly 16 and 17 years of age) screened in 2000.

Laboratory surveillance data from 2003 found an incidence of 5.9% for females aged 20–24 in the Waikato/Bay of Plenty area and 3.8% in the Auckland region. Internationally, the prevalence of *Chlamydia* infection has been found to vary widely in different populations. In asymptomatic women in Europe, for example, it ranged from 1.7 to 17% depending on setting, context, and country. A large nationally representative survey of adults aged 18 to 26 years conducted in the United States from 2001–2 found a prevalence of 4.7% in women.

The risk factors for *Chlamydia* infection found in this study provide some guidance for the design and targeting of prevention programmes. In terms of demographic risk factors, the increased rate among non-European populations is consistent with the elevated rates of *Chlamydia* among Maori and Pacific attendees at sexual health clinics. It is also consistent with the pattern seen in antenatal testing.

Behavioural risk factors of irregular use of condoms and previous STI have also been widely reported and have a high level of biological plausibility. Unlike some previous studies, this present one found an inconsistent relationship between having >1 partner in the previous year and the risk of infection.

This study confirms that a *Chlamydia* screening programme can be incorporated into an established student health service and provides some insights into its acceptability. The uptake of 60% in this study is similar to the response rate found in New Zealand
high school students who were offered a questionnaire and screening, and to the uptake rate of 64% found in the only published randomised trial of *Chlamydia* screening—but less than the 76-84% uptake found in recent UK pilot studies. Higher uptake rates might be expected if testing was offered routinely as part of a screening programme where completion of a questionnaire would not be required.

The case for systematic screening for *Chlamydia* has been made by many authors in New Zealand and internationally. Before embarking on a national *Chlamydia* screening programme, we need to be satisfied that the programme will be the most cost-effective way of preventing infection and its long-term consequences. We also need to decide who should be targeted, in which settings, and with which screening method.

Firstly, although *Chlamydia* screening is widely advocated, there are important gaps in the evidence base supporting this intervention. Evidence in favour of screening has mainly come from uncontrolled trials, modelling studies, and cost-effectiveness analysis. The later review included 10 eligible studies and found screening to be cost-effective at prevalences of 3.1–10%, and with cost saving at a prevalence as low as 1.1%. However, there is little evidence concerning the natural history of *Chlamydia* infection and a lack of rigorous trials demonstrating effectiveness of screening at a population level. Available cost-effectiveness analyses are highly sensitive to assumptions about the predicted costs of treatment of the complications that are avoided.

Secondly, it will be necessary to decide how to target such a programme. The two main options are population-based screening and opportunistic screening. Population based approaches use very broad criteria based on sex and age and seek to screen everyone within that demographic group. Opportunistic or selective approaches screen specific groups who are in contact with health care services or specific agencies. New Zealand researchers and sexual health practitioners have advocated the latter approach for pregnant women and sexually active high school students. A refinement is to use selective criteria (such as self-reported symptoms or behavioural risk factors) to improve the efficiency of screening though such approaches appear to have varying degrees of success. A related issue is whether to extend such screening to males. Given that they often have similar or higher *Chlamydia* infection rates to females, there is a strong argument for including them.

Thirdly, New Zealand will need to consider the preferred method of screening and its cost effectiveness. These issues include considerations of which mix of tests to use, the most appropriate specimen type, and the optimal frequency of screening. In England, for example, the National Health Service has recently decided to convert all *Chlamydia* diagnostic tests from enzyme immunoassay assays to the more sensitive nucleic acid amplification tests, as part of a range of measures to improve sexual health services. As in all programmes, it will be necessary to carefully consider the sensitivity and specificity of the available screening tests. It will also be important to consider potential adverse effects of screening.

Given these uncertainties, our findings provide qualified support for *Chlamydia* screening of sexually active female university students. Such a programme should be considered in the context of comprehensive screening guidelines covering high prevalence groups (such as pregnant women) as well as sexually active young women.
and men generally. Findings from this present study do not provide support for the use of selective criteria (such as self-reported symptoms or behavioural risk factors) to improve the efficiency of screening, although this approach could be investigated further in a larger study.

Findings from this study also reinforce the importance of primary prevention of Chlamydia and other STI. A significant proportion of sexually active young women were not using condoms, or using them irregularly, and this behaviour was associated with higher rates of Chlamydia infection.

This study has a number of limitations. The choice of study population limits the generalisability of the findings to other groups, particularly males. The relatively low participation rate also introduces potential selection bias. Conclusions about sub-populations within the sample are limited by the small study size. Therefore, further research is essential to assess the prevalence of Chlamydia in other populations. Such research should be carried out in the context of intervention studies, preferably one or more pilot screening programmes.

In conclusion, New Zealand needs an adequately resourced and evidence-based Chlamydia control strategy. A good starting point would be a set of national guidelines covering screening in a range of settings, including student health services. These guidelines should include recommendations on laboratory testing methods. Specifically, it would be useful to consider one or more pilot programmes (following the example of the United Kingdom) to assess the performance of such guidelines in New Zealand conditions and gather data to inform a cost-effectiveness analysis of systematic screening.

Improvements to STI surveillance, such as laboratory reporting and notification, would help in evaluating the impact of screening at a population level. This strategy also needs to include primary prevention of Chlamydia and other STI. While national guidelines are being developed, clinicians treating university-aged students should consider opportunistic Chlamydia screening for all females and males who are sexually active. The only consistent risk factors from this investigation, and other New Zealand data sources, are young age and non-European ethnicity. Promotion of condom use should be part of all such patient counselling.

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Correspondence: Dr Michael Baker, Wellington School of Medicine and Health Sciences, Box 5013, Wellington. Fax: (04) 389 5319; email: michael.baker@wnmeds.ac.nz

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25. Macleod J, Smith GD. Chlamydia screening can have high take-up rates if right methodology is used. BMJ. 1999;319:188.
Low birth weight and cardiovascular risk factors in Auckland adolescents: a retrospective cohort study

Barbara Daly, Robert Scragg, David Schaaf, Patricia Metcalf

Abstract

Aims. To determine whether birth weight is inversely associated with cardiovascular risk factors in a multiethnic sample of New Zealand adolescents.

Methods. A retrospective cohort with birth weight collected from hospital records of 855 (68%) out of 1260 Auckland-born students who had blood pressure, fasting blood lipids, and glucose measured while in Year 11–13 at high school.

Results. After controlling for sex, age, and ethnicity, none of the following cardiovascular risk factors were associated with birth weight (p>0.05): systolic and diastolic blood pressure, total cholesterol, HDL cholesterol, triglycerides, and glucose. Serum cholesterol came closest to statistical significance: regression coefficient being —0.10mmol/L (SE=0.06, p value=0.11). In contrast (after controlling for age, sex, and ethnicity), current Body Mass Index (BMI) was significantly (p<0.05) related to all above cardiovascular risk factors. The proportion of students with elevated serum cholesterol levels (top 20%) attributable to elevated BMI (>30 kg/m2) was 18%, and that attributable to low birth weight (<2.5kg) was 2%.

Conclusion. These results do not support for the ‘fetal origins’ hypothesis. The very low proportion of adolescents with elevated coronary risk factors attributed to low birth weight suggests that the focus of cardiovascular disease prevention should remain in adolescence and adulthood, rather than in pregnancy.

Epidemiological research, originally from the United Kingdom, has shown that low birth weight infants have an increased mortality from cardiovascular disease in adulthood compared with normal weight infants. \(^1\)\(^2\) This has led to the formulation of the ‘fetal origins’ hypothesis—i.e. that fetal undernutrition (manifested primarily by low birth weight, ‘underweight for length’, or ‘short for dates’ babies) induces changes in organ size and in hormones that are known to influence fetal growth and development. \(^3\) These changes in early life, particularly if followed in later life by excess nutritional consumption leading to obesity, may predispose to a range of cardiovascular diseases in adulthood—including hypertension, coronary heart disease, and diabetes. \(^4\)

Studies of New Zealand populations offer the opportunity for new insights into the association between birth weight and cardiovascular disease. The ‘fetal origins’ hypothesis is consistent with the adult pattern of cardiovascular disease in Maori who have lower birth weights\(^5\) and increased risk of coronary heart disease, \(^6\) diabetes, \(^7\) and hypertension \(^8\) compared with Europeans. However, it is not consistent with the adult pattern of cardiovascular disease in Pacific Island people living in New Zealand who, despite their higher birth weight, \(^5\) also have a higher risk of these same three diseases compared with Europeans. \(^6\)\(^–\)\(^8\)
The only previous New Zealand reports, from the mainly European sample in the Dunedin longitudinal study, have found no association between birthweight and blood pressure in subjects at the age of 18 years or 26 years although systolic blood pressure was found to be significantly higher at age 7 years, in those who were considered to have Intrauterine Growth Retardation (light and short for dates), compared to normal weight babies, after controlling for gestation, sex and current weight. We report findings from a retrospective cohort study with a large proportion of Maori and Pacific participants to see whether the association between birthweight and cardiovascular risk factors in adolescence are consistent with the “fetal origins” hypothesis.

Methods
A cross-sectional survey was carried out with 2,518 adolescents (78% response of class roll on day of recruitment) attending 10 secondary schools (Year 11–13) that are representative of schools (n=32) with high proportions (>15%) of Pacific Island students within the Auckland area. The schools had low Ministry of Education decile scores (range 1–4, median decile=3) which will have limited any confounding from socioeconomic status (as low decile schools equate to low socioeconomic areas).

All students within each school were invited to participate. Recruiting was carried out class by class during form periods. At all schools, once consent was obtained, the survey team saw students on two occasions in groups of 10. On the day before the interview, students were seen briefly and given: instructions to fast overnight; a food frequency questionnaire to complete at home that night; and a sterile urine container to collect an early-morning urine sample. A questionnaire was also given for students to take home for completion by their parents or guardians.

On the morning of the interview, a 20 ml fasting venous blood sample was collected from each student to measure glucose, serum lipids, iron indices, and haemoglobin. Each student also completed a self-administered questionnaire that included date of birth, ethnicity (self assigned), and pubertal onset based on age of menarche in girls and of underarm hair growth in boys.

Height and weight were measured (in light clothes with shoes removed) and BMI was calculated (kg/m²). Duplicate measurement of blood pressure was carried out with participants in a sitting position using an electronic Omron sphygmomanometer with a standard cuff size after 15 minutes rest. If duplicate blood pressures differed by >10 mmHg, a third measure was carried out.

Details about the birth of each student (date of birth, country of birth, birth hospital if born in New Zealand, and recall of birth weight) were collected in a questionnaire completed at home by parents. Of the 1,260 students born in Auckland, 855 birth records between the years 1978 to 1983 from three of the major Auckland public maternity hospitals (National Women’s Hospital, St Helens Hospital, and Middlemore Hospital) were identified and examined for collection of birth weight information and other obstetric variables (including gestation and crown-heel length available at the latter two hospitals [n=416]). Ponderal index, a measure of growth retardation, was calculated as birth weight (kg) / birth length (m²).

To access hospital birth records for birthweight and information related to this study, written consent was obtained from all students and their parents. Ethical approval was obtained by the North Health Ethics Committee. All statistical were carried out using SUDAAN version 9.0.0 (Research Triangle Park, NC) to correct standard errors for clustered sampling by school.

Adjusted relative risks were calculated by the Mantel-Haenszel method for cohort studies. Multiple linear regression was used to calculate regression and partial correlation coefficients. Analysis of variance was used to calculate means. The population attributable risk was calculated from adjusted relative risks by estimating the attributable proportion for the exposed cases (or students) using standard methods.

Results
Of the 1,260 students born in Auckland, birth weight data were examined from 855 (68%) students, after excluding two students with high serum cholesterol levels (>9 mmol/L, birth weights 3.10, 3.62 kg) to prevent any influence by these outliers on
the findings. Their demographic distributions were: male 51.1%; age 14–15 years 33.0%; 16 years 37.7%; 17 years or older 29.4%; Pacific Island ethnicity 46.1%; European 32.1%; Asian 3.9%; and Maori 18.0% (Table 1). Mean levels for all cardiovascular risk factors did not significantly differ between Auckland-born adolescents with and without hospital birth weight data (Table 1).

Table 1. Comparison of demographic, anthropometric, and cardiovascular risk variables between Auckland-born adolescents for whom hospital birth weight information was (or was not) collected (n=1260)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Hospital birth weights collected</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n=855)</td>
<td>No (n=405)</td>
</tr>
<tr>
<td><strong>Demographic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (%)</td>
<td>51.1%</td>
<td>51.1%</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;16</td>
<td>33.0%</td>
<td>29.4%</td>
</tr>
<tr>
<td>16</td>
<td>37.7%</td>
<td>43.0%</td>
</tr>
<tr>
<td>&gt;17</td>
<td>29.4%</td>
<td>27.7%</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maori</td>
<td>18.0%</td>
<td>20.3%</td>
</tr>
<tr>
<td>Pacific Island</td>
<td>46.1%</td>
<td>41.5%</td>
</tr>
<tr>
<td>Asian</td>
<td>3.9%</td>
<td>4.2%</td>
</tr>
<tr>
<td>European/Other</td>
<td>32.1%</td>
<td>34.1%</td>
</tr>
<tr>
<td><strong>Cardiovascular risk factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SE)</td>
<td>Mean (SE)</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>170.5 (1.6)</td>
<td>70.8 (1.7)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>74.1 (1.1)</td>
<td>73.0 (2.0)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.5 (0.6)</td>
<td>24.9 (0.4)</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>112.8 (1.3)</td>
<td>112.0 (1.6)</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>70.9 (0.7)</td>
<td>70.8 (0.6)</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>4.38 (0.04)</td>
<td>4.34 (0.03)</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>1.31 (0.02)</td>
<td>1.32 (0.03)</td>
</tr>
<tr>
<td>Triglyceride (mmol/L)</td>
<td>0.90 (0.02)</td>
<td>0.88 (0.03)</td>
</tr>
<tr>
<td>Glucose fasting (mmol/L)</td>
<td>4.83 (0.03)</td>
<td>4.84 (0.04)</td>
</tr>
</tbody>
</table>

BMI=body mass index; BP=blood pressure; HDL=high-density lipoprotein; SE=standard error.

Analysis of variance was used to compare adolescent mean hospital birth weights between males and females, age, and ethnic subgroups (Table 2). The results showed that mean birth weights were significantly higher in males compared to females; higher in Pacific adolescents compared with all other ethnic groups, while Maori had lower mean birth weights compared with European adolescents. In contrast, mean birth weight did not vary with current age. Table 2 also shows the prevalence of low birth weight (<2.50 kg), which did not vary (p>0.05) between demographic subgroups—perhaps because of the moderate sample size.
Table 2. Prevalence of low birth weight (<2.50 kg) and mean birth weights (SE), by level of demographic variable

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Low birth weight (%)</th>
<th>Hospital birth weights (kg)</th>
<th>P value (compared with reference)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mean (SE)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>437</td>
<td>2.8%</td>
<td>3.504 (0.022)</td>
<td>0.036</td>
</tr>
<tr>
<td>Female</td>
<td>418</td>
<td>5.0%</td>
<td>3.347 (0.062)</td>
<td>–</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;16 years</td>
<td>282</td>
<td>2.8%</td>
<td>3.419 (0.031)</td>
<td>–</td>
</tr>
<tr>
<td>16 years</td>
<td>322</td>
<td>4.6%</td>
<td>3.397 (0.037)</td>
<td>0.53</td>
</tr>
<tr>
<td>&gt;17 years</td>
<td>251</td>
<td>4.0%</td>
<td>3.475 (0.051)</td>
<td>0.25</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maori</td>
<td>154</td>
<td>5.2%</td>
<td>3.235 (0.055)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pacific</td>
<td>394</td>
<td>2.3%</td>
<td>3.550 (0.037)</td>
<td>–</td>
</tr>
<tr>
<td>Asian</td>
<td>33</td>
<td>3.0%</td>
<td>3.258 (0.052)</td>
<td>0.0012</td>
</tr>
<tr>
<td>European</td>
<td>274</td>
<td>5.5%</td>
<td>3.379 (0.044)</td>
<td>0.0070</td>
</tr>
<tr>
<td>Total</td>
<td>855</td>
<td>3.9%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SE=standard error.

The relationship between hospital birth weight and the major cardiovascular risk factors (systolic and diastolic blood pressure, total cholesterol, HDL cholesterol, fasting triglycerides, and fasting glucose) were examined after adjusting for age, sex, and ethnicity (Table 3). None of these risk factors was associated with birth weight after adjusting for age, sex, and ethnicity (p>0.05); with total cholesterol having the lowest p value (0.11).

Table 3. Regression coefficients (and partial correlation coefficients [r]) for cardiovascular risk factors associated with birth weight and current BMI adjusted for age, sex, and ethnicity for students with hospital birth records (n=855)

<table>
<thead>
<tr>
<th>Cardiovascular risk factors</th>
<th>Hospital birthweight (kg)</th>
<th>Current BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β (SE)</td>
<td>r</td>
</tr>
<tr>
<td>Current BMI (kg/m²)</td>
<td>0.97 (0.26)</td>
<td>0.11</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>-0.29 (0.45)</td>
<td>-0.01</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>-0.20 (0.45)</td>
<td>-0.01</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>-0.10 (0.06)</td>
<td>-0.07</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>0.01 (0.02)</td>
<td>0.02</td>
</tr>
<tr>
<td>Log triglycerides (mmol/L)</td>
<td>-0.03 (0.03)</td>
<td>-0.04</td>
</tr>
<tr>
<td>Fasting glucose (mmol/L)</td>
<td>-0.01 (0.04)</td>
<td>-0.01</td>
</tr>
</tbody>
</table>

BMI=body mass index; BP=blood pressure; HDL=high-density lipoprotein; SE=standard error.

Current BMI was positively associated with birth weight after adjusting for age, sex, and ethnicity (p=0.0047, Table 3). For each risk factor, adding BMI to models (containing age, sex, and ethnicity) strengthened the association between birth weight and each cardiovascular risk factor. The regression coefficient (SE) of birth weight with total cholesterol was -0.13 (0.06) mmol/L/kg (p=0.047) and with the natural logarithm of triglycerides was -0.06 (0.02) mmol/L/kg (p=0.046). However, even with
BMI in the model, birth weight still was not associated significantly (p>0.05) with systolic and diastolic blood pressure, HDL cholesterol, or fasting glucose (data not shown).

The presence of possible non-linear associations between birth weight and cardiovascular risk factors was investigated by grouping participants by birth weight using the following cut-points: 3.00, 3.40, and 3.80 kg. Mean levels of all cardiovascular risk factors (adjusted for age, sex and ethnicity) did not vary across the four birth weight groups (p>0.05), thus indicating the absence of non-linear associations.

The possible presence of an interaction between Pacific and non-Pacific students from the effect of birth weight on cardiovascular risk factors was also examined by analysing birth weight as a continuous variable and creating interaction terms. However, the regression coefficients for all risk factors (specifically blood pressure, the three lipids and fasting glucose) did not differ between these two ethnic groups (p value for interaction term >0.05), thus indicating the absence of any interactions related to Pacific ethnicity.

The effect of puberty on associations was also examined. Adding onset of age of menarche in girls, or of underarm hair growth in boys, to models had no effect on regression coefficients thus indicating that onset age of puberty did not confound the associations between birth weight and cardiovascular risk factors. Controlling for gestation did not change the regression coefficients between birth weight and all cardiovascular risks factors (data not shown).

The relationship (adjusting for age, sex, and ethnicity) between the cardiovascular risk factors and the Ponderal index was also analysed in those participants with data on birth length (n=416). However, the Ponderal index was not associated (p>0.05) with any of the cardiovascular risk factors or current BMI (data not shown).

As expected, current BMI was positively associated with blood pressure (systolic and diastolic), total cholesterol, triglyceride levels, and fasting glucose; and negatively associated with HDL cholesterol [after controlling for age, sex and ethnicity in those for whom hospital birth weight data were obtained] (Table 3).

The contribution that low birth weight and elevated current BMI each made to the proportion of students with elevated total cholesterol (the risk factor which came closest to being associated with birth weight in our data [p value=0.11, Table 3]) was estimated by calculating population attributable risks from relative risks adjusted for sex and ethnicity, but not for age since the latter was not associated with cholesterol (Table 4).

Standard cut-points to define exposure were used for each risk factor: birth weight <2.5 kg, current BMI > 30 kg/m². The proportion of students with elevated serum cholesterol levels attributable to elevated BMI was 18%, and that attributable to low birth weight was 2%. The very small attributable risk for low birth weight primarily is due to the low prevalence of low birth weight (3.9% with birth weight <2.5 kg), compared with the higher prevalence of obesity (17.8% with BMI >30).

Using the upper 95% confidence limit of the relative risk for low birth weight (3.25) gave an attributable risk still only of 4%. Increasing the cut-point of low birth weight
up to <3.0 kg, so that now 20.0% of students were classified as exposed to low birth weight, did not increase the attributable risk (data not shown).

In contrast, the attributable risks for being in the top quintile of a cardiovascular risk factor (bottom quintile for HDL cholesterol) associated with elevated BMI (>30) were all much higher—being 8% for systolic blood pressure >122 mmHg; 12% for diastolic blood pressure >77 mmHg; 17% for HDL-cholesterol <1.09 mmol/L; 16% for triglycerides >1.18 mmol/L; and 6% for fasting glucose >5.1 mmol/L.

Table 4. Relative risk of having elevated serum cholesterol (>5.00 mmol/L), and population attributable risk (PAR), associated with low birth weight (<2.5 kg) and elevated current body mass index (BMI >30 kg/m²)

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Total cholesterol (mmol/L)†</th>
<th>Relative risk (95% CI)*</th>
<th>PAR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt;5.00</td>
<td>≤5.00</td>
<td></td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2.5</td>
<td>9 (28.1%)</td>
<td>23</td>
<td>2.00 (0.89–3.25)</td>
</tr>
<tr>
<td>≥2.5</td>
<td>157 (19.8%)</td>
<td>635</td>
<td>1.00</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;30</td>
<td>55 (37.4%)</td>
<td>92</td>
<td>2.12 (1.64–2.74)</td>
</tr>
<tr>
<td>≤30</td>
<td>111 (16.4%)</td>
<td>566</td>
<td>1.00</td>
</tr>
</tbody>
</table>

BMI=body mass index; CI=confidence interval; *Adjusted for sex and ethnicity; †Top 20% defined as having elevated total cholesterol.

Discussion

We found that birth weight in Auckland-born adolescents is not associated with any cardiovascular risk factors (including blood pressure), in contrast with the significant associations between BMI and all cardiovascular risk factors (Table 3). The similar distribution of demographic and cardiovascular risks factors among students with hospital birth weight (compared with those without) suggests that the sample of students in our analyses is representative of the wider study sample (Table 1). While recruiting students from low socioeconomic decile schools may have limited the generalisability of our results to all New Zealand adolescents, it will also have limited confounding from any socioeconomic factors related to birth weight.

Our findings are consistent with previous studies which have found that current body weight or BMI are both stronger determinants (than low birth weight) of increased blood pressure among adolescents,9,12–15 insulin resistance,16,17 and increased risk of cardiovascular disease.17

Our findings are also consistent with the findings of Huxley et al, who re-analysed the data from 55 studies and found that there was no association between birth weight and blood pressure.18 Huxley et al also found a very weak inverse association between birth weight and serum cholesterol in a meta-analysis of 58 studies.19 In their latter study, the association was so weak that a 100 gram increase in birth weight (the maximum that is achievable) would result in a 0.005 mmol/L decrease in serum cholesterol in adulthood—much lower than the 0.4 mmol/L reduction in cholesterol achievable by dietary modification in adulthood.20
The lack of a U-shaped association between birth weight and any of the cardiovascular risk factors in our study also contrasts with some previous research. Furthermore, the lack of an association between the Ponderal index and all cardiovascular risk factors does not suggest that growth retardation during pregnancy is a risk factor for elevated cardiovascular risk factors in adolescence.

When the effect of current BMI was also adjusted (in addition to age, sex, and ethnicity) in the multivariate analyses, birth weight became more strongly associated with total cholesterol and triglycerides. This is consistent with previous criticism of the ‘fetal origins’ hypothesis—i.e. that adjusting for BMI and or current weight causes spurious associations between birth weight and cardiovascular risk factors, since BMI or current weight are associated positively with both cardiovascular risk factors and also birth weight.

Inappropriately adjusting for current weight (because it is an intermediate variable along the causal pathway) may explain many of the reported negative associations reported between systolic blood pressure and birth weight, including the Dunedin cohort study when children were aged 7 years.

The lack of an association between birth weight and blood pressure may be due partly to the error arising from measuring blood pressure (at least twice) on a single occasion; while measurement error may have occurred with fasting triglycerides and glucose if students did not fast prior to blood collection. However, our finding of the expected strong association between current BMI and all cardiovascular risk factors (Table 3) suggests that any measurement error, if present, is likely to be small, and cannot explain the absence of any association between birth weight and all risk factors.

It also could be argued that the general lack of association between birth weight and cardiovascular risk factors (particularly blood pressure) in our study of adolescents is due to the confounding effects of puberty, since the tracking of blood pressure from childhood to adulthood may be perturbed by the adolescent growth spurt. There has been criticism that studies which have reported no association did not control for puberty. In support of this, an adolescent study (that observed an inverse association) also found during puberty that the inverse relationship between birth weight and future systolic blood pressure was weaker than after puberty.

However, this viewpoint is not supported by other previous studies—as one of the studies which found no association did control for puberty while four of the five adolescent studies which found an inverse association also did not control for puberty.

A review of 47 studies of blood pressure and birth weight published up until 2000 found that the distribution of the mid-point of the participant age range did not vary between studies reporting an inverse association compared with those which found none. Furthermore, in our study, adjusting for onset of puberty had no effect on the strength of regression coefficients between birth weight and cardiovascular risk factors. In addition, the review by Huxley et al found no clear association between current age and the effect of birth weight on current blood pressure among studies not done by researchers associated with the generation of the Barker hypothesis.
Therefore, given the above findings, possible confounding from puberty is not a plausible explanation for the general lack of an association between birth weight and cardiovascular risk factors in our study. Gestation was the only other possible confounder that we examined, and it also had no effect on regression coefficients between birth weight and cardiovascular risk factors when added to regression models.

Use of birth weight as a marker for fetal growth retardation has been criticised—as birth weight is only a crude indicator of fetal undernutrition, which in early gestation has a profound effect on body size at birth, while in later gestation it influences body proportions rather than body size.\(^{30}\) However, to fit with the diversity of findings across the various studies on the programming hypothesis,\(^4\) as pointed out by Joseph and Kramer,\(^{31}\) there have been changes made to the ‘fetal origins’ hypothesis as well as changes to the proposed programming effects consequent to undernutrition during specific periods in fetal life.

Initially, low birth and low infant weights were responsible for increased rates of coronary heart disease.\(^1\) However, over time, the hypothesis has become much more complex with different markers being used to indicate fetal undernutrition. For example, Barker et al have suggested that normal birth weight infants may also have suffered nutritional deprivation in fetal life\(^4,32\) and furthermore that ‘both reduced and accelerated liver growth in late gestation are early determinants of coronary heart disease.’\(^33\)

Our attributable risk calculations can be used to decide about the public health significance of our findings. They indicate that current BMI explains a much higher proportion of students with elevated serum cholesterol in adolescence than low birth weight (Table 4). In contrast, low birth weight explains only a very small percentage (2%) of students with elevated cholesterol, which suggests that efforts to prevent low birth weight in New Zealand infants will have only a marginal role in preventing future cardiovascular disease caused by hypercholesterolaemia.

This conclusion is consistent with overseas estimates—that increasing birth weight by 100 grams (which is achievable) would decrease coronary heart disease mortality in adult men and women by 1.9% and 2.5%, respectively.\(^{34}\) By comparison, recent NZ research indicates that 24% of coronary heart disease mortality can be attributed to elevated adult BMI (>22 kg/m\(^2\)).\(^{35}\)

Furthermore, other authors have concluded that weight control in adolescence probably has a more important role to play in preventing adult hypertension, than does improving the nutrition of pregnant women,\(^{15,36}\) although we are unaware of any studies linking cardiovascular risk factor levels in adolescence with adult cardiovascular mortality. These finding support targeting resources into programmes, which help normalise body weight within the New Zealand adolescent population, rather than trying to achieve higher birth weights among at-risk populations.

In summary, the results from this study provide no support for the ‘fetal origins’ hypothesis, as birth weight was not related to any cardiovascular risk factor. Even if there is a weak association between birth weight and cardiovascular risk factors (which was not detected by this study), only a very small proportion of adolescents with elevated coronary risk factors can be attributed to low birth weight. The ‘fetal origins’ hypothesis may be of intellectual interest to medical researchers, but is...
unlikely to result in any substantial health gains in adulthood. Instead, the focus of cardiovascular disease prevention should remain in adolescence and adulthood.

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**References:**


Coeliac disease diagnosed at Starship Children’s Hospital: 1999–2002

Elisabeth Westerbeek, Stephen Mouat, Alison Wesley, Simon Chin

Abstract

Aim. To retrospectively review the clinical presentation and serological testing of children diagnosed with coeliac disease at Starship Children’s Hospital (Auckland, New Zealand) over a 4-year period between January 1999 and December 2002.

Methods. A review of Starship Hospital medical records of all children diagnosed with coeliac disease by small bowel biopsy between January 1999 and December 2002 was conducted. Patients had anti-gliadin, endomysial, and tissue transglutaminase antibodies performed prior to small bowel biopsy.

Results. There were 48 patients, median age of 6.9 years (range 1.6 to 15.7 years). Comparing symptomatic age groups older and younger than 5 years, the former age group presented significantly more often with abdominal pain (p=0.005) and the latter age group presented significantly more often with failure to thrive (p=0.02). Screening at-risk groups yielded nine children (19%) with asymptomatic disease. Thirty-three of 36 (92%) patients tested positive for the anti-endomysial IgA antibody, and 26 of 27 (96%) patients tested positive with the anti-tissue transglutaminase IgA antibody. Three patients (aged 3, 4, and 6 years of age) were negative for anti-endomysial antibodies (including one also negative for anti-tissue transglutaminase antibody), but all three were positive for anti-gliadin antibody.

Conclusions. Our study found that children with coeliac disease are being diagnosed at an older age. Older children also presented with more abdominal pain while younger children presented with more failure to thrive. At-risk groups for coeliac disease may be asymptomatic and form a significant group of patients diagnosed with coeliac disease. Anti-endomysial and tissue transglutaminase antibodies are reliable tests for coeliac disease. However, in younger patients or if there is a high clinical index of suspicion of coeliac disease, small bowel biopsy should be performed even if the anti-endomysial and tissue transglutaminase antibody tests are negative.

Coeliac disease, previously thought to be infrequent, has now become a common condition. Recent population studies have shown prevalences ranging from 1:83 to 1:300.1–5 In New Zealand, adult data indicate a prevalence as high as 1:83.5 Recent evidence also shows that the incidence of coeliac disease in New Zealand has increased.6

Coeliac disease is thought to be an auto-immune multigenic disorder which is strongly associated with certain HLA alleles-HLA-DQ2 and HLA-DQ8. It is characterised by a permanent intolerance to gluten, resulting in immunologically mediated inflammation to the small-intestinal mucosa.7
Classically, in the paediatric population, coeliac disease has been considered a disease of infancy. Patients presented at variable intervals soon after weaning onto solids, with symptoms of growth failure, diarrhoea, and a distended abdomen. In recent times, more children with coeliac disease have been diagnosed at an older age. Indeed, a wider clinical spectrum of more atypical non-gastrointestinal symptoms such as short stature and anaemia, and mild non-specific gastrointestinal symptoms (such as recurrent abdominal pain in this group) is now increasingly being recognised. At-risk populations for coeliac disease (including first-degree relatives of index cases, and children with Down’s syndrome and Type 1 diabetes mellitus) have also been recognised.

Amongst several possible explanations for this evolving clinical spectrum, a change in dietary habits with a delay in introduction of gluten containing foods to infants being weaned onto solids has been postulated. Increasing recognition of patients with coeliac disease has also been aided by improved serological markers. Newer coeliac antibodies such as the anti-endomysial and tissue transglutaminase antibodies are more reliable than the anti-gliadin antibodies traditionally used before. Increasing availability of flexible endoscopy in infants and children has also helped to more reliably obtain small bowel biopsies.

The purpose of this study was to see if similar changes in the age at diagnosis and a wider clinical spectrum of symptoms were also occurring in children diagnosed with coeliac disease at a tertiary referral paediatric centre, Starship Children’s Hospital. Serological testing was also evaluated to determine their reliability.

Methods

Methodology—A personal database (from one of the authors who performed all of the small bowel biopsies in the study patients) formed the basis for this study. A retrospective chart review of Starship Hospital records was undertaken of these patients with coeliac disease, diagnosed over a 48-month period between January 1999 and December 2002. Information was obtained from clinical notes, referral letters, and laboratory results.

All patients were diagnosed as having coeliac disease based on histological confirmation by duodenal biopsy. At least four duodenal biopsies from the second part of the duodenum were obtained, and biopsies were interpreted by a paediatric pathologist. Histological features considered consistent with coeliac disease included partial to total villous atrophy, crypt hyperplasia, increased intraepithelial lymphocytes, and increased infiltration of lymphocytes and plasma cells in the lamina propria.

Anti-gliadin antibodies were tested by an enzyme-linked immunosorbent assay (ELISA), anti-endomysial antibodies by immunofluorescence (IFA), and anti-tissue transglutaminase antibodies by ELISA. Features of iron deficiency included high iron binding, low iron saturation, or low ferritin levels.

For the purposes of this review, ‘failure to thrive’ is defined as a concern on behalf of the referring physician that the child was either not growing as expected or losing weight. It is included regardless of whether this concern was actually borne out by measurements. Growth was established (using the Hamill growth chart for children) for measuring the 3rd, 50th, and 97th percentile for height, weight. All measurements were calculated into Z scores, according to the formula:

\[
Z \text{ score} = \frac{x-p50}{SD}
\]

where x stands for the patient’s measurement, p50 stands for the 50th percentile at the child’s age, and SD stands for the standard deviation for that age.

For Down’s syndrome patients, a Down’s syndrome growth chart was used. They were not included in the final calculations of mean/median Z scores as they are considered as a population with abnormal growth characteristics.
Proportions were compared using a Chi-squared test. Where the expected counts were less than 25%, a Fisher’s Exact Test was used. A p value <0.05 was considered to be significant.

**Results**

There were 48 patients (19 male, 29 female) with coeliac disease in the study; 44 patients identified as Caucasian (92%), 2 as Indian, 1 as mixed Caucasian/Pacific Island, and 1 as mixed Caucasian/Asian. The number of patients detected annually from 1999 through to 2002 were 13, 7, 14, and 14.

The median age of diagnosis when the small bowel biopsy was obtained was 6.9 years, with a range of 1.6 to 15.7 years (Figure 1). Of these 48 patients, 16 (33%) were younger than 5 years of age, and 32 (67%) were older than 5 years of age at the time of diagnosis. There were 39 symptomatic patients (81%) and 9 asymptomatic patients (19%). Of those patients who were symptomatic, 15 patients (38%) were younger than 5 years and 24 (62%) patients were older than 5 years. Eight out of nine asymptomatic patients were older than 5 years.

**Figure 1. Age of children at diagnosis of coeliac disease**

The 9 patients who were asymptomatic (mean age: 10.5 years) were identified mainly on the basis of screening. Three of them were first-degree relatives of patients with coeliac disease (one with iron deficiency), 3 patients had Down’s syndrome (1 with iron deficiency), and 1 patient had both Down syndrome and Type 1 diabetes mellitus. One patient had Type 1 diabetes mellitus and iron deficiency. One patient had short stature, but otherwise had no other symptoms.
Presenting symptoms included failure to thrive, vomiting, diarrhoea, lethargy, anorexia, abdominal pain, abdominal distension, irritability, and constipation (Table 1). Overall, the most frequent symptoms reported were failure to thrive (44%), diarrhoea (44%), abdominal pain (41%), and poor appetite (31%). Patients older than 5 years of age tended to have more abdominal pain compared to patients younger than 5 years (Table 1, p=0.005). Failure to thrive was present more often in the younger age group (p=0.02). No other significant difference in other symptoms was noted between the two age groups with symptoms.

Table 1. Symptomatic group (n=39) presenting symptoms

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Patients &lt; 5yr n=15(%)</th>
<th>Patients &gt; 5yr n=24(%)</th>
<th>All symptomatic patients n=39(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure to thrive</td>
<td>10(67)*</td>
<td>7(29)</td>
<td>17(44)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6(40)</td>
<td>3(13)</td>
<td>9(23)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>7(47)</td>
<td>10(42)</td>
<td>17(44)</td>
</tr>
<tr>
<td>Lethargy</td>
<td>5(33)</td>
<td>6(25)</td>
<td>11(28)</td>
</tr>
<tr>
<td>Poor appetite</td>
<td>6(40)</td>
<td>6(25)</td>
<td>12(31)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>2(13)</td>
<td>14(58)**</td>
<td>16(41)</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>4(27)</td>
<td>2(8)</td>
<td>6(15)</td>
</tr>
<tr>
<td>Irritability</td>
<td>3(20)</td>
<td>1(4)</td>
<td>4(10)</td>
</tr>
<tr>
<td>Constipation</td>
<td>3(20)</td>
<td>2(8)</td>
<td>5(13)</td>
</tr>
<tr>
<td>Other</td>
<td>2(13)</td>
<td>9(38)</td>
<td>11(28)</td>
</tr>
</tbody>
</table>

Values given as percentage of the group; *p=0.02 compared to patients >5 years; †p=0.005 compared to patients <5 years.

In the group older than 5 years of age, a variety of clinical presentations were noted. Two patients had nonspecific recurrent abdominal pain only, one patient had recurrent vomiting and a hoarse voice as the main symptoms, one patient had joint symptoms as well as gastrointestinal symptoms, one patient had mainly lethargy and iron deficiency, and two patients with Type 1 diabetes presented with nonspecific recurrent abdominal pain.

One patient had Down’s syndrome, Type 1 diabetes mellitus, and hypothyroidism. Four patients had started a gluten-free diet before diagnosis, and had needed to undergo re-exposure to gluten before small bowel biopsy to confirm the diagnosis. In those patients younger than 5 years with symptoms, most presented with a combination of failure to thrive, poor weight gain, loose stools, abdominal distension, irritability, and lethargy.

A positive family history for coeliac disease was found in 16 patients (33%), with 12 of these patients (25%) having a first-degree relative with coeliac disease.

There were six patients with Down’s syndrome (13%) including one with both Type 1 diabetes mellitus and hypothyroidism. Four of these patients were asymptomatic at the time of diagnosis of coeliac disease and detected as part of a screening schedule for Down syndrome children in New Zealand.21

There were 9 patients with Type 1 diabetes mellitus (19%), including 1 previously mentioned with both Down’s syndrome and hypothyroidism. Two of these patients were asymptomatic at the time of screening for coeliac disease.
After excluding 6 patients with Down syndrome and 1 patient with developmental delay, weight was available for 40 patients and height for 32 patients within 3 months before the diagnosis of coeliac disease was made. For patients who had growth measurements available, mean Z score for weight was –0.17 (n=40) and for height – 0.35 (n=32). Amongst the symptomatic group with measurements available, there was no significant difference in Z scores for weight (-0.26 vs –0.11 ns) and height (-0.48 vs –0.32 ns) between those younger and older than 5 year (Table 2).

**Table 2. Z scores for height and weight-symptomatic patients > and < 5 years; all patients**

<table>
<thead>
<tr>
<th>Z score</th>
<th>Patients &lt; 5 years</th>
<th>Patients &gt; 5 years</th>
<th>All patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Height</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No statistical difference in Z scores for height and weight between age groups with symptoms.

Serological testing was performed in all patients prior to small bowel biopsy. In the earlier time period of the study, anti-gliadin antibodies or a combination of anti-gliadin and anti-endomysial antibodies tended to be done, while in the latter part of the study, anti-endomysial and transglutaminase antibodies tended to be done. Eleven of 17 patients (65%) were positive for anti-gliadin IgA antibodies and 16/17 (94%) were positive for anti-gliadin IgG antibodies (Table 3).

There were 2 patients (aged 3 and 6 years) negative for anti-endomysial but positive for anti-gliadin antibodies; and 1 patient aged 4 years negative for both anti-endomysial and transglutaminase antibodies but positive for anti-gliadin antibody, despite the former antibodies being more sensitive and specific. Thirty-three of 36 patients (92%) were positive for anti-endomysial IgA antibody, and 26/27 patients (96%) were positive for ant-tissue transglutaminase IgA antibody.

Sixteen of 39 patients (41%) showed features of iron deficiency. Thirty-one of the 48 patients had a serum IgA documented and none were below the laboratory reported reference range for age.

**Table 3. Screening antibody tests**

<table>
<thead>
<tr>
<th>Screening tests</th>
<th>Total number of patients who were positive / total number of patients tested (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gliadin IgA</td>
<td>11/17 (65%)</td>
</tr>
<tr>
<td>Gliadin IgG</td>
<td>16/17 (94%)</td>
</tr>
<tr>
<td>Endomysial IgA</td>
<td>33/36 (92%)</td>
</tr>
<tr>
<td>Tissue transglutaminase IgA</td>
<td>26/27 (96%)</td>
</tr>
</tbody>
</table>

**Discussion**

The clinical spectrum of childhood coeliac disease has evolved from being a disease previously more common at a younger age, to now being detected more frequently...
at an older age. In our series of patients, the median age of diagnosis was 6.9 years, comparable to other studies,\textsuperscript{18,23} and supports the observation that the classic presentation in early childhood of growth failure, distended abdomen and diarrhoea has become less common.

While ‘failure to thrive’, diarrhoea, abdominal pain, and poor appetite were the most common symptoms overall in our study, there were some differences. The older patients tended to have more abdominal pain and younger patients more failure to thrive. There were no significant differences in other symptoms between the age groups, but this may be because of the small numbers of our study. Atypical symptoms in our older children included recurrent abdominal pain, recurrent vomiting, anaemia, short stature, and joints symptoms. A wide range of other atypical symptoms that have been noted by others include delayed puberty, dental enamel defects, hepatitis, ataxia, seizures, and constipation.\textsuperscript{4}

Nine (19\%) of our patients were detected as a result of screening at-risk groups including first-degree relatives, Down’s syndrome, and Type 1 diabetes mellitus. These at-risk groups formed a significant proportion of the children being diagnosed with coeliac disease in our series. There were 9 children with diabetes (19\%), some of whom had nonspecific abdominal pain and/or poor glycaemic control. Coeliac disease should therefore be considered in those diabetic patients whose glycaemic control is difficult or who have mild gastrointestinal symptoms.

Studies indicate that about 3–7\% of Down’s syndrome children also have coeliac disease.\textsuperscript{13,14} As children with Down’s syndrome tend to have abnormal growth characteristics, early recognition of coeliac disease is important so that growth is not significantly impaired (as abnormal growth is mistakenly attributed to Down’s syndrome).

There was a high positive family history of coeliac disease in our study, with 16 (33\%) patients having some family member with coeliac disease. Twelve (25\%) of the patients had an affected first-degree relative, a high frequency probably due to screening and selection bias in our series. When populations have been studied, the reported overall frequencies of coeliac disease in first degree relatives have been 1–18\%.\textsuperscript{8} This reflects the strong genetic component of this disease, and reinforces the need to screen first-degree relatives of index cases.

Z scores for weight and height in our study were not particularly low, and there were no statistically significant differences in growth measurements between younger and older children who were symptomatic. This may be because of the small and incomplete numbers in the study. It is also possible that patients were being detected before significant growth impairment occurred, although this could not be verified in our study.

Our study showed that the anti-endomysial and transglutaminase antibodies are reliable. Reported sensitivities vary from 85–98\% and specificities from 94–100\%.\textsuperscript{9} Due to the limitations of this retrospective study, true antibody sensitivity and specificity could not be obtained. Three patients (aged 3, 4, and 6 years of age) had negative anti-endomysial antibodies (including one with negative anti-transglutaminase antibody), but positive anti-gliadin antibodies. Anti-endomysial antibodies have been reported to be less reliable in children younger than 2 years of
Reliance on the anti-endomysial and transglutaminase antibody may therefore miss younger patients with coeliac disease.

With this exception, anti-gliadin antibodies, because of lower sensitivity and specificity compared with anti-endomysial and transglutaminase antibodies, are no longer being widely used. However, if there is a strong clinical suspicion of coeliac disease, particularly in the younger child, small bowel biopsy should be performed regardless of the results of the serological tests.

In 39 patients who had iron studies performed, 16 (41%) had features of iron deficiency, supporting the observation that nutritional deficiencies are common.9 While up to 10% of patients with selective IgA deficiency have coeliac disease,25 this was not detected in our patients. However this may reflect the small numbers in our study.

Four of the patients had been on a gluten-free diet before biopsy. It is important that empirical withdrawal of gluten is discouraged, and that small bowel biopsy is obtained first to confirm the diagnosis histologically. Without a positive small bowel biopsy, the special food authority for gluten-free food products cannot be obtained in New Zealand, thereby possibly financially disadvantaging families in the long-term.

While other studies suggest that the incidence of coeliac disease appears to be increasing,6,26 in the 4 years of our study, we did not detect any obvious increase. However, the time period of our study was relatively short. Further observation over a longer period of time is therefore required to determine whether the incidence is increasing.

In summary, our review suggests that coeliac disease in children is being diagnosed in an older age group, many of whom have atypical symptoms. Recurrent abdominal pain is a more frequent presenting symptom in the older child and failure to thrive more frequent in the younger child. At-risk screening detects a significant number of patients, some of whom may be asymptomatic. Anti-endomysial and transglutaminase antibodies are reliable serological markers—except possibly in the younger child where (if the clinical index of suspicion is high) a small bowel biopsy should be done regardless of the serological test results.

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**References:**


Sore throat management in New Zealand general practice

Marjan Kljakovic, Peter Crampton

Abstract

**Aim.** To describe the sore throat management practices by New Zealand general practitioners (GPs) and compare the rate of sore throat presentation over time.

**Method.** Data were collected from the *National Primary Medical Care Survey* carried out over 2001/2002. Analyses were done on patients who presented to the GP with the symptom of a sore throat as one of their reasons for visit. A systematic review of the New Zealand literature was done for sore throat presentation to GPs since 1966.

**Results.** There were 10,506 records of visits gathered from 246 GPs and 335 patients presented sore throat as a reason for visit. Patients presented sore throat at a rate (SE) of 3.6 (0.26) per 100 encounters and varied by age (p=0.004), but not by socioeconomic deprivation (p=0.415) or by ethnic group (p=0.165). Patients’ perceived urgency of visit had a greater impact in the rate of presentation for the 0–4 year age group than in the at-risk age group of 5–14 years (p=0.001).

GPs recorded a ‘Read code’ diagnosis at a rate of 59.2 (3.96) recordings per 100 encounters. Among the 306 recorded diagnoses, 11.4% were explicit recordings of viral diagnoses. 7.6% of GPs ranked themselves as ‘moderately’ and 2.3% as ‘highly’ uncertain of their diagnosis. Throats swabs were taken at a rate of 6.6 (1.68) swabs per 100 encounters. Antibiotic prescribing rate was higher when sore throat was recorded as a reason for visit than not (p<0.001). There were no significant differences in throat swabs taken for sore throat patients prescribed an antibiotic or not (p=0.623). No Pacific person had a throat swab taken. Patients with sore throat who were Maori (73.5 [7.2]) or Pacific people (80.2 [17.3]) were more likely to be prescribed an antibiotic than Europeans (57.4 [4.62]).

Since 1966, there were 16 New Zealand studies of patients presenting with respiratory disorders to their GP. Seven of these studies measured GP management of sore throat, and only 3 of these measured the rate of patients’ sore throat symptom presentation. The rate of patients’ sore throat presentation remained similar when compared with the Waikato study of 1991 (2.8%) that had a similar methodology.

**Conclusion.** Sore throat continues to be a common symptom that GPs manage in their work. Ethnic differences may have a part to play in how GPs manage sore throat. More research is needed to discover those factors that would encourage a greater proportion at-risk 5–14 year old children to attend their GP with sore throat.

Sore throat is among the top 10 symptoms that patients present to their general practitioner (GP) in New Zealand—a finding similar to other Western countries. Patients vary in how they choose primary health care for their sore throat care. For example, the rate of sore throat presentation in a Wellington GP-run after-hour service (10 per 100 encounters) was nearly double the rate of presentation to Waikato GPs working in their consulting rooms (4.7 per 100 encounters).
The variation in the presentation rates of sore throat between different types of primary care services may help explain why, in some areas of New Zealand, rheumatic fever is still an important sequela of throat infections.\(^4\) Those most at risk are children aged 5–14 years (69% of cases) and Maori and Pacific Island people (89% of cases).\(^2,3\) However, a 1991 morbidity survey in the Waikato found that Maori and Pacific Island people, in the at-risk age group (5–14 years) and with a sore throat, consult their GP less often than Europeans.\(^3\)

The rationale for treating sore throat is to eliminate the possibility of streptococcal sequelae such as rheumatic fever.\(^4\) Previous studies in New Zealand primary care have indicated that there appears to be no bias in favour of treating sore throats in the 5 to 14 year age group of patients with antibiotics, despite this group of patients being particularly at risk for rheumatic fever in New Zealand.\(^2,4\)

Over the last decade there has been increasing public health pressure towards a more rational approach to sore throat treatment in New Zealand (for example discouraging antibiotic prescribing for viral infections).\(^5,6\) Informing policy on how primary care services might best manage sore throat around New Zealand requires understanding not only the patients’ consulting patterns for sore throat, but also the GPs’ management of them.

The aims of this study was to compare the rate of sore throat presentation over time; to describe the sore throat management practices by New Zealand GPs; and to test two hypotheses. Our first hypothesis is that ethnic difference in sore throat presentation remains as it was in the Waikato study of 1991. Secondly, we hypothesise that GPs do not bias in favour of treating sore throats in the 5 to 14 year age group of patients with antibiotics.

**Method**

**Sample data**—The data used in this study were collected from the National Primary Medical Care Survey (*NatMedCa*), carried out over 2001/2002. This was a nationally representative, multistage, probability sample of GPs and patient visits. The primary purpose of the survey was to collect data on the content of patient visits. For two periods (of 1 week’s duration), each selected GP completed a questionnaire for a 25% systematic sample of patient visits. The questionnaire was adapted from the annual US National Ambulatory Medical Care Survey (*NAMCS*).\(^7\)

To obtain a nationally representative sample:

- Geographic locations were sampled, and
- GPs were sampled from locations, stratified by organisation type (independent; independent practitioner association; capitated; community-governed non-profit) and rural/urban (metropolis and cities; towns and rural areas).

GP and visit weights were calculated to take account of different sampling probabilities, so that approximately unbiased estimates of proportions, means, and measures of association could be calculated.\(^8\)

**Selection criteria analysis**—All the patients were selected for analysis if they presented to the GP with the symptom of a sore throat as one of their reasons for visit. The GPs could record up to four reasons for a visit.

The following data elements were selected in the analysis:

- Patient characteristics: age, sex, ethnicity, and NZDep (socioeconomic deprivation).
- Process details where sore throat was the reason for the visit: READ coded diagnoses, throat swab, and prescribing of antibiotics.

The denominator for the analyses was patient encounters with the GP in routine general practice. Three age bands of patients were used in the analysis: 0–4 years, 5–14 years, and 15+ years.
Ethnicity was grouped as either European, Maori, or Pacific (Island) peoples (such as Samoan). Socioeconomic position was measured using the NZDep2001 index of socioeconomic deprivation, a census-based small-area index of deprivation.\(^9\) The index scale used here is from 1 to 5, where 1 = the least deprived 20% of areas, and 5 = the most deprived 20% of areas. Comparisons were carried out using the SUDAAN statistical package,\(^10\) thus allowing estimates to take account of clustering, stratification, and weights.\(^11\)

**Collection of morbidity data for sore throat studies over time**—The *New Zealand Family Physician* and the *New Zealand Medical Journal* were hand-searched for studies on morbidity surveys in general practice or primary care. People in the academic centres around New Zealand were contacted for unpublished data. The 1966–2000 MEDLINE index was searched with the keywords: sore throat, general practice, general practitioner, morbidity survey, and New Zealand.

**Results**

The total visit sample consisted of 10,506 records, gathered from 246 GPs. The overall GP response rate was 71.7%. The response rate was calculated as the proportion of eligible GPs in the sample who completed patient visit survey forms for the two 1-week survey periods. The unweighted number of visits to GPs with sore throat as a reason for visit was 355, which equated to a nationally representative weighted total of 10,392 visits during the 2-week data collection period and 270,192 sore throat visits annually. By sex, the proportion of sore throat visits was 41.7% male and 58.3% female; and 38% of these visits were for (subsidised) Community Services Card-holding patients.

**Patient presentation of sore throat**—The rate (standard error [SE]) of sore throat presentation to GPs was 3.6 (0.26) per 100 encounters. Table 1 compares patient characteristics of social deprivation (NZDep), ethnicity, and perceived urgency of consultation for the three age groups of patients. Overall, the rate of sore throat presentation per 100 encounters varied by age (p=0.004), and perceived urgency of consultation (p=0.001)—but not by NZDep2001 (p=0.415) or by ethnic group (p=0.165).

**Uncertainty of diagnosis by GPs**—The rate (SE) of sore throat visits that had a ‘Read code’ diagnosis was 59.2 (3.96) per 100 encounters. Table 2 shows the frequency of ‘Read coded’ diagnoses. Among the 306 listed diagnoses, 224 (73.2%) were throat-related diagnoses; 35 (11.4%) were explicitly viral diagnoses; 35 (11.4%) were other respiratory diagnoses; and 12 (3.9%) were non-respiratory diagnoses.

When GPs were asked to rank how uncertain they were of their diagnosis, 50.2% said they were ‘certain’, 39.9% ranked their uncertainty as ‘low’, 7.6% as ‘moderate’, and 2.3% as ‘high’ (52 sore throat visits were not ranked by GPs).

**Throat swab and antibiotic prescribing by GPs for patients with a sore throat**—When sore throat was a reason for visit, the rate (SE) of throat swabbing taken was 6.6 (1.68) swabs per 100 encounters. The rate (SE) of antibiotic prescribing was 60.7 (4.29) prescriptions per 100 encounters, which was significantly higher than the rate (SE) of antibiotic prescribing when sore throat was not recorded as a reason for visit (18.5 [0.75]) prescriptions per 100 encounters (p<0.001).

In patients presenting with a sore throat, there were no significant differences between the age-standardised average number of throat swabs taken per 100 encounters for patients prescribed an antibiotic (6.0 swabs per 100 encounters) versus no antibiotic (7.6 swabs per 100 encounters) (p=0.623).
Table 1. Comparison of patient characteristics (Social deprivation, Ethnicity, and perceived urgency of visit) with the rate of sore throat presentation to GPs for three age groups of patients (n= 355 patients)

<table>
<thead>
<tr>
<th>Patient characteristic</th>
<th>Rate (SE) of sore throat presentation per 100 encounters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
</tr>
<tr>
<td>Social deprivation (NZDep grade)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2.6 (0.47)</td>
</tr>
<tr>
<td>2</td>
<td>3.3 (0.53)</td>
</tr>
<tr>
<td>3</td>
<td>3.5 (0.61)</td>
</tr>
<tr>
<td>4</td>
<td>4.0 (0.70)</td>
</tr>
<tr>
<td>5</td>
<td>4.1 (0.69)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>3.4 (0.26)</td>
</tr>
<tr>
<td>Maori</td>
<td>5.2 (0.82)</td>
</tr>
<tr>
<td>Pacific person</td>
<td>3.3 (1.12)</td>
</tr>
<tr>
<td>Perceived urgency of visit</td>
<td></td>
</tr>
<tr>
<td>As soon as possible</td>
<td>4.5 (1.78)</td>
</tr>
<tr>
<td>Today</td>
<td>52.0 (3.92)</td>
</tr>
<tr>
<td>This week</td>
<td>40.4 (3.89)</td>
</tr>
<tr>
<td>This month</td>
<td>3.1 (1.08)</td>
</tr>
<tr>
<td>All sore throat patients</td>
<td>3.6(0.26)</td>
</tr>
</tbody>
</table>
Table 2. Frequency of ‘Read’ diagnostic categories made by GPs (Sore patients could have more than one diagnosis.) N=306 diagnoses

<table>
<thead>
<tr>
<th>Read Diagnostic Category</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Throat related diagnoses</strong></td>
<td></td>
</tr>
<tr>
<td>Acute pharyngitis</td>
<td>74</td>
</tr>
<tr>
<td>Acute tonsillitis</td>
<td>70</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>39</td>
</tr>
<tr>
<td>Sore throat / throat symptoms</td>
<td>25</td>
</tr>
<tr>
<td>Throat infection</td>
<td>6</td>
</tr>
<tr>
<td>Streptococcal sore throat / tonsillitis</td>
<td>4</td>
</tr>
<tr>
<td>Tonsillectomy</td>
<td>2</td>
</tr>
<tr>
<td>Examine throat</td>
<td>2</td>
</tr>
<tr>
<td>Acute laryngitis</td>
<td>2</td>
</tr>
<tr>
<td><strong>Explicitly viral diagnoses</strong></td>
<td></td>
</tr>
<tr>
<td>Viral URTI</td>
<td>19</td>
</tr>
<tr>
<td>Viral infection /illness/measles/rubella</td>
<td>11</td>
</tr>
<tr>
<td>Influenza</td>
<td>3</td>
</tr>
<tr>
<td>Infectious mononucleosis</td>
<td>1</td>
</tr>
<tr>
<td>Herpes simplex viral infection</td>
<td>1</td>
</tr>
<tr>
<td><strong>Other respiratory diagnoses</strong></td>
<td></td>
</tr>
<tr>
<td>Otitis media</td>
<td>8</td>
</tr>
<tr>
<td>Acute bronchitis</td>
<td>5</td>
</tr>
<tr>
<td>Acute sinusitis</td>
<td>4</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>4</td>
</tr>
<tr>
<td>Post nasal drip</td>
<td>3</td>
</tr>
<tr>
<td>Chest infection</td>
<td>2</td>
</tr>
<tr>
<td>Nasal obstruction</td>
<td>2</td>
</tr>
<tr>
<td>Respiratory infection NOS</td>
<td>2</td>
</tr>
<tr>
<td>Airways obstruction irreversible</td>
<td>1</td>
</tr>
<tr>
<td>Acute gingivitis</td>
<td>1</td>
</tr>
<tr>
<td>Acute tracheitis</td>
<td>1</td>
</tr>
<tr>
<td>Mouth ulcer</td>
<td>1</td>
</tr>
<tr>
<td>Oral thrush</td>
<td>1</td>
</tr>
<tr>
<td><strong>Non-respiratory diagnoses</strong></td>
<td></td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>3</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>2</td>
</tr>
<tr>
<td>Back pain</td>
<td>1</td>
</tr>
<tr>
<td>Follow up consult</td>
<td>1</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>1</td>
</tr>
<tr>
<td>General examination of patient</td>
<td>1</td>
</tr>
<tr>
<td>Headache</td>
<td>1</td>
</tr>
<tr>
<td>Oesophageal reflux</td>
<td>1</td>
</tr>
<tr>
<td>No abnormality (NAD)</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 3 compares the rates of throat swab and antibiotic prescribing per 100 encounters for patients presenting with a sore throat in the three age groups and three ethnic groupings. Overall, there were no significant differences in rates of throat swabbing or antibiotic prescribing by age or ethnicity.
Table 3. Rate of GP throat swab taking and antibiotic prescribing for three age groups and ethnic groupings of patients (n= 355 sore throat patients)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rate (SE) per 100 encounters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Throat swab</td>
</tr>
<tr>
<td><strong>Patients’ age groups</strong></td>
<td></td>
</tr>
<tr>
<td>0-4 years</td>
<td>5.8 (3.83)</td>
</tr>
<tr>
<td>5-14 years</td>
<td>8.1 (2.95)</td>
</tr>
<tr>
<td>15+ years</td>
<td>5.9 (2.09)</td>
</tr>
<tr>
<td><strong>Patients’ ethnicity</strong></td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>7.1 (1.97)</td>
</tr>
<tr>
<td>Maori</td>
<td>6.1 (3.36)</td>
</tr>
<tr>
<td>Pacific person</td>
<td>0</td>
</tr>
<tr>
<td><strong>All sore throat patients</strong></td>
<td>6.6 (1.68)</td>
</tr>
</tbody>
</table>

Sore throat presentation and diagnosis over time—There were 16 New Zealand studies identified between 1966 and 1999 where GP respiratory disease management was described—14 of those studies were morbidity surveys of GP management of patients encountered in general practice (with any primary health care problem), and sore throat was one of the problems managed. One study focused only on sore throat management in a single general practice, and one study only focused on sore throat management in an after-hours services run by GPs.

Table 4 shows there was considerable variation over time in how GPs diagnosed all respiratory diagnoses, upper respiratory tract infection diagnoses, and sore throat related diagnoses.

Seven studies provided data on the GPs’ management of sore throat related diagnoses, but only three of these studies measured the rate of patients’ presentation of sore throat symptom. The rate of sore throat presentation in this study (3.96%) had changed little from the 2.8% rate found in the 1991 Waikato study which used a very similar methodology.

Discussion

Principal findings—The rate of sore throat related diagnoses identified by GPs in this 2001 study (3.96%) had changed little from the 2.8% rate found in the 1991 Waikato study that used a very similar methodology. Comparisons with previous data need to be made with caution because of variation of data definition and collection between studies done over time. Nevertheless, sore throat remains one of the top 10 symptoms patients present to the GP across all studies over time.

This study rejected our first hypothesis in that the ethnic difference in sore throat presentation did not remain as it was in the Waikato study of 1991. We found more Maori than European patients presented with sore throat, but fewer Pacific people. This finding is the reverse of Waikato study for Maori, and although there was no reversal among Pacific people overall, there was a considerable increase in the proportion of 5–14 year of Pacific People who attended the GP for sore throat.

This study also rejected our second hypothesis because we found that the variation in patients presenting with sore throat was affected by age. Our finding that the 5–14 age...
group attended more often than other age groups is the reverse of earlier New Zealand studies.  

The rejection of both hypotheses is encouraging because Maori and Pacific children in the 5–14 year age group make the bulk of patients who suffer rheumatic fever in New Zealand. However, the real impact of social factors influencing attack rates of rheumatic fever following sore throat will only be measured when research identifies the proportion of patients who do not attend their general practice with a sore throat.  

Our study found the patients’ perceived urgency of visit to the doctor was for sore throat was greatest for the less-than-4 years age group, whereas the 5–14 year and over-14 years age groups did not differ. This is understandable behaviour for parents worried about their young children. However, a wait for over 1 week with a sore throat among the at-risk group of 5–14 years may influence the attack rate of rheumatic fever.

Previous research from the 1980s found that New Zealand patients did not consider sore throat to be a serious illness requiring urgent attention. More research is needed to identify those factors that will increase the speed with which patients in the at-risk age group of 5–14 years present their symptom of sore throat for medical attention.

Our study found that few GPs were uncertain of their diagnoses, and that 59 per 100 sore throat encounters resulted in a throat-related diagnosis recorded in the records. However, viral throat diagnoses accounted for only 14.8% of diagnoses explicitly stated by GPs which is less than would be expected with the higher prevalence of viral causes of sore throat. We found the GPs were more likely to prescribe an antibiotic for a sore throat than not—and the rate of 61% of sore throat patients prescribed an antibiotic was similar to previous New Zealand studies.  

Our study found that the rate of throat swabbing by GPs for patients with sore throat was lower (6.6% versus 14%) than in the 1991 Waikato study.

There are conflicting international guidelines on whether GPs should swab patients who present with a sore throat. However, in our study we found that there was less swabbing of the throat and more prescribing of antibiotics for Maori and particularly Pacific Island patients compared to European patients. This suggests GPs may have different management policies for patients with sore throat who come from different ethnic backgrounds.

Limitations of this study—A strength of this study is that the data describe the sore throat management of a nationally representative sample of GPs. Bias may have been introduced due to the overall GP response rate of 71.7%. Non-responders tended to be male and reported greater than average patient loads. If the busiest GPs differ in some systematic way in their characteristics or activities, this may bias the results. The magnitude and direction of such bias is unknown. The magnitude of many of the observed differences reduces the chance of spurious conclusions being drawn. Similarly, there may have been bias associated with incomplete recording and assignment of ICD-9 codes (83.9% of visits had at least one disease code assigned), although the magnitude is likely to be small.

NatMedCa was a practitioner, rather than a population-based, survey. The data refer to the actual work of primary care practitioners rather than to population utilisation or
to the needs of different populations. As a visits-based study, NatMedCa (by its nature) over-represents frequent users. For this reason, care must be exercised when generalising results to the general population: the results of this study apply to users of primary care services rather than to the general population. Therefore, more studies are needed that link community behaviour with sore throat management in primary care.

**Significance of this study**—Sore throat continues to be a common symptom that patients present to their GP. Ethnic differences may have an important part to play in the behaviour of patients with their sore throat and how GPs manage sore throat. More research is needed to discover those factors that encourage a greater proportion of patients in the at-risk age group of 5 to 14 years to attend their GP with sore throat.

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**References:**


Sexually transmitted diseases and HIV/AIDS in Vanuatu: a cause for concern and action

Dominik Zenner, Steven Russell

Abstract

Aims. This article argues that sexually transmitted infections (STIs) and HIV/AIDS in Vanuatu are a cause for concern and that a strong response is needed to stem an epidemic.

Methods. Three sources of data are used: studies and policy documents on STIs and HIV/AIDS in Vanuatu; analysis of reported STI cases from public health facilities; and key informant interviews with 14 policy stakeholders.

Results. In Port Vila (capital of Vanuatu), more than a quarter of the women attending antenatal clinics were positive for at least one STI. Although Vanuatu Ministry of Health (MoH) case records for gonorrhoea, genital ulceration, and syphilis show national prevalence rates have remained relatively constant between 1.2% and 2%, there is probably gross under-reporting because MoH data exclude trichomoniasis and chlamydia cases; surveillance systems are poor; and patient access to services is limited. High STI prevalence and several socioeconomic factors create a high-risk environment for the rapid spread of HIV/AIDS.

Discussion. The need for a strategic response in Vanuatu is pressing. Priorities for action include the scaling up of awareness programmes for young people, particularly girls, and the development of surveillance systems. Government capacity weaknesses mean the MoH should explore possible partnerships with the non-government organisation (NGO) sector and point to the need for international support to implement a new government Strategic Plan.

The number of officially reported cases of HIV and AIDS in the Pacific Island countries remains low compared to other parts of the developing world (Table 1), but in some countries, notably Papua New Guinea, reported cases are rising. Estimates also show that reported cases may only be the tip of the iceberg, with 16,000 (7,800–28,000) infected people in Papua New Guinea—an overall prevalence rate of 0.6%.

Much higher prevalence rates are estimated among high risk groups (up to 17% in female sex workers). As far back as 1996, the United Nations Development Programme (UNDP) warned of an epidemic in the region, and these warnings have been repeated recently by United Nations Programme on HIV and AIDS (UNAIDS).

Vanuatu recorded its first HIV case in September 2002, and a second has now been officially reported. It is likely that more people are HIV-positive but remain invisible to the scanty reporting and surveillance systems in the country. Infections may be concentrated among high-risk groups such as sex workers, but a high prevalence of other sexually transmitted infections (STIs) and the risk environment in Vanuatu discussed below mean that HIV infections are likely to spread to the wider population if effective preventive actions are not taken.
Table 1. Reported HIV and AIDS cases (end of 2003) in Melanesian countries

<table>
<thead>
<tr>
<th>Country</th>
<th>HIV reported</th>
<th>AIDS reported</th>
<th>HIV estimated¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fiji</td>
<td>142</td>
<td>25</td>
<td>600</td>
</tr>
<tr>
<td>New Caledonia</td>
<td>263</td>
<td>99</td>
<td>n/a</td>
</tr>
<tr>
<td>Papua New Guinea</td>
<td>7,320</td>
<td>1,336*</td>
<td>16,000</td>
</tr>
<tr>
<td>Solomon Islands</td>
<td>2</td>
<td>1</td>
<td>n/a</td>
</tr>
<tr>
<td>Vanuatu</td>
<td>2</td>
<td>2</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Source: South Pacific Commission¹; *as of December 2001; n/a=not available.

This article aims to fill a gap in current knowledge as the first situational report on STIs and HIV/AIDS in Vanuatu, using the limited data available. STIs are the focus of attention because potential HIV cases remain hidden and because STIs themselves increase susceptibility to HIV transmission. High STI prevalence rates may also indicate behavioural patterns that contribute to greater transmission risk, such as multiple partners, commercial sex, and low condom-use rates.

The paper examines the evidence on STI prevalence rates, monitoring, and surveillance system weaknesses and the factors contributing to the high-risk environment in Vanuatu. The viewpoint expressed is that these findings are a cause for grave concern to the public health and development community in Vanuatu and the wider region, and concludes by reviewing capacity response weaknesses and policy priorities.

Methods

Quantitative and qualitative data were collected in May 2003 for a small research project approved by the Vanuatu Ministry of Health (MoH) and the National Statistics Office (NSO). Data were derived from three sources.

- A review of studies and policy documents on STIs and HIV/AIDS in Vanuatu.
- An analysis of STI cases reported by public health facilities (dispensaries, health centres, and hospitals) through standard Monthly Statistical and Epidemiological Reports.
  (These information sheets record case numbers for gonorrhoea, syphilis, and genital ulcers (not chlamydiasis or trichomoniasis) and should be processed by the Statistics Unit of the MoH into an Annual Epidemiological Report. Some non-government organisation (NGO) facilities also report to the MoH but many private-for-profit surgeries do not. Procedure dictates that any HIV cases should be reported directly to the MoH.)
- Semi-structured key-informant interviews with 14 policy stakeholders, (4 with government officials and 10 with NGO workers).

Respondents were selected because of their involvement with policy and practice and to obtain a spectrum of perspectives and opinions. A standardised question guideline was used and the interviews were taped, transcribed, coded, and analysed. This method generated complementary qualitative data on the risk environment, monitoring and surveillance capacity and other policy matters. Anonymity was guaranteed as part of the ethical procedures of the research.

Results

STI prevalence rates in Vanuatu

Data on STI incidence and prevalence rates in Vanuatu is severely limited. All key informants working in the field of reproductive health believed that STI rates were
rising (particularly in urban areas), a conclusion based on the limited data available, anecdotal evidence, and their overall perception that risk factors were increasing (see below).

The first body of evidence comes from two STI prevalence surveys. The first was a World Health Organization (WHO)-funded survey of 545 pregnant women conducted by the MoH in Port Vila in 2000. In this relatively low-risk sample, 27.5% of the women were positive for *Trichomonas vaginalis*, 21.5% for *Chlamydia trachomatis*, and 5.9% for gonorrhoea (Table 2). Out of the 66 teenage women tested, 58.1% had at least one infection and the study concludes that these findings are ‘of major concern’ and that ‘the unexpectedly high burden of disease among a traditionally low-risk population of antenatal women argues for policy and community-level interventions….’

Table 2. Sexually transmitted infections (STI) rates in Port Vila from an antenatal survey

<table>
<thead>
<tr>
<th>STI</th>
<th>Women tested</th>
<th>Women infected</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Trichomonas vaginalis</em></td>
<td>545</td>
<td>150</td>
<td>27.5</td>
</tr>
<tr>
<td><em>Chlamydia trachomatis</em></td>
<td>545</td>
<td>117</td>
<td>21.5</td>
</tr>
<tr>
<td><em>Neisseria gonorrhoea</em></td>
<td>545</td>
<td>32</td>
<td>5.9</td>
</tr>
<tr>
<td>Treponemal antibody seroactivity</td>
<td>537</td>
<td>13</td>
<td>2.4</td>
</tr>
<tr>
<td>HIV</td>
<td>537</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Source: WHO

The second survey, conducted by the Vanuatu Family Health Association (VFHA) in cooperation with the WHO and MoH in West Ambae Island, found lower prevalence rates (5.2% and 1.5% for *Trichomonas* and *Chlamydia* respectively) in a random sample of clinic attendees. The lower infection rates in these more remote rural areas are not surprising, but the results of the urban and rural studies are difficult to compare because of the different sampling and also age composition of the two surveys.

In the urban study, the median age was 25 years and in the rural study 35 years; and given that 60% of Ambae’s population is below 24 years, the rural sample of older women does not reflect the ‘normal’ population nor the most sexually active group.

The second body of evidence comes from the authors’ analysis of routine MoH case returns from facilities. Weaknesses in public sector STI monitoring and surveillance systems and data quality should be highlighted. Facility reporting rates were found to vary considerably between provinces; for example, ranging from an 18% questionnaire return rate in Penama Province in 2002 to 72% in Sanma Province in the same year, and seemed to depend on provincial and facility capacities such as staffing levels, training and motivation to complete returns. Penama had the lowest average return rate from 1995 to 2002 (62% of questionnaires) and its understaffed hospital lacking an STD treatment room and appropriate laboratory facilities underlines this. The 2002 country-wide return rate (48%) was markedly lower than previous years (64–83%), probably as a result of a change to the information sheet that led to some confusion. The public sector’s weak capacity to manage the case
reporting system is illustrated by the fact that since 1988 the MoH has not processed monthly returns into an Annual Epidemiological Report.\(^8\)

Acknowledging the weaknesses of Vanuatu’s STI reporting system and the crude results generated, STI case numbers have been estimated by taking the cases recorded by MoH facilities and adjusting for the respective under-reporting rates of each province in each year:

\[
\text{Estimated cases} = \text{reported cases} \times \text{reporting rates}^{-1}
\]

The total case numbers of all three recorded STI entities between 1995–2002 (gonorrhoea, genital ulceration, and syphilis) are presented in Figure 1 and corresponding adult prevalence rates for each STI in Table 3.

**Figure 1. Countrywide STI estimates (gonorrhoea, genital ulceration, and syphilis) in Vanuatu**

![Graph showing STI estimates for Vanuatu](No image provided)

<table>
<thead>
<tr>
<th></th>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonorrhoea</td>
<td>1.31</td>
<td>1.23</td>
<td>1.57</td>
<td>1.88</td>
<td>1.44</td>
<td>1.32</td>
<td>0.99</td>
<td>1.22</td>
</tr>
<tr>
<td>Genital ulceration</td>
<td>0.02</td>
<td>0.02</td>
<td>0.01</td>
<td>0.08</td>
<td>0.09</td>
<td>0.11</td>
<td>0.13</td>
<td>n/a</td>
</tr>
<tr>
<td>Syphilis</td>
<td>0.01</td>
<td>0.01</td>
<td>0.02</td>
<td>0.03</td>
<td>0.03</td>
<td>0.05</td>
<td>0.07</td>
<td>0.19</td>
</tr>
<tr>
<td><strong>Cumulative prevalence</strong></td>
<td><strong>1.34</strong></td>
<td><strong>1.26</strong></td>
<td><strong>1.6</strong></td>
<td><strong>1.99</strong></td>
<td><strong>1.56</strong></td>
<td><strong>1.48</strong></td>
<td><strong>1.18</strong></td>
<td><strong>1.42</strong></td>
</tr>
</tbody>
</table>

*Prevalence was calculated for the adult population using 1999 National Census data and incorporates inter-census population growth rates derived from the NSO demographic analysis report.*

Table 3. Prevalence rates for gonorrhoea, genital ulceration and syphilis (total cases as a percentage of the adult population aged 15–59 years for 1995–2002*)
Gonorrhoea cases were far more numerous than syphilis and genital ulcer cases nationally; for example, in 2000 there were 1358 gonorrhoea cases compared to only 166 syphilis and genital ulcer cases. A steep rise in male gonorrhoea cases and a decline in female cases between 2001 and 2002 may have been exaggerated by changes to the MoH reporting form.

Reported case levels and prevalence rates of about 1.2–2% for the three STIs appear to have been fairly consistent over time, but two important gaps in the MoH data justify the inference that STI prevalence is likely to be much higher. First, MoH data exclude trichomoniasis and chlamydiasis due to lack of adequate testing methods (i.e. polymerase chain reaction), and these STIs are far more prevalent according to WHO survey data (Table 2). Second, it is likely that poor surveillance systems, low awareness of STIs, and poor patient access to services mean a gross under-reporting of cases.

Patient under-reporting is illustrated when looking at Shefa Province which saw a dramatic rise in reported syphilis and genital ulceration cases (notably by females) after a new reproductive health clinic (Kam Pussum Hed Clinic) was opened by the Wan Smolbag NGO in 1999 and submitted its first case reports to government in 2000 (Figure 2).

Shefa Province’s steep rise in reported cases after its clinic’s establishment indicates that it was addressing unmet needs; improving service delivery in other provinces could lead to a similar rise in reported STI cases through improved access. The accessibility of care provided to women at Kam Pussum Hed Clinic and its discreetness on the outskirts of Port Vila were important factors explaining the rise in utilisation.

Figure 2. Genital ulceration and syphilis estimates in Shefa Province based on reporting rates there each year
The risk environment for STIs and HIV/AIDS in Vanuatu

High STI prevalence and several socioeconomic factors interact to make a range of people susceptible to infection, thus creating a risk environment for the rapid spread of STIs and HIV/AIDS:

**Demographic structure**—Young people are particularly vulnerable to HIV infection (globally half of new cases are among 15–24 year olds). In Vanuatu, 59% of the population are under 24 years and 18% aged between 15 and 24 years old thus making a large section of the population vulnerable now (and in the near future) at a time of rapid socioeconomic change through urbanisation, migration and transition to cash economy among others.

**Poverty and inequality**—Until recently, Vanuatu has experienced comparatively low economic growth rates which have caused rising unemployment and impoverishment. Unequal gender relations add to these risk factors. Women’s greater physiological and societal susceptibility to STI and HIV transmission is internationally recognised, and key informants gave abundant examples to illustrate women’s limited bargaining power over when and how they have sex (rooted in cultural and social norms that expect women to be timid and to obey their husbands), as well as fears of abuse and violence.

**Political and social institutions**—Vanuatu’s rural society (and to a lesser extent its urban society) is hierarchical and patriarchal (male dominated)—with leading roles ascribed to the male chief, the pastor, and village elders. Key informant interviews confirmed that public talk about sex and reproductive issues is generally taboo and perceived by community leaders as a threat to the sociocultural integrity of the community—thus imposing serious barriers to reaching rural areas and women with sexual health awareness campaigns.

Condom distribution is sometimes equated with the encouragement of casual sex or promiscuity. Even in Port Vila, a large randomised Knowledge, Attitudes, and Practice (KAP) survey (n=1053)—conducted by the NGO Vanuatu Young People’s Project (VYPP)—found considerable resistance to condom use, and women were accused of promiscuity if they suggested condoms. MoH staff themselves are embedded in this sociocultural context which one government informant argued contributes to a degree of ‘ambivalence about the distribution of condoms.’

**Economic activity and risky livelihoods**—The South Pacific Commission (SPC) warns that high levels of migration and lifestyle changes associated with new economic activity and rapid urbanisation are risk factors for the spread of STIs and HIV. An estimated 19% of the Ni-Vanuatu (indigenous) population do not live on their home islands but migrate to urban centres for work. The tourist industry is also large, accounting for 40% of GDP and employing 4000 people. For example, in 2000, 57,500 tourists and 50,000 cruise ship passengers visited Vanuatu (compared to Vanuatu’s 186,678 inhabitants).

Although more sex education is recommended by UNGASS, the Government admits that only limited sex education is available in tourist hotels and workplaces. Key informants also argued that the rapid transition to a cash economy and
urbanisation were driving increases in risk factors such as the commercial sex industry and alcohol consumption.

**Service infrastructure and biomedical knowledge**—According to key informants, a widespread lack of knowledge about prevention or treatment of STIs is a key risk-factor. The UNDP adult literacy rate is only 34%\(^{24}\) and 56% of the population receive only primary education up to class 6 (age 12) with no learning about reproductive health matters. Awareness campaigns achieve low coverage outside the main urban centres due to limited geographical access, people’s limited access to television and radio media, and the social taboos around sex noted above.

Key informants at the MoH saw lack of awareness and lack of access to curative services as mutually reinforcing, because if people are not interacting with services then they are not receiving information and advice. Information delivery by rural health workers may be further restricted by taboos if they come from the communities where they work.

**Discussion**

The high STI prevalence rates found by a WHO antenatal survey in 2000, and the first officially reported case of HIV 2 years later, are a cause for concern for the public health community in Vanuatu. Although routine MoH STI-case reporting shows no clear pattern of increase, complacency would seem misplaced given reporting system gaps and the likelihood of under-reporting, notably in rural areas. Poverty, gender inequality, and poor health service and awareness coverage interact to make a range of people susceptible to infection.

Policy lessons for Vanuatu come from countries that have successfully tackled the epidemic and reduced incidence, either at an early and concentrated stage of the epidemic (e.g. Thailand) or after the disease had spread to the general population (e.g. Uganda).

These lessons include the early strengthening and implementation of STI/HIV surveillance systems; high-level political leadership and commitment to HIV/AIDS prevention; treatment and surveillance strategies; a multi-sectoral response across ministries; response partnerships with a range of civil society actors; and strict promotion of condom use in the commercial sex industry.\(^{25,26}\)

The need for such responses in Vanuatu is pressing, and the Government recently published its response with the *Vanuatu Policy and Strategic Plan for HIV/AIDS and Sexually Transmitted Infections 2003–2007.*\(^{23}\) The core aims and policies of the Strategic Plan are to improve monitoring and surveillance systems; to increase awareness about STIs and HIV/AIDS (particularly among high-risk groups); to promote condom-use; and to reduce the incidence of STIs through better prevention and treatment measures.

Despite the Strategic Plan’s good intentions and ambitious aims, government capacity and political commitment will be the key to success. Government capacity is clearly limited in terms of budget constraints, shortages of skilled and motivated staff;\(^{22}\) and weak information systems. The MoH recognises the importance of improving its crude and erratic STI and HIV surveillance systems in order to identify needs and to monitor incidence and evaluate planned interventions—and some of these investments could be covered through the recurrent budget.\(^{27}\)
More ambitious HIV surveillance systems (noted in the Strategic Plan), or surveys to evaluate awareness and prevention programmes that conform to international standards, are likely to require external funding and human resource support from the international community.

Targeting awareness campaigns and services at high-risk groups is also fraught with difficulties because such groups are hard to identify or reluctant to be found. According to key informants, sex workers are particularly difficult to reach due to societal attitudes. NGOs working with this group emphasised the need for great caution and discretion to avoid negative community reactions to their work. Indeed, reaching other vulnerable groups such as women in rural communities will be difficult due to the aforementioned political and social institutions and taboos around public talk about sex, gender inequalities, and access difficulties.

Even if a range of vulnerable groups can be reached, greater awareness will not necessarily empower them to change risky behaviours (if poverty and gender inequalities persist), and changing underlying social relations that play a role in STI transmission is never easy. These challenges, however, should neither deter action nor prevent successes, as the examples of Thailand and Uganda have demonstrated, and peer education among young people, particularly girls, may be the most appropriate and feasible point to begin interventions. Such engagements might also build capacity and facilitate more ambitious initiatives with vulnerable groups in the future.

MoH-capacity weaknesses mean that Government should explore the possibility of partnership with the NGO sector to deliver services. Indeed, several NGOs in Vanuatu have already demonstrated they can deliver reproductive health campaigns and services, and partnerships with NGOs and community-based organisations will strengthen capacity for reaching vulnerable groups.

NGO programmes were identified during the situational analysis, and included: two reproductive health clinics in Port Vila (including Kam Pussum Hed) and one in Luganville; a community theatre group that promotes awareness about sexual health matters and tours the islands six times every year; several peer-to-peer education initiatives with youth in urban areas; and radio shows. The MoH Strategic Plan acknowledges the significant contribution that NGOs can make to the fight against HIV/AIDS, and partnerships are most likely to be successful if relationships of trust, equal collaboration, and mutual support can be developed.

Government-capacity weaknesses also point to the need for international support to implement the Strategic Plan. At a recent UNAIDS workshop in Fiji, the scaling up of HIV awareness and prevention programmes for young people in the region was emphasised as an urgent priority to prevent an HIV/AIDS epidemic in the Pacific—and both the Global Fund to Fight AIDS, TB, and Malaria (GFATM) and the Australian Agency for International Development (AUSAID) have committed funds to strengthen a regional AIDS strategy and capacity to deliver services.

Another priority in Vanuatu is to develop monitoring and surveillance systems; and a response by a re-invigorated National AIDS Council—to coordinate government actors within the MoH and National Statistics Office, NGOs, and international agencies (such as WHO or GFATM)—would be an important contribution to the fight against HIV/AIDS.
HIV is new to Vanuatu, and although many organisations seem determined to fight its spread, strong political leadership will be needed to overcome rivalries and push for such a coordinated response.28

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McArdle’s disease (myophosphorylase deficiency) presenting as acute renal failure

Navdeep Sidhu, Thomas Thompson

McArdle’s disease is a rare genetic metabolic myopathy characterised by exercise-induced myalgia, cramps, early fatigue, and muscle weakness resulting from an inability to break down glycogen in response to intense or sustained muscular activity.\(^1,2\) We report the case of a patient with McArdle’s disease presenting with acute renal failure.

**Case report**

An 18-year-old male was referred with a 3-day history of nausea and vomiting. His last meal was a burger on the night prior to the onset of his symptoms. Since then, he had not tolerated any food and had managed to keep down only small amounts of fluid. He complained of occasional epigastric pain but had no diarrhoea or bloody stools. His urine output had decreased and he thought that his urine was orange but not particularly dark. He denied having any fever, rash, joint pain, or myalgia and he had not experienced similar symptoms in the past. He had been on a 12-month course of isotretinoin for acne treatment that was completed 3 months earlier, but had no other medical history of note.

His temperature was 37.9\(^\circ\)C. His pulse was 64/min and blood pressure 136/88 mmHg. His venous pressure was 2 cm and there was no oedema. His chest was clear. He had mild right-upper-quadrant tenderness.

His sodium was 131 mmol/L, potassium 5.9 mmol/L, urea 32.3 mmol/L, and creatinine 970 umol/L. His calcium was 2.25 mmol/L and phosphate 1.6 mmol/L. An ultrasound scan showed enlarged kidneys with increased echogenicity. He managed to pass a small amount of dark urine that showed 3+ of protein, 4+ of haemoglobin, and only 25x10\(^6\) red blood cells /L. A creatine kinase (CK) level was requested and was found to be markedly elevated at 271440 U/L.

On further questioning, the patient recalled that, during the evening prior to becoming unwell, he had run about 50 metres—being forced to stop because of pain and stiffness in his thighs and calves, which had resolved by the next morning. He gave a history of exercise intolerance for as long as he could remember, with varying degrees of myalgia depending on the intensity of exercise.

The patient did not improve with intravenous fluids and the following morning was transferred for dialysis, which he required for 7 days. His creatinine returned to normal but his CK was persistently elevated above 1000 U/L. A subsequent neurological referral and muscle biopsy established the diagnosis of McArdle’s disease.
**Discussion**

McArdle’s disease is an autosomal recessive disorder, with the primary defect being a mutation in the phosphorylase gene on chromosome 11. It is a rare disorder, with an estimated prevalence of 1 in 100,000 people, but is also the most common of the glycogen-storage diseases.

The lack of myophosphorylase activity prevents glycogenolysis and the mobilisation of glucose-1-phosphate into the glycolytic pathway during exercise. The availability of fatty acids as an alternative source of energy is limited during the early stages of exercise and this, coupled with the depletion of intracellular glucose and ATP, results in the onset of symptoms.

Over-exertion of muscles results in acute local muscle damage (rhabdomyolysis) causing a painful hardening and shortening of the muscles. Damage to the myocyte membrane causes a release of intracellular components such as myoglobin, potassium, and CK; the plasma level of the latter is almost always persistently raised in patients. Severe rhabdomyolysis leads to myoglobinuria and possibly acute renal failure.

McArdle’s disease is usually not diagnosed until the second or third decade of life. Diagnostic delay is related to the rarity of the condition; the fact that symptoms are typically less severe during childhood and are often mistaken for ‘growing pains’; or because the symptoms are attributed to poor physical condition, poor motivation, or both. Patients frequently recall episodes of exercise intolerance during childhood.

Treatment of McArdle’s disease remains a challenge. Patients should avoid intense exercise to prevent muscle damage. However, they should be encouraged to undertake regular, moderate exercise to help maintain cardiovascular fitness and muscle mitochondrial activity to enhance the ability of muscle to oxidise available fuels, especially fatty acids. Many patients can continue to exercise with increased endurance if they rest briefly at the first signs of pain; this is termed the ‘second wind’ phenomenon and has been attributed to either a shift in the metabolic pathway or to a circulatory adjustment resulting in enhanced intramuscular capillary perfusion.

Ingestion of sucrose prior to exercise has been shown to improve exercise tolerance in patients, with possible protection against exercise-induced rhabdomyolysis. Short-term, low-dose creatine monohydrate supplements have been shown to have some benefit in enhancing work capacity, although higher doses worsened the symptoms of exercise intolerance. A single case report suggested that vitamin B₆ supplementation may improve muscle performance.

In conclusion, this case describes a patient with previously undiagnosed McArdle’s disease presenting with life-threatening acute renal failure related to exercise-induced rhabdomyolysis and myoglobinuria. This near-death experience may have been prevented if the diagnosis had been made earlier in life—as guidance on exercise methods and limitations would have minimised the risk of him developing severe muscle breakdown and its associated complications.

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Recovery from pancytopenia and liver dysfunction after administration of propylthiouracil for Graves' disease

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A case of hyperthyroidism associated with pancytopenia is described. Hyperthyroidism can be associated with various haematological disorders related to several mechanisms. It should be suggested that the aetiology of pancytopenia might be due to hyperthyroidism. In the literature to date, pancytopenia is reported in only five cases of hyperthyroidism. Although the mechanism of pancytopenia in patients with hyperthyroidism is unclear, it might be related to the reduced lifespan of whole blood components—partially due to the autoimmune mechanism and/or disturbances in maturation and differentiation of the pluripotential stem cells.1,2

Case report

A 53-year-old woman was referred to our hospital complaining of pretibial nonpitting oedema, diarrhoea, and loss of weight during the previous 2 months. The physical examination revealed excessive sweating with sinusal tachycardia (110 beats per minute), associated with high blood pressure, which allowed us to suspect that hyperthyroidism was responsible.

The measuring of thyroid functions and autoantibodies confirmed the diagnosis. Thyroid function tests revealed a pattern of primary hyperthyroidism FT3: 7.9 pg/ml (normal: 1.57–4.71), FT4 >6 ng/ml (normal:0.8–1.9), TSH< 0.004 uIU/mL (normal: 0.4–5.0). The antithyroglobulin antibody and antimicrosomal antibody titres were normal, and the TSH receptor antibody (TRAb) titre was 124 U/L (normal range:0–9 U/L).

Thyroid function tests showed a pattern of overt primary hyperthyroidism. In thyroid ultrasonography, the thyroid gland diffusely enlarged without nodule. In laboratory findings, the white blood cell count was 3200 uL; significant leucopaenia with a relative neutropaenia (39.5%) and lymphocytosis (48.2%) were present, haemoglobin (Hb) was 9.1 gr/dL, the mean corpuscular volume (MCV) was slightly decreased (78 fL), haematocrit (Hct) was 28.5%, and platelet count 71000 uL. Pancytopenia was present.

Slightly elevated transaminase levels; aspartate aminotransferase(AST) 68 U/L (normal:1–32 U/L), and alanine aminotransferase (ALT) 65 U/L (normal:1-31 U/L) were observed (Figure 1).

Haematological examinations showed hypochromic anaemia, leucopaenia, and thrombocytopenia (Figure 1) with normoplastic bone marrow biopsy. In the laboratory examination, neither haemolytic anaemia nor vitamin B12 or iron deficiency were observed.
Figure 1. Diagram to show the clinical course of the patient over 5 weeks

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1 week</th>
<th>2 weeks</th>
<th>3 weeks</th>
<th>4 weeks</th>
<th>5 weeks</th>
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<tr>
<td>WCC x 10^9/l (NR:4000-10300)</td>
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<td>3820</td>
<td>4200</td>
<td>5900</td>
<td>3800</td>
</tr>
<tr>
<td>Neutrophil count</td>
<td>1280</td>
<td>1620</td>
<td>2310</td>
<td>3420</td>
<td>1740</td>
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<tr>
<td>Lymphocyte count</td>
<td>1540</td>
<td>1680</td>
<td>1430</td>
<td>1770</td>
<td>1600</td>
</tr>
<tr>
<td>Platelet x 10^9/l (150,000-373,000)</td>
<td>71000</td>
<td>128000</td>
<td>187000</td>
<td>187000</td>
<td>145000</td>
</tr>
<tr>
<td>Hgb g/dl</td>
<td>9.1</td>
<td>9.5</td>
<td>10.7</td>
<td>10.9</td>
<td>10.4</td>
</tr>
<tr>
<td>MCV fl (80.7-95.5)</td>
<td>78</td>
<td>78.3</td>
<td>80.7</td>
<td>82.5</td>
<td>81</td>
</tr>
<tr>
<td>ALT U/L (1-31)</td>
<td>65</td>
<td>21</td>
<td>11</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>FT4 (0.8-1.9)</td>
<td>6</td>
<td></td>
<td>1.02</td>
<td>2.6</td>
<td></td>
</tr>
<tr>
<td>FT3 (1.57-4.71)</td>
<td>7.97</td>
<td>3.41</td>
<td>5.2</td>
<td></td>
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</tr>
<tr>
<td>TSH (0.4-5)</td>
<td>0.004</td>
<td>0.004</td>
<td>0.004</td>
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</tbody>
</table>
At the end of 3 weeks of treatment with 300 mg propylthiouracil (PTU) daily for Graves’ disease; the patient’s free thyroid hormones returned to normal. Other abnormal laboratory findings such as pancytopaenia and abnormal mean corpuscular volume plus liver dysfunction also disappeared (Table 1).

After 1 month of treatment for Graves’ disease, PTU medication was withdrawn for 1 week to allow for a $^{131}$I radioactive uptake test. Thyroid scintigraphy showed changes consistent with classical Graves’ disease: 4-hour $^{131}$I uptake was 50.8% and 24-hour $^{131}$I uptake was 56.3%. After the administration of $^{131}$I for uptake, a 370 megabecquerel $^{131}$I dose was given as a single oral dose to the patient. The second appearance of the pancytopaenia coincided with the recurrence of hyperthyroidism after discontinuation of PTU due to $^{131}$I radioactive medication (Figure 1).

**Discussion**

Hyperthyroidism can be associated with various haematological disorders related to several mechanisms. Single lineage abnormalities related to hyperthyroidism are much more commonly reported than pancytopaenia.

Graves’ disease is frequently associated with anaemia (34 %). It is usually mild and resolves with antithyroid therapy. However, anaemia is unresponsive to haematinic therapy; anaemia and mean corpuscular volume returns to normal when thyrotoxicosis is controlled.

Relative lymphocytosis is frequently found in the peripheral blood due to neutropaenia (18 %). Relative lymphocytosis with a normal or slightly low total white cell count are the characteristic blood findings of Graves’ disease. In our case, neutropaenia and lymphocytosis returned to normal when thyrotoxicosis was controlled. Antigenicity between human TSH receptor and polynuclear neutrophils may be the cause.

Graves’ disease is also rarely associated with mild thrombocytopaenia (4 %), and occasionally with idiopathic thrombocytopaenic purpura. This can be due to autoimmune pathogenesis of both diseases. Mild thrombocytopaenia disappears spontaneously when a patient's free thyroid hormones returned to normal; if severe, it may respond to glucocorticoid treatment.

Pancytopaenia is a rare complication of hyperthyroidism. Although drug-induced pancytopaenia should be considered, our patient never took any drug during (and for several months prior to) her first hospital visit. There was no evidence of viral infection, sarcoidosis, tuberculosis, or malignant lymphoma—all of which can cause pancytopaenia.

Hepatic dysfunction occurs in hyperthyroid patients, particularly when thyrotoxicosis is severe and raised serum ALT and AST levels may be present. Hepatic dysfunction occurs in hyperthyroid patients when splanchnic oxygen consumption increases, whereas splanchnic blood flow is essentially unchanged. As a result, the arteriovenous oxygen difference across the splanchnic bed is increased; hence, hypoxia may contribute to hepatic dysfunction.

Another theory is that a virus infection, possibly subclinical, may have triggered the Graves’ disease and also caused transient hepatitis, either directly or by anti-liver autoimmunity. In this case, our patient had no anti-mitochondrial or anti-smooth-
muscle antibodies, nor anti-soluble liver antigens. Furthermore, she was not a hepatitis B virus (HbsAg) carrier. These data indicated that she did not have autoimmune hepatitis (AIH) or viral hepatitis infection due to liver dysfunction. All liver dysfunction disappeared when the patient became euthyroid.

Abnormal liver function test results (in hyperthyroid patients) make the differential diagnosis of concomitant, unrelated liver disease difficult until the euthyroid state has been established.

The clinical importance of immunosupression and induction of apoptosis, compared with inhibition of thyroid hormone formation, is still unclear. Recent in vitro culture studies show that, following antithyroid drug treatment for active Graves’ disease, expression of HLA-DR\(^9\) antigen on the surface of thyroid epithelial cells can be inhibited, thus affecting production of cytokines and reactive oxygen metabolites. And the reduction in these inflammatory mediators may explain the site-specificity of the immunomodulation produced by antithyroid drugs.\(^{10}\)

In this case, we thought that the pancytopenia recurrence, noticed after cessation of PTU treatment (due to preparation for radio-iodine treatment), is an observation in favour of PTU’s therapeutic effects on pancytopenia. Moreover, various laboratory abnormalities were normalised by antithyroid therapy alone, thus indicating that the hyperthyroidism itself was closely related to the pathogenesis of haematologic and liver dysfunction.

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The right to remain in ignorance about genetic information—can such a right be defended in the name of autonomy?

Phillipa Malpas

Abstract

Within the field of medicine, it has become widely accepted that respecting the autonomy of individuals justifies their right to know. More recently, commentators have asked whether such respect also justifies an individual’s right not to know; that is, their right to remain in ignorance. In this paper, I examine what the concept of autonomy entails and whether one is justified in exercising a right not to know genetic information about oneself in the name of autonomy. An important distinction is drawn between autonomous choices generally and autonomous choices about how we shall conduct our lives. Against this theoretical discussion, I consider two hypothetical cases. I conclude by claiming that ignorance cannot be justified in the name of autonomy, and furthermore that where genetic information is pertinent to one’s future autonomy, one cannot exercise a right not to know.

Within the field of medical ethics, in the last 20 years or so, there has been a growing awareness and respect for the patient’s right to know information about themselves. As a result of the Cartwright Report in 1985, the Code of Rights for Health and Disability became law on 1 July, 1996.¹

Patients are recognised as having a number of important rights, including the right to be fully informed and the right to effective communication. One’s right to be fully informed includes being told the results of tests and procedures as well as an explanation of their condition and the treatment options available. Thus, the right to know requires that individuals are given personal information—this enables them to make informed choices and to give their informed consent. John Harris² claims: since autonomy is necessary in order that every individual can pursue freely and in their own way the things that for them make life valuable or meaningful, they have the strongest entitlement to whatever information about themselves will, in their own judgement, best help them to do this.

If for the sake of argument we agree that individuals have a right to know—grounded in respect for their autonomy—perhaps individuals also have a right not to know that also stems from respect for their autonomy. According to Wertz et al,³ autonomy includes both the right to know and the right not to know one’s genetic status. When we consider trivial examples—revealing the score of a sports game I want to watch later or the ending of a movie I hope to go and see—we assume that others will respect our wish not be informed (of such information) when we ask them not to tell us.

I am probably right to think that you should respect my desire not to know such information (out of minimal consideration, if nothing else) but am I correct in believing that my right not to know can be defended in the name of autonomy?
Certainly, if we consider recent anti-smoking advertisements on television, it is clear that the State considers that we do not have a right to remain ignorant regarding certain information; namely the health effects of smoking on ourselves and others (passive smokers). Graphic illustrations of the consequences of smoking on our internal organs clearly aim to inform individuals about the harmful costs of smoking on our health. Presumably such advertising—aside from the financial costs to our healthcare system—is motivated by two features: harm to one’s own health and the health of others.

The same could be said for drunk driving and speeding campaigns on television. Behind such campaigns is the assumption that upsetting visual imagery and statistics will shock individuals into taking certain information on board and thereby change their behaviour.

In the cases above there are three important points to make clear:

Firstly, where not knowing certain information is likely to lead to third parties’ being harmed, it is clear that we may not have a right not to know—i.e. to remain in ignorance. Consider the two children who confront their mother because they are concerned about her health. They ask her to see a doctor because they think she is ill however, she refuses claiming she’d rather not know such information. They respond saying that ‘her not knowing if she is sick’ may harm them as she is their only caregiver, and that (if she is ill) their future wellbeing may be at stake. Ignorance is not a defence when others may be harmed by our actions (or inactions).

Secondly, individuals may not have a right to remain in ignorance where not knowing certain information is likely to lead to their being harmed. An important function of any society is to educate and enable its citizens to be able to live their own lives as they so determine. Respecting self-determination requires that individuals have access to information so that they can make informed decisions. To that end, our healthcare system is obliged to provide an extensive range of health care services to its citizens. Presumably what underlie television campaigns of the kind described above are concerns about how ignorance may harm individuals. Informing individuals about the consequences of certain actions provides them with information they can use to make decisions in reasonable knowledge.

Thirdly, the examples above also imply a more challenging and contentious position; that individuals cannot demand a right not to know in the name of autonomy. When we consider what the demanding philosophical theory of autonomy entails (one may claim) that ignorance (of important information) is inimical to autonomy. Moreover, ignorance may go on to thwart our future autonomous choices. Thus, it may be prima facie that where ignorance is likely to frustrate our future autonomous goals, we cannot have a right not to know which is grounded in autonomy.

Genetic information is different to other types of information. Not only does it tell us details of our own genetic makeup, it gives us information about those genetically related to us. It also can predict with increasing accuracy and scope, disorders that we will come to exhibit in the future (unless we die of something else beforehand). Such knowledge has important implications for us in understanding the ways in which we think about ourselves and those related to us.
In this paper, I will explore the notion of a right not to know. Throughout the discussion I will talk both of a right not to know and a right to remain in ignorance. I use both terms interchangeably. Leaving aside the claim that individual’s may not have a right not to know where not knowing may lead to others being harmed, I will focus on one’s putative right not to know genetic information about oneself where such a right is defended in the name of autonomy. Specifically, I will examine whether it is consistent to defend the claim that one has both a right to genetic knowledge and a right to remain in ignorance of genetic knowledge in the name of autonomy.

In the context of this discussion, my right not to know simply means I am morally permitted to exercise my right and everyone else has a duty to let me not know; that is, they have a duty not to interfere with my ignorance. Does autonomy justify me exercising a right not to know important genetic information that is pertinent to many future choices I may make? To answer this question, it is necessary to give a brief account of personal autonomy and what I claim it entails of us as moral agents.

**Autonomy**

Although the notion of autonomy is understood in a variety of different ways, and criticised accordingly, it is a commonly held assumption that autonomy is a feature of persons and it is a desirable quality to have. Deriving from the Greek terms, autos (self) and nomos (rule or law), the autonomous person is essentially one who is free to determine their own life—that is, the individual is able to choose from a variety of different options without interference or coercion from others.

In the liberal philosophical tradition, autonomy assumes an elevated role because it is central to how we understand ourselves and the world around us. The way we perceive of ourselves as distinct from inanimate objects, the way in which we interact with our surroundings, and the way in which we understand the causes and responsibility for the events which take place around us are wrapped up in our conception of autonomy.

Immanuel Kant is perhaps the most influential philosopher linked with the notion of personal autonomy. He argued that it was the ability to reason that gave human beings their intrinsic value and set them apart from all other beings. The capacity to make rational decisions and guide one’s life accordingly sits at the heart of Kant’s idea of autonomy. An important consequence of his position is that the autonomous agent is themself an end, and can never be used solely as a means to the ends of others.

For John Stuart Mill, personal autonomy was connected with personal liberty; as far as possible individuals should be free to live their lives as they so desire, as long as their actions did not harm others. Thus, Mill was explicit that society was not to interfere in the self-regarding actions of others. Over one’s self, and over their own body and mind, the individual is sovereign. In order to live as one rationally chooses, Mill argued it is important that the individual receive an education that exercised the various faculties—he who chooses his plan for himself employs all his faculties. He must use observation to see, reasoning and judgment to foresee, activity
What motivates both accounts of autonomy, in fact what is central to autonomy in philosophical literature generally, is that individuals exercise their capacity to reason in determining how they shall live. If individuals are to build the kinds of lives they desire, they must have access to information that concerns them. This is why the right to know is so important.

According to Haworth, personal autonomy demands critical reflection; namely having the ability to reflect critically on one’s needs, wants, and situation. Seen in this way, autonomy is extremely demanding because it requires thoughtful and considered deliberation—this entails assessing the consequences of acting in particular ways, considering not only the impact on oneself but also on others, and taking responsibility for the decisions we make. Seeing autonomy in this way involves our making particular deliberative choices. It requires that we pursue information and knowledge so that the choices we make are informed—that they truly reflect what we want for ourselves (and those we care about). Thus, when we speak of autonomy, we are speaking of a reasoned, deliberate way of living.

Autonomy understood in this way refers to an extended process through time. It is important to be clear about the distinction made here, for one may make autonomous choices, but live a life that is not autonomously chosen. Those individuals incarcerated in prison may make many autonomous choices day to day, but they do not govern their own lives, thus they lack autonomy in the wider sense that I distinguish as important. One may make autonomous choices such as deciding what to wear or when and what to eat, yet be unable to make autonomous choices about how we shall conduct our lives. It is the latter understanding of autonomy that is crucial to this discussion.

It is important that my choices are freely made. We value being able to make choices because, in deciding what to do (or not to do), we exercise our decision-making capabilities which in turn reflect what we want for ourselves. That is, we decide amongst an array of different options what we intend for ourselves (and others), with understanding and without controlling influences that determine our action.

**The right not to know**

Having discussed a philosophical conception of autonomy and what it requires of us, let us consider whether one can autonomously decide to remain in ignorance about one’s genetic information. Consider the following hypothetical cases:

Sandra’s mother, Lily, died of breast cancer at the age of 31 when Sandra was 10 years old. Lily’s sister and several aunts also died of the disease. There is also a history of ovarian cancer. Sandra has grown up knowing that she is at risk for both breast and ovarian cancer. Her GP has recommended to her that she should consider susceptibility testing because it is known that a family member carries a germ-line mutation at \textit{BRCA 1}. If Sandra carries the mutation, she has greater chance of developing breast and ovarian cancer and is more likely to develop the disease younger than someone without the mutation. She refuses, claiming that (as an autonomous adult) she has a right not to know whether or not she carries the genetic mutation.

After months of deteriorating health, Tom’s father is diagnosed with Huntington’s disease. Tom and his brother know they have a 50% risk of carrying the gene for the disease. Tom
refuses to be tested for the disease. He claims that as there is nothing that can medically benefit him now if he tests positive for the disease, he’d rather not know. Furthermore, having weighed up the available options, it is his informed view to prefer remaining in ignorance: he, like Sandra, believes that he has a right not to know.

Can respect for autonomy justify their exercising a right to remain in ignorance? One can empathise with both Sandra and Tom’s situation. Having both lost family members to diseases that are clearly manifest within their extended families, it is easy to understand their desire—perhaps in an attempt not to have to confront the reality of disease—not to want to know. And we well may agree that no-one has the right to force them to know. But assuming that such claims were not made ‘in the heat of the moment’, and they had sufficient time to reflect on the ramifications of their situation, can their exercising a moral right not to know genetic information about themselves be defended in the name of autonomy?

Tom argues that he has weighed up the options available to him which suggests that he is reasonably informed about the disease’s progression. Perhaps he has spoken to various specialists about the likely course of the disease, or has read literature within the area and feels that, given existing knowledge in the area of Huntington’s disease, he would prefer to maintain his current lifestyle whilst remaining hopeful of a cure in the future. He may claim that exercising his right not to know is consistent with his autonomy, because his choice not to know is informed: he knows all there is to know about Huntington’s disease. He argues that because he knows enough about the disease, he doesn’t want to know any more (for instance, what it will mean if he is found to carry the faulty gene), such an act is consistent with his autonomy because it is an informed choice not to know.

Tom claims that he knows enough about the disease to make an informed choice not to know, yet what Tom does not know about Huntington’s disease is the all important (with regard to his future) fact—whether or not he carries the gene for it. And because it is his own future relation to Huntington’s disease he is refusing to know, he is giving up his autonomy, not exercising it.

Therefore it seems incompatible for Tom to claim that not knowing certain genetic information is consistent with him exercising his autonomy. This is for two reasons:

- Firstly, remaining ignorant about whether he carries the HD gene means that he cannot make informed decisions about his future because he does not have significant information to hand.

- Secondly, his choice not to know may frustrate his future autonomous goals: he may go on to make choices that are self-defeating. For instance, if Tom wrongly assumes he carries the Huntington’s gene, then he may decide to forego having children of his own in the mistaken belief that they too would be at risk for the disease. He cannot exercise a right to ignorance in the name of autonomy because some of the important decisions he goes on to make in uncertainty (ignorance) may thwart his future life goals.

As I discussed earlier, making autonomous choices involves being cognisant of the consequences of one’s decisions. It entails weighing up the various options available however difficult and distressing they may be. It also involves being honest with oneself about what the choices will mean for the future which means, for example, recognising when one’s choices are being unduly influenced by fear or guilt.
Sandra’s decision not to be tested may be influenced in part by trepidation of what she remembered her mother enduring. She may rationalise ignorance of her risk as a way of postponing having to confront her own fears about illness and death. Or she may feel that only she truly knows her mental strengths and weaknesses and at this point in time ignorance is bliss. Such rationalisations are understandable, but we should not be tempted into assuming that remaining ignorant is consistent with autonomy.

Part of deciding how to live our lives is taking responsibility for ourselves and the choices we have to make, which means confronting what the future may hold for us even when we would rather not know it. I undercut my own autonomy if I reject knowledge pertinent to my future choices and life because autonomy involves shaping my own life with knowledge, but I do not undercut it if I reject knowledge which is not pertinent to any choice I could possibly make in the future.

When Tom says that he does not wish to know whether he carries the gene for Huntington’s disease, and Sandra says that she does not want to undergo susceptibility testing for breast cancer, we ought to be sensitive to their position. Although sensitivity does not imply that we should agree with their position, their putative right not to know may be defended, for example, by a consequentialist argument. Having weighed up the benefits and burdens of remaining ignorant, it may be that more benefits will ensue overall in not knowing. For instance, Tom may claim that ‘not knowing and remaining hopeful’ benefits him far more greatly than knowing for certain (even allowing for the fact that he may not be at risk for the disease at all). This is because he knows (better than anyone) his psychological strengths and weaknesses in coping with such knowledge. He may reason that, were he to be tested and found to carry the gene, such an unbearable burden would lead him to consider suicide.\textsuperscript{15–18}

We are the architects of our lives and require knowledge if we are to build the kinds of lives we want to live, thus it appears contrary to autonomy to claim that one has a right to know genetic information whilst at the same time defending a right not to know genetic information. We can understand and sympathise with the individual who claims a right not to know—perhaps they would be willing to sacrifice autonomy in preference to knowing one’s imminent death—but such an individual cannot justify such a right in the name of autonomy.

**Conclusion**

In this discussion I have examined the claim that one can exercise a right to remain ignorant on the grounds that it is consistent with one’s autonomy. In the hypothetical cases presented, I focused on whether an individual has a right to remain in ignorance when the information concerned is their genetic knowledge.

I began by considering what the notion of autonomy entails. When autonomy (as self-determination) is understood as involving critical self-reflection, deliberation, and thoughtful and informed decision-making, it becomes clear that one must have relevant information at one’s disposal to be autonomous.

We are responsible for our own lives and as such have an obligation to be informed. Such an understanding of autonomy is demanding and justifies our right to know. When information is denied to us, or is unavailable or too complex to understand, we
cannot make autonomous choices because we are ignorant about the options available
to us. We are not responsible for our lives when we cannot make informed choices.

The individual who claims a right not to know on the basis that exercising such a right
is compatible with one’s autonomy is mistaken. Their motives may be
understandable, indeed we may find their reasons clear and compelling, but autonomy
does not (and cannot) tolerate remaining ignorant (about important information that
may have significant implications for our life) when central to being autonomous is
making informed choices with as much knowledge as is available to us.

Thus we cannot defend a right not to know our genetic information in the name of
autonomy alone. It may well be that the right not to know can be successfully
defended on consequentialist grounds, the justification being that the benefits of not
knowing genetic information outweigh the burdens of knowing. Autonomy, however,
demands that we exercise our capacity to reason and this surely entails the pursuit of
pertinent genetic information not the rejection of it.

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PHARMAC and Ventolin in New Zealand

John Gillies, Jeff Brown, Cass Byrnes, Alan Farrell, David Graham

Abstract

Recently, PHARMAC undertook an unfortunate experiment on asthma sufferers when it fundamentally changed its funding support for reliever medications. Ventolin® metered dose inhaler (MDI), the backbone of asthma relief for over 30 years, was dropped in favour of Salamol®, a post-patent salbutamol in a device which, within the first few weeks of use, has been found to be ineffective by many patients, and thus potentially dangerous. PHARMAC has agreed to reconsider its decision, but how was this decision reached in the first place?

Drug: Ventolin® metered dose inhaler (MDI)

Indication: Bronchodilator for relief of asthma symptoms

Recommended dose: 1–2 puffs (100-200 μg) inhaled when necessary for control of asthma symptoms. Delivery via spacer recommended in children.

Clinical efficacy: Since the early 1970s, salbutamol delivered from the Ventolin® MDI has been the cornerstone of acute asthma management. It produces a rapid onset of bronchodilation with a duration of action of 4–6 hours. Other bronchodilator drugs, delivered in different devices, have required rigorous assessment before adoption, and some have proved inappropriate leading to their withdrawal due to safety concerns. Ventolin® MDI is the commonest bronchodilator used by asthmatics in New Zealand and worldwide. It is used by most people with asthma in New Zealand to relieve asthma symptoms due to airflow obstruction, which for some people may be life-threatening.

Serious adverse events are rare, and none have been reported from device failure.

Background: In the 1980s, New Zealand had one of the highest asthma mortality-rates in the world. Since then, the rate has fallen but the prevalence of asthma in New Zealanders remains amongst the highest in the world.
As exacerbations of asthma are potentially life-threatening, it is essential that bronchodilator therapies offered are proven to be effective, safe, and reliable.

Earlier this year, PHARMAC indicated its decision to withdraw a subsidy for Ventolin® MDI prescribed for asthma, in favour of Salamol®, an after-patent preparation of salbutamol. Salamol® had not been used significantly in New Zealand prior to this announcement, and its introduction would mean changing successful treatment for hundreds of thousands of asthma sufferers currently using Ventolin® MDI.

Early distribution of Salamol® has resulted in significant anxiety to asthma sufferers (children and adults) who regularly used Ventolin®, not only because of the change, but also because of technical difficulties with the device, resulting in them sensing it was less effective. Those wishing to continue with Ventolin® can do so, but now face an additional charge of at least NZ$2.00 per inhaler. We believe this charge will be unsustainable for many, particularly those with more than one asthmatic in the family, or with children who often require a number of relievers to be available (home, school, car, other carers, etc).

There has been no direct consultation by PHARMAC about the introduction of Salamol® with any expert groups such as the Thoracic Society of Australia & New Zealand, the Australasian Paediatric Respiratory Group, or the Paediatric Society of New Zealand.

Salamol® is being imported by Air Flow Products Ltd, a commercially independent wholly owned subsidiary of the Asthma and Respiratory Foundation of New Zealand (ARFNZ).

Clinical Issues:

Most often, the first an asthma sufferer or family has heard about this fundamental change to their therapy has been when they present to their pharmacy with a prescription for Ventolin® MDI and when the product is delivered, they are told that Ventolin® MDI is no longer available with the same subsidy, and that Salamol® is the replacement.

Acute asthma can not only be provoked by anxiety in some asthmatics, but also in acute events anxiety can worsen the severity of the event. An unexpected change from a trusted medication may have serious consequences in these patients.

Already, asthmatic children and adults have expressed concern about how ‘different’ the inhaler feels, in taste, physically, and in its delivery of medication. Indeed, several children have complained of the taste and some have been more reluctant to use the medication. The device is smaller and wider, and may be more difficult for especially elderly asthmatics or those with
arthritis to manage. The typical patient grips the Ventolin® MDI in the palm of the hand and uses the thumb to activate it. The Salamol® device is too small to comfortably grip this way, and it may slip through the palm when the patient attempts to activate it.

A more serious issue is the tendency for the device to block its outlet thereby failing to deliver any medication. There has been a response by the supplier that the device should be washed regularly, with specific instruction about drying it. This is problematic for a number of reasons. Users may not remember to regularly clean the device per the manufacturers instructions, thus increasing risk of malfunction. The advice given does not specify a drying method, and there is a risk that a patient requiring medication acutely might only have a currently wet and unusable device. Finally, the manufacturer’s instructions specifically require that the device not be washed in detergent. This is directly contrary to the washing instructions for spacer devices necessary for use in children and many adults, and will surely result in confusion.

Disregarding the issues of palatability etc, it would seem that the most dependable way (of ensuring that patients always had access to a reliable Salamol® inhaler) would be to provide them with two, rather than one inhaler. Clearly this would not be a cost-effective measure.

The device has alcohol in the propellant in sufficient quantities for a user to fail a traffic alcohol screening test. As paediatricians, the authors are also concerned that children are unnecessarily being exposed to alcohol.

**Published research:**

A search of the National Library of Medicine using PubMed for ‘Salamol®’ on 29 June 2005 produced only three papers. One described the failure of a roadside alcohol breath test, a second discussed Salamol® as a nebulising solution, and the third discussed the lung bioavailability of salbutamol (Salamol®) which the researchers reported to be the same as Ventolin®. There was no comment on the device being prone to clogging. Clearly there has not been enough published clinical research of this drug/device combination to enable doctors to support its adoption.
Role of the Asthma & Respiratory Foundation of New Zealand: This decision has created a potential conflict of interest for the Asthma & Respiratory Foundation of New Zealand because its subsidiary, Airflow Products Ltd, imports and distributes Salamol®. The ARFNZ states that its vision is “to create an environment in which people with respiratory conditions can breathe more easily” and its mission is “to advocate on behalf of all people with respiratory conditions”. Despite its policy of not advocating any specific medication, the Foundation now stands to gain financially from Salamol®.

Discussion: These events would appear to the authors to represent a poorly considered decision by PHARMAC. PHARMAC has chosen a potentially defective product as the sole salbutamol MDI for use without charge in New Zealand. The disruption and potential risk to asthma sufferers in New Zealand does not seem to justify the purported annual savings of less than NZ$2 million over 16 months.8

PHARMAC has managed to confuse and potentially endanger the asthma sufferers of New Zealand by this unfortunate experiment, and alienated the medical practitioners who strive to do their best for patients with asthma.

Perhaps this is a lesson not to assume that an apparently small change (in this case a change of medication brands and their delivery systems) cannot have an adverse outcome. Certainly there are sufficient experts in the field that could have advised on this, if asked.

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Human instincts, normal and pathological: the sexual instinct


The sexual instinct requires very careful management at the period of puberty. I have often wondered how much longer we alienists are to be as “voices crying in the wilderness” regarding the grave moral dangers which beset the child at this great physiological crisis, and still, just at the period when the most anxious care and the most tactful management are required, the grossest carelessness on the part of parents exists. At this momentous epoch strange new feelings appear which, if well directed, are capable of the highest good, but which, on the other hand, are readily perverted to evil. Parents, in the majority of cases through feelings of entirely false modesty, do not explain the real nature of these natural feelings, but allow their children to learn the truth, often in a highly perverted form, from extraneous sources, with correspondingly disastrous results, only too frequently irretrievable and lifelong.

A quiet, confidential chat between mother and daughter, father and son, would be entirely beneficial and productive of untold good; and yet instead of quietly guiding and regulating the sexual feeling of their children the majority of parents allow matters to drift and drift until too late, and are then unaccountably surprised at the moral delinquencies of their offspring. In spite of numerous examples of the evil results of this criminal neglect, each new generation of parent persists in following in the old paths, and we are constantly being confronted with the spectacle of children born of really good and well-meaning parents going rapidly to the bad.

There seems to be a lack of the happy medium of overstrictness and utter laxity. In the former case there is no confidence between parents and children—the least error is visited by condign punishment, the love of child for parents is in abeyance, and lie kicks over, the traces in the end. On the other hand, laxity is just as reprehensible; and I am sadly afraid that parental control is at a low ebb in this colony. We are constantly having introduced into our legislation Bills aiming at the taking-over by the State of functions which properly belong to parents and which should be left to them. In fact, I would go further and say that oftentimes parents should be punished for the sins of their children. If children are but properly trained from their earliest years corporal punishment would never be necessary and the love which they bear towards their parents would be an all-sufficient guarantee for future good and useful lives.

In speaking of the various affections of the sexual instinct I shall be very brief, as it is in many respects an unsatisfactory and unsavoury subject. The various affections—such as salism, tubadism, masturbation in women, sodomy, and so forth—have been so adequately dealt with by Krait Ebbing and Havelock Ellis that I cannot offer anything new. As Dr. King remarked at the last general meeting of this association, many symptoms and varieties have been labelled as separate diseases which should properly be included under the general heading of “sexual inversion.”
**Whooping cough in adults**

Methuselah, and I suspect, many of his colleagues have considered pertussis a disease that affects only children. Apparently not so. A recent review claims that, in the USA, pertussis is responsible for approximately 20% to 30% of cases of cough lasting more than 2 weeks in adults and adolescents. In support, the reviewer quotes more than 100 articles in prestigious American journals. It appears that childhood immunisation with pertussis vaccine does not provide lifelong immunity. Furthermore, the characteristic whoop is present in less than 50% of cases in adolescents and adults. Serologic tests and/or nasopharyngeal aspirate or swab for polymerase chain reaction and culture can confirm the diagnosis but are unreliable, and the reviewer concludes that testing for pertussis is not sufficiently sensitive for treatment decisions to be guided by test results alone. And the treatment—14 days of macrolide antibiotic.

*Annals of Internal Medicine 2005;142:832–4*

**Hysterectomy options**

An international team (headed from National Women’s, Auckland) has performed a review of trials evaluating the most appropriate surgical method of hysterectomy (abdominal, vaginal or laparoscopic) for women with benign disease. The conclusions, drawn from their review of 27 trials (total of 3643 participants), were that vaginal hysterectomy is preferable to abdominal hysterectomy where possible. The reasons for this is that this technique results in significantly speedier return to normal activities and other improved secondary outcomes (shorter duration of hospital stay and fewer unspecified infections or febrile episodes). And if vaginal hysterectomy is not possible, laparoscopic hysterectomy is preferable to abdominal hysterectomy, although it brings a higher chance of bladder or ureter injury.

*BMJ 2005;330:1478–81*

**Diabetes mellitus in pregnancy**

Gestational diabetes may occur in up to 10% of all pregnancies and is associated with substantial rates of maternal and perinatal complications. The latter include macrosomia, shoulder dystocia, birth injuries such as bone fractures and nerve palsies, and hypoglycemia. For women, gestational diabetes is a strong risk factor for diabetes. However, it remains uncertain whether screening and treatment to reduce maternal glucose levels reduces these risks. In a randomised trial reported from Adelaide, it has been shown that intervention (dietary advice, blood glucose monitoring and insulin therapy as needed) does reduce serious perinatal morbidity and may also improve the woman’s health-related quality of life. Unsurprisingly, women in the intervention group had a higher rate of induction of labour than women in the routine-care group and more infants of women in the intervention group were admitted to the neonatal nursery. So, intervention causes more work and higher costs, but better results.

Migraine and acupuncture

Migraine is a common and disabling condition. In most cases it is sufficient to treat the acute headaches, but many patients require interval treatment as attacks occur often or are insufficiently controlled. Treatment with β-blockers, calcium antagonists or other agents has been shown to reduce the frequency of migraine attacks; however, the success of treatment is usually modest. So what about acupuncture? Researchers in Munich have reported upon a three way randomised trial—acupuncture, sham acupuncture, or no treatment. And the results? Acupuncture was no more effective than sham acupuncture in reducing migraine headaches, although both interventions were more effective than no treatment. Vive the placebo effect!

JAMA 2005;293:2118–25

Another bad move

We know that hospitals in the UK are managed by Trusts within the National Health Service (NHS). But did you know that the Blair government wants the healthcare trusts to compete with each other for business, and thus theoretically raise standards and provide patients with a choice? Hospitals which run out of money will simply go to the wall, it says. In reporting this move, an observation was made that “there is not a shred of evidence that this is either workable or desirable”. Too true, as we who have lived through the Crown Health Enterprise (CHE) fiasco in New Zealand can testify.

Guardian Weekly, 1–7 July 2005, p9
PHARMAC responds to Stewart Mann on dihydropyridine calcium channel antagonists

Associate Professor Stewart Mann recently described changes in PHARMAC’s funding of dihydropyridine calcium channel antagonists (DHP CCBs) and resultant changes for patients over the past 5–10 years (http://www.nzma.org.nz/journal/118-1218/1569/). We found the article to be a good summary of a complex issue.

We make the following observations:

PHARMAC’s processes

PHARMAC’s legislative objective is “to secure for eligible people in need of pharmaceuticals, the best health outcomes that are reasonably achievable from pharmaceutical treatment and from within the amount of funding provided.” Two of the ways in which PHARMAC achieves this is by reference pricing and by negotiating sole supply contracts with pharmaceutical suppliers. When managed appropriately, these strategies free up funding to invest in other unsubsidised medicines, gaining additional clinical benefit elsewhere.

Reference pricing and sole supply occurs only where it is clear that a loss of choice between one equivalent brand of drug and another is not considered critical. PHARMAC bases such decisions on available clinical evidence; it is not part of PHARMAC’s Operating Policies and Procedures to conduct compliance and/or bio-equivalency testing. Before a medicine can be marketed in New Zealand it must first meet the necessary standards set by the Ministry of Health. As part of the registration process, the New Zealand Medicines and Medical Devices Safety Authority (Medsafe) requires safety and compliance testing of all medicines.

With every reference pricing initiative, PHARMAC seeks independent expert clinical advice from PTAC, and consults (and is required to consult) with relevant clinical and patient groups to ensure it has all the information before making a decision. PHARMAC is always looking to improve its processes, and although for practical reasons we may not have replied individually to each consultation response we received, every response is (and was) provided to and considered by PHARMAC’s Board before a decision is made. This is an obligation that the PHARMAC Board takes extremely seriously.

Reference pricing

Reference pricing is a commonly used strategy to control the cost of multiple drugs within a drug class, and in New Zealand is based upon the principle that reimbursement is set at the price of the least expensive member(s) of a drug class. Reference pricing happens in a number of countries including Germany, Canada, The Netherlands, France, Japan, Sweden, and Australia, and has been used in New Zealand since PHARMAC’s inception in 1993.
There is limited evidence on the impact of reference pricing of DHP CCBs on health outcomes:

- PHARMAC did commission an independent follow up evaluation of the DHP CCB reference pricing in 1999, analysing data from the 1–2 consultations per patient funded by PHARMAC for GPs to monitor changes in blood pressure. This analysis provided some evidence that there were no clinically significant changes in blood pressure following the switch, although there were limitations with the data.

- We are aware of one other example where outcomes data are available following the reference pricing of DHP CCBs. In British Columbia (Canada) there was no associated increase in rates of physician visits, hospitalisations, and long-term care admissions—as also occurred with ACE inhibitor reference pricing.

The putative lack of any significant observable impact on blood pressure control in New Zealand may of course have been more short-term due to increased awareness and medical monitoring (Hawthorne effect) than the change to the newly subsidised DHPs themselves, and there was no evidence that such improvements would be maintained long-term with just routine management of blood pressure. Nevertheless, there was no evidence that changing to the newly subsidised DHPs caused deterioration across users, at least short term in the context of more intensive dedicated monitoring.

Although the British Columbian data are less than ideal, they are possibly the best available under the circumstances.

As noted by Associate Professor Mann, PHARMAC put in place Special Authority provisions to allow fully funded access to alternative DHP CCBs based on advice from PTAC’s Cardiovascular Subcommittee and the Cardiac Society.

While we acknowledge arguments around patient inconvenience and resistance to change, these must be considered against the alternative – that when funds are constrained, tradeoffs must be made, so that patients elsewhere in the health sector are less likely to have to pay for their own treatment, or simply miss out.

**Bioequivalence**

It is important to note that Adalat CC (coat core) was assessed and approved by Medsafe, the Medicines Regulator, as a new medicine on the basis of clinical trial and other data supplied by the sponsor of the product in New Zealand. Medsafe has advised PHARMAC that it did not consider Adalat CC to be either bioequivalent to, or interchangeable with, Adalat Oros (Medsafe, personal communication).

When it was considering a submission by the supplier (separate to the application for Medsafe registration), the Cardiovascular Subcommittee of PTAC noted that several pharmacokinetic parameters of the CC product differed from those seen for Adalat Oros. The subcommittee also raised questions about whether these differences would impact on patient well being if patients were changed from other formulations of Adalat to the CC formulation. The subcommittee took advice on this issue from both the Cardiac Society and Associate Professor Richard Robson (who is the current Chair of Medsafe’s Medicines Assessment Advisory Committee (MAAC)) before making a recommendation on funding within this therapeutic group.
The Cardiovascular Subcommittee also took into account several other factors including dropout rates and adverse effects in the CC groups versus the Oros groups, the overall blood pressure control in the Glasser et al study, and also the fact that the CC preparation was unlikely to gain registration in New Zealand for the angina indication.

Medsafe advises that Adalat CC and Adalat Oros utilise distinct dose release systems and are designed to have different release characteristics. This is not the case for Felo and Plendil, where both were designed to be taken once daily and were amenable to standard bioequivalence testing. While MAAC’s Generic Subcommittee (GSC) did note and discuss differences in the bioequivalence studies conducted to demonstrate that Felo and Plendil were bioequivalent, these issues were resolved as more data were provided. Medsafe is of the opinion that it is inappropriate to link the issues of the differences in pharmacokinetics between Adalat CC and Adalat Oros with those noted and discussed by the GSC with respect to Felo and Plendil (Medsafe, personal communication).

**Generic changes**

Generic substitution of brands of the same active ingredient (such as Felo ER for Plendil ER) is a very regular occurrence internationally, with it being common place in counties such as Hungary, Canada, Italy, Germany, the United Kingdom and Australia. Furthermore, in many of these countries the patient is potentially switched (again and again) every time they go back to the pharmacy. Some countries, for example Denmark, have mandatory substitution at pharmacy level. This is accepted in those countries because of the regulatory requirement that bioequivalence is to be shown before a generic can be marketed.

The regulatory requirements in New Zealand are no different—bioequivalence must be demonstrated. As well, the guidelines for showing equivalence used in New Zealand are based on the guidelines used internationally. Generic medicines are also required to meet the same quality and manufacturing standards as all manufacturers of branded medicines; this makes it difficult to compare them to used cars.

**Comment**

It is not uncommon for a greater than usual number of people to report adverse events when reference pricing, or a brand change through the tender, occurs. We understand from Medsafe that usually there is a “spike” in reports to Medsafe’s Medicines Adverse Reactions Committee (MARC), which then quickly returns to a normal level. It is difficult to ascertain the exact reason for this phenomenon, or indeed how many additional patients are able to take the ‘new’ medicine when they were unable to tolerate the previously subsidised one. The same “spike” can occur when there is no change to a drug other than the name—for example as occurred with simvastatin’s brand name changing from ‘Zocor®’ to ‘Lipex®’ (Medsafe, personal communication).

Reference pricing and generic substitution are methods that are accepted in many countries as a clinically acceptable way of managing pharmaceutical expenditure. PHARMAC is careful to consult with interested parties and take clinical advice before undertaking reference pricing, and hopes to maintain a constructive line of communication with the medical community. To deem these processes “experiments”
is comparable to calling every prescription a doctor writes an experiment, as none of
us know with absolute certainty how a particular patient is going to react to a
particular drug. Provided we are all aware of the risks and benefits generally
associated with a particular treatment as they are highlighted in clinical studies, we
can manage changes in medication both from a funding and clinical perspective.

Remember too that all on-patent medicines are sole supply. PHARMAC considers
that tendering for off-patent medicines is an effective way to secure the supply of
pharmaceutical agents and to achieve lower prices for generic medicines. Reference
pricing frees up funding from the pharmaceutical budget that can then be reinvested
into other priority areas. In this sense, reference pricing has a positive effect on health
outcomes, as it allows PHARMAC to invest in new medicines that either extend or
improve the quality of life that otherwise would not happen.

Footnotes:

*The analysis was careful to caveat that evaluators had no control over experimental design or data
collection, and that the reliability and the validity of the raw data (which had not been collected in a
controlled research environment) could not be assessed – particularly the accuracy of the blood
pressure recordings. It was stated that deficiencies in claim form design, lack of standardised protocols
for blood pressure measurement, and some inconsistencies in interpretation of claim form items meant
that these results must be reported cautiously.

†To clearly determine whether there were excessive risks from switching associated with reference
pricing would require a very large randomised controlled trial (to control for confounding and other
bias), for what is likely to be small difference between the drugs. Such studies would be unlikely to be
feasible/affordable, particularly in New Zealand. Otherwise there are ongoing issues of comparability
(differences in measurement, different patient populations, selection bias, measurement bias etc.). The
only alternative would be to allow the original supplier’s patented monopoly to remain in perpetuity.

Conflict of interest: Scott Metcalfe is externally contracted to work with PHARMAC for public health
advice. Andrew Davies, Wayne McNee and Peter Moodie declare no conflicts.

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References:

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Richard Milne responds to PHARMAC on discounting future health benefits and costs

I thank PHARMAC for responding to my recent Viewpoint article on discounting of future health benefits and costs, in which I argued that a high social discount rate, when used in economic evaluation, militates against both preventive medicine and many public health policies.

I concur with PHARMAC that economic evaluation, in its various forms, should be used more widely in evaluation of Government programmes, including those initiated by the Ministry of Health (MOH) and District Health Boards. When this happens, the discount rate will become crucial to prioritisation of healthcare programmes. It is encouraging that PHARMAC has now reduced the discount rate from 10% to 8% and that it plans to ‘consult widely within the next 12 months.’ However, the issue is much broader than PHARMAC.

My main concern is with the valuation of future health benefits of novel interventions. High discount rates for health benefits can be fatal to Government prioritisation and funding of public health strategies such as new screening and infant vaccination programmes, a range of which will compete for limited funding in the next 5 years.

The Public Health Intelligence Unit of the MOH follows the World Health Organization (WHO) in using a discount rate of 3% in its Burden of Disease studies, to reflect the results of research into individuals’ time preference for future compared to present health benefits. It is puzzling why the MOH and PHARMAC utilise such different discount rates: if the MOH (by discounting at 3%) places a moderately high value on future disability (e.g. lung cancer at age 50 resulting from decades of nicotine addition), why does PHARMAC (by discounting at 8%) implicitly place such a low value on the future benefits accruing from interventions that reduce or avert future disability (e.g. smoking cessation therapies for adolescents)?

PHARMAC states: ‘There are many examples of health related behaviour suggesting that New Zealanders actually have a very high preference for health now at the expense of health in the future.’ Examples of devaluing the future can indeed be found (e.g. young males who consistently drive after binge drinking) but counter-examples are readily found (many women with young families; tertiary students preparing for lifetime careers). The social discount rate for health benefits must represent all New Zealanders; ideally it is the weighted average across all types of behaviour pertaining to health and survival.

The Ministry of Health’s current emphasis on disease prevention is more compelling than anecdotes. The main health benefits of routine infant vaccination and screening for type 2 diabetes, cardiovascular disease, breast cancer, and cervical cancer all occur in the future. Implementation and widescreen acceptance of these programmes therefore suggests that both the MOH and the New Zealand public implicitly accept a moderately low social discount rate for health benefits. Research is needed: in the meantime, we can and must learn from other nations, which set the discount rate for health benefits generally between zero and 5%.
In accord with international recommendations,\textsuperscript{4} most countries (including New Zealand [NZ]) set the discount rate for costs equal to that for health benefits. PHARMAC justifies its discount rate for both costs and benefits on purely financial grounds. These are:

- The ‘capital charge’ that is used for evaluating capital investments (currently 8\% per annum); however, as PHARMAC acknowledges, international authorities\textsuperscript{3} and Treasury\textsuperscript{5} advise using the rate of return on a risk less asset (e.g. the 5-year or 10-year government bond rate) as the basis for setting the discount rate. PHARMAC states that this is ‘currently 4\% to 6\% in the NZ context’;\textsuperscript{1}

- Comparison with Land Transport NZ (LTNZ), which still uses an historic discount rate (10\%). However, this is unsurprising because LTNZ is advised by Treasury and the 10\% rate is used as a default by Treasury for discounting costs. But when challenged, Treasury could provide no justification for continuing to use such a high rate; one of its own analysts in 2002 estimated a discount rate of 5.6\% for costs;\textsuperscript{5} and

- Treasury has no declared policy on setting a discount rate for health benefits\textsuperscript{(2)}. Comparisons with LTNZ are therefore unhelpful.

Unfortunately PHARMAC’s revised discount rate for both costs and benefits (8\%) is still substantially higher than that recommended in all published international consensus guidelines for economic evaluation (2.5\% to 5\% except for Spain at 6\%\textsuperscript{6}), and the difference matters, especially for health benefits.\textsuperscript{2,7}

While I agree with PHARMAC that New Zealand should not ‘blindly’ follow historic decisions by the UK and the US because our current economy is different, I note that:

- The discount rate in international guidelines for economic evaluation bears no relationship to population or per capita GDP.\textsuperscript{2}

- The UK revised its discount rate to 3.5\% just last year; and

- Our major trading partners help determine the economic environment in which NZ healthcare decisions are made; their policies therefore should not be ignored. Discount rates are 5\%, 3.5\%, and 3\% for Australia, the UK, and the US, respectively.

Rather than PHARMAC canvassing the opinions of pharmaceutical suppliers and clinician groups again, it would be more helpful if the MOH were to set up processes for informed discussion and decision making for all stakeholders. These discussions should take into account internationally agreed principles and practice, empirical research, and the Ministry of Health’s general policy objectives including its current emphasis on disease prevention.\textsuperscript{2} Lowering the discount rate will lend support to prioritisation of disease-prevention strategies without affecting the global health budget. It’s a small ask, if we are interested in both rational decision-making and disease-prevention.

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References:


Findings and methodological lessons from a small case-control study into campylobacteriosis in Wellington

**Background**—Campylobacteriosis is the most commonly notified enteric disease in New Zealand and one for which notifications have increased nearly every year since it became notifiable in 1980.

**Aim**—To report the major findings of an unpublished case-control study into campylobacteriosis. This study was conducted by a group of fifth year medical students as part of an educational training experience (with assistance from medical school staff).

**Methods**—The 50 cases were based on notifications between 25 February and 13 March 2003 in the greater Wellington region (Lower Hutt, Upper Hutt, Porirua and Wellington). This investigation was carried out to investigate peak summer notification levels that were two to three times higher than usual. The 50 controls were recruited by telephone and matched by age-group and Territorial Local Authority area. Cases and controls were interviewed by telephone.

**Main findings**—The strongest association was for consuming “chicken not cooked at home” in the last three days, but this was not at a statistically significant level (adjusted odds ratio = 2.13, 95% confidence interval = 0.91 – 4.92, p = 0.11). Eating some foods was found to be protective when considering either the three or five day window period ie, bacon in the past five days (p < 0.01), eating pork in the last three days or five days (both p = 0.02), and eating yoghurt in the last three days (p = 0.045). The statistically significant non-food exposures were: drinking water from a water cooler in the last seven days (p = 0.03), and travel outside the Wellington region in the last seven days (both being protective). Further detailed results are available on request from the authors.

**Discussion**—Although a case-control study was considered early in the community outbreak of campylobacteriosis affecting this region in the summer of 2002/03, there were various delays before the study could begin (eg, study protocol and questionnaire development and ethical approval). This meant that weekly notification levels were returning to normal by the time the study started. Therefore the findings are likely to relate more to endemic campylobacteriosis risk factors in the region rather than those for a specific outbreak.

The findings for chicken are consistent with other evidence from larger New Zealand case-control studies, and various outbreak investigations. It is also consistent with the evidence for frequent contamination of New Zealand poultry with Campylobacter (and reviewed by Lake et al).

The other food associations found in this study might have been due to a substitution effect (ie, a food associated with “protection” may merely displace from the diet of the control a food associated with increased risk).

A particular strength of this study was that the control selection was via systematic changes to telephone numbers that allowed those with unlisted phone numbers to be
included as controls. However, this greatly increased the number of phone calls required. Another strength was that the questionnaire was fairly comprehensive and it made use of exposure windows (of 3, 5 and 7 days). This refinement allows for analysis of exposures that correspond to the most common rather than the maximum incubation period of infectious diseases, and is considered particularly useful for investigating common food exposures such as eggs, poultry, and meat.12 It was reported by the interviewers that the interviewees did not appear to have any problem with understanding this method of questioning.

Nevertheless, specific limitations of this study included the following:

- The size of the study was likely to be too small to have adequately investigated many of the key associations of interest. Having such a broad age range of cases (<1 to 88 years) may have lowered the quality of the study.
- The response rate for potential controls agreeing to participate was very low at 25%, and this may have introduced bias. The finding that more than twice as many controls than cases were smokers also suggests differences between the two groups.
- The large number of different interviewers involved (n = 11) as a result of the educational objectives of the project. Also, the medical student interviewers self-reported that they were not that confident with their interviewing skills.

Conclusions—This case-control study is of fairly limited value owing to its small size and various other methodological concerns. Nevertheless, it does provide some limited additional evidence for chicken consumption being a risk factor for campylobacteriosis in the New Zealand setting. The study also indicates the difficulty of achieving a high response rate from using population-based controls and that exposure window assessment can be feasibly included in questionnaires used in case-control studies.

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Calling obituary writers

Obituaries do not write themselves, oddly enough. They require organisation, time, and respect for our departed colleagues.

Many decades ago, our medical practitioners were Otago graduates with a sprinkling of Brits. Things have changed. With the Auckland Medical School and our overseas-trained colleagues coming from a wide variety of medical schools, it is no longer a tight little club where everyone knows everyone else.

Thus we need a network to tell us who has died and who amongst family and colleagues can best give the rest of us some overview of the life, both professional and social, of our dead colleague.

For several years I have tried to rejuvenate this part of the Journal. I have been greatly helped in this task by colleagues in Auckland, Wellington, and Dunedin who scan the local newspapers. Anyone whose death notice does not appear in one of the four main dailies is liable to miss out.

Who is to write the obituary? Someone who cares. It need not be a literary masterpiece but should give something of the texture of the person’s life. Most funerals have a eulogy and the eulogist is often in the best position to help with an obituary.

About 400 words is usual but, with the electronic journal, space is no longer the problem it was in the days of hard copy.

The next time a colleague dies, ask yourself: “Who is going to do the obituary?” It could be you or someone whose arm may need only a gentle twist.

Most of the Journal belongs to the younger and brighter of us but the obituaries belong to us all. Even the old and cranky.

Roy Holmes
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Guide to Arthrocentesis and Soft Tissue Injection


Curricular training in musculoskeletal medicine is evidently limited in the US (as in New Zealand) thus motivating the author over there to write this guide as a “starting point” for clinicians interested in gaining expertise.

Each chapter covers a specific region of the body, and starts with a list of differential diagnoses. Diagnoses are discussed individually, with clear and concise accounts of pathology and clinical findings, followed by more detailed advice on treatments (many involving physical modalities), injection techniques, and aftercare.

My main criticism is the lack of details on interpreting symptoms and signs; local anaesthetic blocks to help make a diagnosis is often emphasised. Although injection techniques are well described, line drawings of injection placement lack details and clarity. Instructions on injection aftercare appear overcautious and defensive. The author notes a paucity of research on musculoskeletal medicine, then seems to overlook available evidence on the treatment of nonspecific back pain—the use of bed rest, corsets, and crutches for walking are advocated. The small print size may be a challenge for older eyes.

This concise and pocket-sized guide, on common musculoskeletal disorders, has helpful advice on injection techniques and physical therapy. Lacking details on clinical diagnosis, it is not ideal for a beginner, but it would be a useful reference for the clinician who is gaining experience and learning on the job.

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The Doctor in Literature: satisfaction or resentment?


In this annotated, indexed anthology of the doctor-patient relationship, as portrayed over the centuries in novels, short stories and plays, Dr Posen refreshingly releases “wad some pow’r the giftie gie us to see ourseles as others see us [sic].”

The first objective was to make accessible 1500 passages from about 600 works of fiction, which describe physicians and their attitudes and activities as perceived from a lay perspective. There are 11 chapters with titles including fees, time, bedside manner, physical examination, communication, degrees of detachment, the ward round, physicians’ social status and the physician in court. The index is comprehensive and whether the book is delved into on a whim or read from cover to cover it is a delightful read. Many themes recur that seem unaffected by time, place or clinical training.

The second objective was to explore specific personality traits among fictional physicians as reflected from the authors’ experiences and prejudices, which tend to stress the more unsatisfactory aspects of medical practice. Posen, the endocrinologist, detects some errors and anachronysms in the lay accounts. The “typical” doctor is usually a man of action rather than contemplation; he tends to be arrogant and paternalistic, frequently fights with his colleagues, and he detests politics, politicians and administrators. This aspect of the book will be of interest to medical students and other health care workers and will provide source material for medical ethics and sociology.

Dr Posen’s third purpose was to introduce the reader to particular passages that he feels have not been given the attention that they deserve and which provide some of the most realistic accounts of contemporary teaching hospitals. “When the painful process was over the surgeon, squeezing her arm with avuncular pride, said “Good girl” as if she were a bright dog that had retrieved a bone.”

Literature has much to teach about life and this book has much to teach us about medical life; how we would all rather meet doctors in works of fiction than on the receiving end; how jargon and delays irritate and how an irrational dislike of doctors which originates in “a deep resentment of powerful experts with their semi-secret knowledge,” has existed from Plato to the present day.

Medical literature, which scholars classify as “technical reporting,” is a one-sided account of the doctor-patient relationship. “Present-day reports of clinical trials provide multiple details concerning subjective and objective findings including “adverse events” or the subjects “quality of life”, but not a hint about how these subjects perceive the personality or the behaviour of the participating physician.”

*The Doctor in Literature: satisfaction or resentment?* does some balancing, is scholarly but amusing, informative but entertaining, and an accessible reference work that draws the reader to the references cited. Astonishing continuity of the doctor-
patient relationship across geographic and historical boundaries is confirmed and when the relationship is suboptimal, the patients’ complaints of two thousand years ago are almost identical with those heard today.

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