Unanswered questions, the epidemiology of a community outbreak: meningococcal C disease in Northland, New Zealand, 2011

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Abstract

Aim We describe the epidemiology of a community outbreak of Meningococcal C disease in Northland in 2011, and national trends in serogroup C disease in New Zealand.

Methods Notification data from EpiSurv for all meningococcal C cases were analysed for 2011 for Northland and for the period 2001-2011 nationally.

Results In 2011, the rate of group C meningococcal disease for the population in the Whangarei district aged less than 20 years was 27.6 cases per 100,000 population (6 cases) compared with 17.6 cases per 100,000 population under 20 years (8 cases) in the Northland District Health Board (DHB). All except one case were under 20 years of age. The case fatality rate was 33%. Nationally the rate of meningococcal C disease has fluctuated over the last decade, with an increasing trend apparent since 2007. There has been a noticeable increase over the last 3 years of group C cases infected with the C:P1.5-1,10-8 strain (including all of the Northland cases). This strain has also been associated with a higher case fatality rate (16% in the period 2007-2011).

Conclusion Meningococcal C disease in New Zealand, although still less common than group B, is poorly understood. The relationships between carriage, invasive disease and community outbreaks deserve greater study. Active monitoring of surveillance data is warranted to ensure timely funded introduction of the highly effective meningococcal C conjugate vaccine on to the national immunisation schedule when appropriate, given increasing disease rates, the high case fatality rate and significant Māori non-Māori inequities in disease incidence.

Invasive meningococcal disease, caused by the Gram-negative diplococcus bacteria Neisseria meningitidis, is a serious illness commonly presenting as meningitis and/or septicemia. The case-fatality rate in New Zealand over the last decade has varied from 4 to 10%.1

The bacteria can be differentiated into groups according to the chemical and immunological properties of the capsular polysaccharide. The most common groups causing human disease are A, B, C, W135 and Y, with groups B and C most common in New Zealand.

During the 1990s through to 2011, the group B meningococcal disease strain B:4:P1.7-2,4 predominated nationally over other strains, reaching a peak of 200 cases per 100,000 population in 2001 in children aged less than 1 year.2,3
Group B meningococcal disease has likewise predominated in Northland; only 7 confirmed cases of group C meningococcal disease were recorded in the 10-year period, from 2001 to 2010.

Group C is the second most common group causing disease in North America and Europe, and is playing an increasing role in Asia. Since 2002 it has been responsible for local outbreaks in China and plays a significant role in Singapore. Most cases of meningococcal C disease are sporadic but clusters, outbreaks and epidemics have been reported globally. Outbreaks of group C meningococcal disease usually resolve in 1-to-3 years. Northland experienced a community outbreak of meningococcal C disease in 2011.

**Methods**

Analysis of the Northland and national meningococcal disease cases is based on data recorded in the national notifiable diseases database, EpiSurv, and the national Meningococcal Reference Laboratory database as at 21 February 2012. Cases reporting multiple ethnicities were prioritised to a single ethnic group according to the following prioritised order: Māori, Pacific Peoples, Asian, Middle Eastern/Latin American/African, European or Other (including New Zealander). Rates were calculated using Statistics New Zealand mid-year population estimates, other than rates by ethnic group. Denominators by ethnic group for 2011 were estimated by applying the ethnic group proportions in the 2006 Census to the population estimates for 2011.

**Results**

**Meningococcal C disease in Northland, 2011**—The first case of invasive meningococcal disease in Northland in 2011 was notified on 10 July, 2011 and was typed as group C, serotype 2a, PorA 1.5-1,10-8. Unusually, three further cases of group C meningococcal disease followed within a month. In the period up to 21 December 2011, a total of 13 confirmed cases of invasive meningococcal disease were notified in Northland. Of these, four cases were group B meningococcal disease and nine cases were group C meningococcal disease (all C:2a:P1.5-1,10-8 strain).

The United States Centers for Disease Control and Prevention and the New Zealand Ministry of Health definition of a community outbreak is “three or more confirmed cases of the same serogroup (and serotype) within a 3-month period and an age-specific incidence or specific community population incidence of approximately 10 cases per 100,000 population, where there is no other obvious link between the cases”. The rates in Northland fulfilled the criteria for a community outbreak in those individuals younger than 20 years.

Of the nine cases of group C meningococcal disease, three cases were Māori and six cases were European or Other (including New Zealander). Eight cases were younger than 20 years of age. The rate of group C meningococcal disease for this age group was 27.6 cases per 100,000 population (6 cases) in the Whangarei district compared with 17.6 cases per 100,000 population under 20 years (8 cases) in the Northland District Health Board (DHB) (Table 1).

Three deaths occurred due to group C meningococcal disease. There were no epidemiological linkages between the cases in Northland.
Table 1. Comparison of group C meningococcal disease rates before the introduction of meningococcal C conjugate vaccine: Northland DHB, New Zealand, Australia, The Netherlands and the United Kingdom

<table>
<thead>
<tr>
<th>Location</th>
<th>Year</th>
<th>Meningococcal C disease rate per 100,000 population</th>
</tr>
</thead>
<tbody>
<tr>
<td>United Kingdom</td>
<td>1999</td>
<td>2.0</td>
</tr>
<tr>
<td>Australia</td>
<td>2001</td>
<td>3.5</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>2001</td>
<td>1.7</td>
</tr>
<tr>
<td>New Zealand</td>
<td>2011</td>
<td>0.7</td>
</tr>
<tr>
<td>Northland DHB (total population)</td>
<td>2011</td>
<td>5.7</td>
</tr>
<tr>
<td>Northland DHB (population aged &lt;20 years)</td>
<td>2011</td>
<td>17.6</td>
</tr>
</tbody>
</table>

National trends in meningococcal C disease—Since 2001, the number of group C meningococcal cases in New Zealand has fluctuated. There was a downward trend overall from 2001 to 2007, decreasing from 0.8 to 0.2 per 100,000 population (30 to 9 cases) over this period. Since 2007, the rate of group C disease has returned to around the 2001 level, with a rate of 0.7 per 100,000 population in 2011 (32 cases).

Figure 1. Rate of group C meningococcal disease in New Zealand, 2001-2011

The increase in group C disease since 2007 has principally been driven by a rise in the number of cases due to the C:P1.5-1,10-8 strain, the strain predominant in Northland in 2011. Disease due to other C strains has been steady at 4 or 5 cases per year over the last 5 years.

The C:P1.5-1,10-8 strain was first detected in New Zealand in 2001. However, routine typing to this level has only occurred since 2007, so the number of cases due to this strain pre-2007 is unknown. There has been a noticeable increase over the last 3 years with 24, 18 and 27 cases infected with the C:P1.5-1,10-8 strain in 2009, 2010 and 2011 respectively.
In 2011, the rate of disease due to this strain was highest in the 1 to 4 year age group (2.4 per 100,000, 5 cases) followed by the 15-19 year age group (1.9 per 100,000 population, 6 cases). The rate of disease due to the C:P1.5-1,10-8 strain was more than three times higher in Māori compared to the European or Other (including New Zealander) ethnic group (1.7 per 100,000 population (11 cases) compared with 0.5 per 100,000 population [15 cases]). Rates were highest in Northland DHB (5.7 per 100,000 population, 9 cases) followed by Waikato DHB (1.4 per 100,000 population, 5 cases).

One third (9) of the 2011 C:P1.5-1,10-8 cases died. However, the case fatality rate for this particular strain of group C disease has varied considerably from year to year, with a case fatality rate of 6% (1/18 cases) in 2010 and 40% in 2007 (2/5 cases). The average case fatality rate due to any group C meningococcal disease over the last 5 years is 16.3% (17/104 cases).

Discussion

Since 2007, rates of meningococcal C disease in New Zealand appear to be trending upwards. In addition, case fatality rates for group C meningococcal disease are substantially higher than for disease due to the predominant B strain (B:P1.7-2,4), resulting in a similar number of deaths from group B and C (16 versus 17) meningococcal disease in the last 5 years, despite the lower number of cases due to group C disease (approximately one third of the number due to group B disease).

Although the lack of routine sub-typing pre-2007 in New Zealand precludes definitive confirmation of the increase in the C:P1.5-1,10-8 strain, this is concerning especially given that all of the 2011 C:P1.5-1,10-8 strain isolates were determined through multi-locus sequence typing to belong to the ST-11 clonal complex. Group C strains from this clonal complex have been associated internationally with higher case fatality rates, and increases in disease due to such strains led to the introduction of group C meningococcal conjugate vaccine on to routine immunisation schedules in a number of European countries.8,9

The reasons for changes in incidence and severity of disease caused by different meningococcal strains are poorly understood. The relationship between carriage and disease has not been fully elucidated.10,11 Although meningococcal carriage is thought to be common, and higher in teenagers, it varies considerably between settings.12,13 Carriage prevalence does not predict incidence of disease or outbreak occurrence.11 Carriage in most people results in the development of protective antibodies but during the carriage state, co-colonisation with other pathogenic and nonpathogenic bacteria may lead to genetic exchange resulting in the emergence of new meningococcal clones.13,14

Capsule switching (for example from serogroup B to C), recombination events involving the porA gene and insertion and transformation of DNA have been described, but there remains little known about trends in genetic types and “hyper-responsive” (i.e. more invasive) lineages.11,14 There is very little difference between the genomes of carrier and invasive strains, suggesting that “on/off” switching of genes may be an important determinant of pathogenesis.15
Community carriage of group C strains and the relationship between carriage and transmission of meningococcal disease, including group C disease have not been well studied in New Zealand. A 2001 study estimated the overall carriage rate of *N. meningitidis* among household contacts in New Zealand was 20.5%.\(^1\) The lower rates of group C disease between 2004 and 2008 coincide with the years when a group B meningococcal disease vaccine (MeNZB) was in use as part of the New Zealand Meningococcal B Immunisation Programme.\(^17\) It is possible that cross-protection from MeNZB™ vaccine against group C disease contributed to this reduction while the vaccine was in use (MeNZB was removed from the routine childhood immunisation schedule from June 2008). A recent MeNZB™ vaccine effectiveness study estimated the effectiveness of MeNZB™ vaccine against non-group B strain disease to be more than 50%.\(^18\) However, the actual contribution of MeNZB vaccine to the observed reduction in group C disease is uncertain given that the effect of residual confounding could not be excluded.

The meningococcal C conjugate vaccine is very effective in reducing the disease burden, but also has a significant impact on carriage. Data from both the UK and the Netherlands have demonstrated that infants can be successfully protected by indirect protection (herd immunity).\(^8\) In the UK, carriage of serogroup C meningococci was reduced by 66% 1 year after vaccination. There were no significant changes in carriage of other disease-associated serogroups.\(^19\)

Currently total population rates of group C disease in New Zealand are still significantly lower (0.7 per 100,000) than those in the United Kingdom (UK), other European countries and Australia at the time of introduction of the meningococcal C conjugate vaccine to the routine childhood immunisation schedule in those countries.

However, the 2011 Northland outbreak suggests that the relationships between carriage, invasive disease and community outbreaks in New Zealand deserve greater study. In addition, given the high case fatality rate, upward trend and significant inequities in meningococcal C disease in New Zealand, it is critical that active monitoring of surveillance data is undertaken to help determine appropriate and timely introduction of the highly effective conjugate meningococcal C vaccine on to the national immunisation schedule.

**Competing interests:** Nil.

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**Acknowledgements:** We acknowledge Heather Davies, Liza Lopez and Esther Lim at ESR for their analytical and administrative support.

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**References:**