Whooping cough—where are we now? A review
Tomasz Kiedrzynski, Ange Bissielo, Mishra Suryaprakash, Don Bandaranayake

ABSTRACT
AIMS: This paper describes the recent trends of pertussis and vaccine uptake in New Zealand based on notifications and immunisation registration information since 2011. It highlights the current risk for the infant in the first months after birth and the crucial role a pertussis booster in pregnancy could play. It also aims to show that protection of infants by the acellular pertussis vaccine can be improved by timely immunisation even in a situation of improving overall uptake rates that are nearing the national target of 95%.
METHODS: We analysed New Zealand notification data for pertussis, extracted from EpiSurv between August 2011 and December 2013, which included the period of the last epidemic. Pertussis immunisation coverage data were extracted from the National Immunisation Register (NIR). Population estimates were based on 2006 census data. Deprivation was analysed using the New Zealand Deprivation Index 2006.
RESULTS: Despite immunisation coverage at 12 months having exceeded 90% New Zealand experienced a large epidemic from 2011 to 2014, with several hundred infant hospitalisations and three deaths. Notification data indicated an average annual rate of pertussis in the New Zealand population of 102 per 100,000 with the highest rates in the youngest age groups. While an overall increase in immunisation coverage in New Zealand was evident and the timeliness showed improvement across ethnic groups and deprivation deciles, there was a marked geographical variation within DHBs and between ethnic groups.
CONCLUSIONS: Given the recent published evidence, pertussis vaccination should be offered to all mothers between weeks 28 and 38 of pregnancy. Further improvements are still possible in coverage at 6 months, particularly in Māori and but also in Pacific populations, as well as in more deprived populations. DHBs work towards achieving the 95% target can contribute to the improvement in the timeliness of immunisation.

Introduction
Whooping cough (pertussis) is a disease affecting all age groups and is often severe in young children, most notably in infants. Pertussis is both an endemic and epidemic disease, with 2-to-5 yearly epidemic cycles. Epidemics last up to 3 years (Figure 1).
Acellular pertussis vaccines replaced the whole cell vaccine in the New Zealand schedule in 2000. In comparison with children who have received an immunisation schedule that includes both whole cell and acellular vaccine, children who have received only acellular pertussis vaccine appear at increased risk of pertussis. Thus, the acellular pertussis vaccines currently in use appear to be less immunogenic than the whole cell vaccines and less effective at preventing infection with and transmission of Bordetella pertussis.

The main goal of the pertussis immunisation programme is to protect infants in the first year of life against severe, life-threatening disease. While timely immunisation is crucial, the first dose of the vaccine is not given until 6 weeks of age, leaving a window of highest risk to the young infant. The risk of infection in infants has however been shown to decrease significantly after the first and the second doses of the vaccine. The World Health Organization (WHO) considers that in general, at least two doses of acellular vaccine are required for protection, and recommends a three-dose primary series,
which is given at 6 weeks, 3 months and 5 months in New Zealand.\textsuperscript{5,6}

To address this immunity gap between birth and the acquisition of vaccine-induced immunity, maternal pertussis immunisation between weeks 28 and 38 of pregnancy is now recommended.\textsuperscript{7} In New Zealand this intervention has been funded since 1 January 2013. The expected effect is protection of the infant's mother against pertussis and passive transfer of protective amounts of maternal antibodies to the infant. A recent study has shown a vaccine efficacy of 91\% for infants younger than 3 months following vaccination during pregnancy.\textsuperscript{8} The safety of the pertussis and tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine in pregnancy has also been demonstrated.\textsuperscript{9,10} An additional strategy to prevent whooping cough in the new-born, ‘cocooning’, involves immunising those living with or caring for infants—particularly the parents and other household contacts who are most often the source of infant infections. These vaccinations are currently recommended but not funded in New Zealand as the degree of their effectiveness is unclear.\textsuperscript{11}

Methods

We analysed New Zealand notification data for pertussis extracted from EpiSurv as of 17 April 2014. EpiSurv is the national database for notifiable disease surveillance. The period of interest for this review was from August 2011 to December 2013, which was the peak activity of the 2011–2014 pertussis epidemic. We included confirmed, probable, and suspect cases as defined in the Ministry of Health's Communicable Disease Control Manual 2012. Hospitalisation information and immunisation status of cases at any time prior to onset of disease were as recorded in EpiSurv (Health professionals use a range of sources to update immunisation status including the NIR, parental recall or Well Child book records. This does not take into account the time needed for the vaccine to elicit an immune response).

Pertussis immunisation coverage data were extracted from the National Immunisation Register (NIR) on 12 August 2014. They included the numbers of eligible children completing 6, 8, 12 and 24 months and their immunisation status for pertussis at these ages. Coverage was the proportion of eligible children who were immunised. Current District Health Board (DHB) of domicile was based on the National Health Index. Progress in the timeliness of immunisation against pertussis was measured using the coverage by three doses of pertussis vaccine of children at 6 and 12 months in the 3-month reporting periods ending March 2011 and December 2013.

Population estimates were based on 2006 population census data. Ethnicity was prioritised. Deprivation was analysed using the NZ Deprivation Index 2006 (NZDep2006).

Figure 1. Number of pertussis notifications and hospitalisations by calendar month-year, January 1998 to September 2014

Note: Includes confirmed, probable, suspect cases and notifications that were still under investigation. Source: ESR, EpiSurv
The population aged less than 1 year was calculated using NZDep2006-specific population proportions in the 0-4 population applied to the known total population in that age group.

We performed descriptive analyses to derive rates, case frequencies and immunisation coverage.

**Results**

Notification data from peak activity of the 2011–2014 pertussis epidemic indicated an average annual rate of notified pertussis in the New Zealand population of 102 per 100,000. A total of 778 cases were reported in infants under 1 year and 386 cases in the age group 12–23 months. The average annual incidence rates were highest in the youngest age groups: 801 per 100,000 under 6 months, 396 in 6 to 7 months, 309 in the 8 to 11 months and 293 in the 12 to 23 months age groups. Three deaths were also notified (2 infants under 1 year and a 3-year-old child).

If we look more specifically at the populations that reached 6, 8, 12 and 24 months of age during the period from August 2011 to December 2013, immunisation coverage for three doses of pertussis vaccine increased from 75% at the age of 6 months to 88% at 8 months, 92% at 12 months and 95% at 24 months. This shows that not enough infants were being immunised early enough during this period.

However, the timeliness of the three-dose immunisation against pertussis has improved during the period between 2011 and 2013. The coverage of children with three doses of the vaccine at the age of 6 months has gradually increased from 67 to 78% between the 3-month reporting periods ending March 2011 and December 2013. Similarly, this coverage at age 12 months has gradually increased from 89 to 94%.

**Table 1. Pertussis vaccine three dose coverage at 6 and 12 months and pertussis incidence rates by deprivation quintile, August 2011–December 2013**

<table>
<thead>
<tr>
<th>NZDep2006</th>
<th>Coverage at 6 months</th>
<th>Annual incidence in infants under 1 year of age per 100,000</th>
<th>Coverage 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>NZDep 1–2</td>
<td>81%</td>
<td>278</td>
<td>93%</td>
</tr>
<tr>
<td>NZDep 3–4</td>
<td>80%</td>
<td>407</td>
<td>93%</td>
</tr>
<tr>
<td>NZDep 5–6</td>
<td>78%</td>
<td>480</td>
<td>93%</td>
</tr>
<tr>
<td>NZDep 7–8</td>
<td>75%</td>
<td>578</td>
<td>92%</td>
</tr>
<tr>
<td>NZDep 9–10</td>
<td>67%</td>
<td>788</td>
<td>90%</td>
</tr>
</tbody>
</table>

Sources: ESR, EpiSurv and Ministry of Health, National Immunisation Register

Deprivation and timeliness of 3-dose pertussis immunisation of infants

Table 1 shows that coverage with the three dose pertussis vaccine in the period August 2011 to December 2013, particularly at 6 months, decreases while pertussis incidence in infants increases with increasing household deprivation. Between the 3 month reporting periods ending in March 2011 and December 2013 the three dose pertussis immunisation coverage at the age of 6 months, while remaining low in deprivation levels 7–8 and 9–10, has improved from 68 and 60% to 77 and 69% respectively. The coverage at 12 months was higher, and increased from 89 and 87% respectively, to 94% for both deprivation levels.

Ethnicity and timeliness of 3-dose pertussis immunisation of infants

Table 2 highlights that ethnicities with higher ‘on-time’ coverage for the three doses of pertussis vaccine had a lower pertussis incidence in infants: Asian infants had the highest coverage at 6 months and the lowest incidence rate. At the opposite end of the range, Māori and Pacific infants had the lowest coverage and the highest incidence. While Pacific infants had better coverage than Māori infants at 6 and 12 months, their pertussis incidence was the highest likely due to other factors, eg environmental, such as overcrowding.
Between the 3 month reporting periods ending in March 2011 and December 2013 the three-dose pertussis immunisation coverage at the age of 6 months in Māori and Pacific infants had improved from 52 and 66% to 64 and 76% respectively. Similarly, coverage at 12 months had increased from 83 and 92% respectively, to 92 and 97%.

Geography and timeliness of 3-dose pertussis immunisation of infants

During the period from August 2011 to December 2013, the three-dose pertussis immunisation coverage at 6 months of age within DHBs varied between 60% in Northland to 84% in Southern. DHBs with the lowest coverage (under 70%) were Northland, Waikato, Bay of Plenty, Tairawhiti, and Whanganui (Figure 2).

Immunisation coverage at age 12 months was higher and ranged from 86% in Northland to 95% in Hutt Valley, with Northland, West Coast, Waikato and Bay of Plenty being the only DHBs with coverage at age 12 months that was <90%.

Pertussis incidence and immunisation status in children under 2 years of age

Figure 3 shows the immunisation status of children with notified pertussis and Figure 4 shows the immunisation status of children hospitalised with pertussis by age for the period 1 August 2011 to 31 December 2013. After a peak at 1 month of age, the number of cases and hospital admission decreases in older age groups. Notified cases aged 1 month or less were too young to be immunised. Fifty-six percent of cases aged 6 months at the time of notification had received three doses of vaccine.
Figure 3 and Figure 4 show that the bulk of cases and hospital admissions are in infants too young to be fully immunised with the primary three-dose immunisation series. However, it is likely that a substantial number of cases and hospital admissions in children aged over 5 months could have been prevented if all vaccine doses had been given on time.12

Conclusions

There has been a substantial improvement in immunisation coverage in New Zealand since 2011. While the protection offered by the acellular vaccine is not optimal, we assume a modified or new vaccine will not be available within the next 5 years.

Currently the uptake of pertussis vaccine during pregnancy in New Zealand is poor, in spite of the recommendations from the CDC7 and strong evidence of its efficacy and safety.8 DHBs, with support from the Ministry of Health, could take steps to improve the situation. This will undoubtedly help reduce disease incidence and severity in infants too young to be immunised.

Further improvements are still possible in coverage at 6 months, particularly in Māori and Pacific populations, as well as in populations living in more deprived households.

In July 2012 the government’s health target was refocused on a 95% coverage at the 8-month milestone age. Between July 2012 and December 2013, the 8 month coverage
progressed from 87 to 91% overall, from 78 to 88% in Māori, from 87 to 91% in Pacific, from 87 to 90% in deprivation deciles 7–8 and from 81 to 90% in deprivation deciles 9–10. Further improvement in the timeliness of immunisation is expected as DHBs work towards achieving the 95% target. DHBs that have difficulties in maintaining or improving their immunisation coverage will require additional support from the Ministry of Health to help them to reach the target.

The priorities before the next epidemic surge of pertussis should be—first of all—pertussis vaccination of all, or most, mothers between weeks 28 and 38 of pregnancy, as well as immunisation coverage at and above 95% for the three doses of pertussis-containing vaccine at age 6 months. In 2015, the Ministry will be leading a pertussis policy workshop with PHARMAC and The Immunisation Advisory Centre support to build on existing programme strengths and review internal strategies for reducing whooping cough.

Competing interests: Nil

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