

Pertussis control strategies: A consistent approach for New Zealand

Synopsis of Ministry of Health Workshop, April 2015

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ABSTRACT

In the past decade, pertussis has made a global resurgence, driving reconsideration of national immunisation schedules and vaccine usage. A workshop held by the Ministry of Health in 2015 discussed New Zealand's pertussis disease control strategies. Data were presented from current research into vaccine safety during pregnancy and the effectiveness of the immunisation schedule in preventing pertussis throughout childhood. The greatest burden of disease and mortality remains in infants under 1 year of age, especially infants too young to be immunised, those of Māori and Pacific ethnicity, and those living in deprivation. The workshop considered strategies including the timing of the scheduled vaccines, maternal immunisation, improving immunisation coverage, vaccination timeliness and service delivery to reduce inequalities and overall disease burden. It concluded that the current infant schedule appears to be working well to protect older infants from severe pertussis. Significant gains for reducing severe disease in vulnerable young infants could be made with improvements in maternal vaccine uptake. Other strategic directions include attention to schedule adherence and timeliness of vaccine delivery, and more effective communication approaches for healthcare professionals and the public.

Pertussis is a highly contagious bacterial respiratory disease characterised by a prolonged paroxysmal cough. A major pertussis epidemic in New Zealand, peaking from August 2011 to December 2013, resulted in the hospitalisation of hundreds of infants aged under 1 year, and the death of three infants under 6 weeks of age—too young to have started the primary immunisation course. A resurgence in pertussis has also been seen internationally, especially in countries using the acellular pertussis vaccines.

The first pertussis vaccines contained whole inactivated *Bordetella pertussis*. Although effective, these whole-cell pertussis (wP) vaccines are more reactogenic. In 2000, the less reactogenic acellular pertussis (aP) vaccine replaced the wP vaccine on the New Zealand National Immunisation Schedule (the Schedule). The currently used New Zealand vaccine contains three pertussis antigens with pivotal roles in pertussis immunity. However, aP vaccines appear not to be as effective, nor produce as long-lived

immunity, as the wP vaccines, and may be associated with the worldwide resurgence of pertussis.^{1,2}

The elimination of pertussis by vaccination is not currently possible, because pertussis is widespread in the community, aP vaccine immunity is not long-lasting, and transmission can occur even with vaccinated individuals. Therefore, immunisation strategies are primarily focused on reducing severe pertussis in infants. In New Zealand, three doses of vaccine are given for a primary course in infancy at 6 weeks, 3 months and 5 months, with boosters at 4 and 11 years of age. Whether this vaccine schedule provides adequate protection, or how rapidly immunity wanes, is unknown.

In 2015, the Ministry of Health (MoH) held a workshop to bring together expertise and experiences to discuss pertussis disease control strategies and a consistent approach for New Zealand. The aim was to minimise the impact of future pertussis outbreaks on those most vulnerable.

Following presentation of current international and national research, key areas were discussed: the effectiveness and timing of the Schedule; the use and delivery of maternal pertussis immunisation to protect infants; improving communication around pertussis immunisation for healthcare professionals and the public; improving immunisation coverage and service delivery to reduce inequalities; and evaluation of data collection, disease reporting and surveillance.

Pertussis disease burden and prevention strategies in New Zealand and internationally

The burden of pertussis is a global issue. Infants too young to have received the primary course are at highest risk of severe disease, hospitalisation, and death. Mild disease, especially in adolescents and adults, is often under reported and/or undiagnosed. Although the vaccines are effective at preventing pertussis disease, including the cough, a study in nonhuman primates has shown that acellular pertussis vaccine did not protect them from acquiring the infection and readily transmitting *Bordetella pertussis* to contacts.³

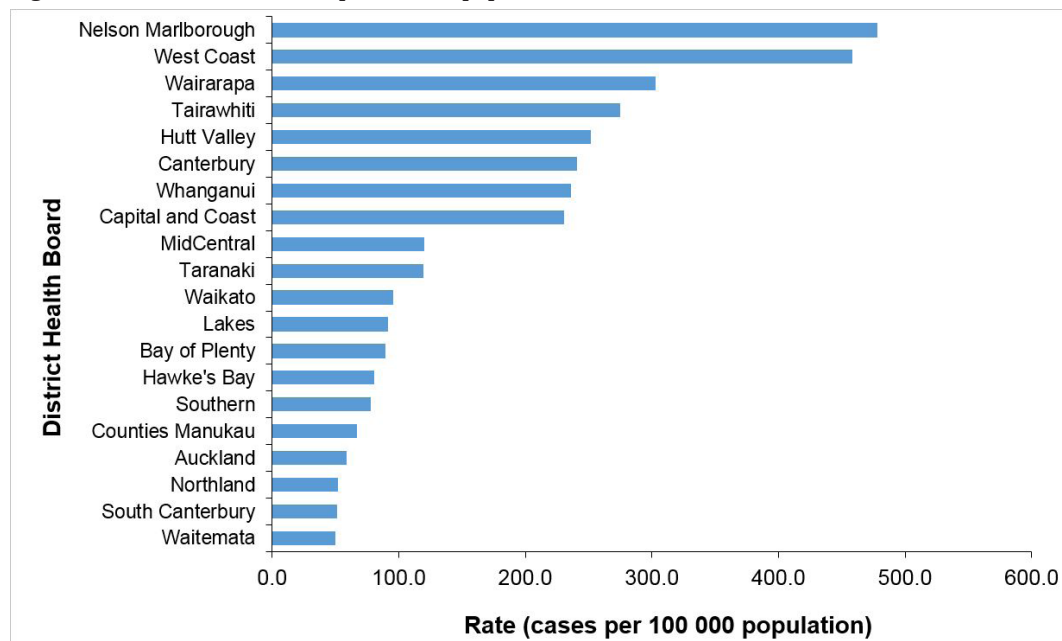
In New Zealand, pertussis epidemics occur every 3 to 5 years. Disease notifications showed that between 2000 and 2014, nine infants under 8 weeks of age and one unvaccinated 3-year-old with underlying chronic lung disease died as a result of pertussis. During the height of the most recent New Zealand epidemic, almost half of all the infant cases notified, aged under 1 year, were hospitalised with pertussis (eg, 182/414 infant cases were hospitalised in 2012). This proportion is approximately ten times greater than across all age groups and demonstrates how vulnerable infants are severely affected. The 70 years or older age group were also at increased risk from severe disease, once they become sick, with about 10% of the notified cases hospitalised. Pacific and Māori pertussis hospitalisations rates were much higher than New Zealand Europeans, eg, three to four times higher in 2012 (Prioritised ethnicity was used in these data analyses).

National Immunisation Register (NIR) data showed that the overall, three-dose coverage at 6 months of age remained under 80% during the period August 2011–December 2013. Ethnicity and high deprivation (NZDep 9–10, in particular) were identified as risk factors for low immunisation coverage. Coverage at 6 months of age improved from 67% in March 2011, to 78% in December 2013, and from 89% to 94% at 12 months of age. Despite good improvements, disparities remain at 6 months of age, particularly for Māori infants, infants living in high deprivation, and to a lesser degree, Pacific infants.

Pertussis-containing vaccines provide a good level of control for severe pertussis, even when delivered through a variety of immunisation schedules worldwide. Adherence to the Schedule and timeliness of delivery of the primary series is most important to prevent severe pertussis.⁴ Although immunisation has reduced the burden of pertussis deaths and severe disease in infants overall, a cohort of infants less than 6 months of age—too young to have completed the primary series—remains susceptible. Various strategies are being evaluated worldwide to prevent severe pertussis in the youngest infants.

The World Health Organization recommended in July 2014 that countries using aP vaccines should consider a booster dose sometime between the ages of 1 to 6 years, preferably in the second year of life, at least 6 months after the last dose of the primary course.^{5,6} Currently, the only high income countries not to include a toddler booster in their schedules are Australia, England and Wales (E/W), and New Zealand, which have had similar rates of reported pertussis deaths in children aged under 1 year over the last decade (average deaths per million per decade [95% CI]: Australia 4.2 [2.2–7.4], E/W 7.4 [5.5–9.7], New Zealand 8.2 [2.7–19.2]).

One key risk factor for pertussis is large family size, with parents or siblings more likely to transmit disease to infants.⁷ The degree to which vaccination reduces transmission is not clear; however, the risk of severe pertussis for infants may be halved when both parents are vaccinated more than 4 weeks prior to disease onset.⁸ ‘Cocooning’ of infants by giving vaccine

Figure 1: Pertussis notifications per 100,000 population in 2012 (ESR)¹²

booster doses to close contacts relies on high coverage, which is difficult to achieve. Toddlers are a likely source of sibling transmission and may be justification for a toddler booster dose.

In general, cocooning strategies have not been shown to work on a population base, and are being superseded by antenatal immunisation. Transplacental transfer of high levels of maternal antibodies help to protect the infant from birth. Maternal immunisation has been shown to be 91% (95% CI 84–95%) effective in preventing pertussis in infants up to 3 months of age.⁹ Since antibody levels decline rapidly between pregnancies, revaccination is required for each pregnancy. Historically, a lack of data on vaccine safety in pregnancy has hindered uptake. However, data are now accumulating: a large study in the UK shows good evidence that acellular pertussis-containing vaccines are safe when given in pregnancy,¹⁰ and as discussed below, New Zealand data support this safety profile.

Immunisation of pregnant women at 28–38 weeks gestation was introduced in 2013 in New Zealand as a control strategy during the epidemic to provide passive antibody protection to infants too young to be fully vaccinated; limited data suggest that the uptake is very low. The 'during epidemic' criteria was removed in August 2015.

Neonatal vaccination is a potential alternative to immunising mothers during

pregnancy. Baboon infants have been shown to be protected against severe pertussis by either maternal or neonatal vaccine.³ A pilot clinical study conducted in Australia demonstrated significantly higher pertussis antibody levels by 2 months of age in infants who receive aP vaccine at birth and 1 month, which persisted to 6 months of age.¹¹ Further studies are underway.

Outbreak control— lessons learnt in New Zealand

During the recent pertussis epidemic in New Zealand, control strategies and improvements in immunisation delivery were necessary. Various lessons were learnt across the country as illustrated by both Hawkes Bay and Nelson-Marlborough District Health Boards (DHBs). Prior to the epidemic, Hawkes Bay DHB was proactive in maintaining high coverage for childhood immunisations. Although approximately 50% of the birth cohort in the district were Māori or from areas of high deprivation—and therefore deemed to be at high risk—during the epidemic fewer cases of pertussis were notified compared to other regions, as shown in Figure 1 for 2012.¹²

In this district, education of parents, childcare and healthcare providers is seen as an important priority. As of December 2014, coverage by 8 months of age was 96%

in Māori, 100% for Pacific people and 98% for those within the most deprived quintile as measure by the New Zealand deprivation score, demonstrating closure of many traditional equity gaps. Antenatal vaccination clinics are run weekly to immunise pregnant women and to promote immunisation of infants: anecdotally, Hawkes Bay DHB has found that mothers who are immunised during pregnancy commonly immunise their infants on time.

In contrast, in the Nelson-Marlborough DHB an outbreak response plan was implemented to manage the high number of pertussis cases during the epidemic. In predominantly rural areas, pertussis spread quickly through schools and preschools to unimmunised children. Further improvements in vaccine education, coverage and timeliness were recognised as necessary. Revised measures were implemented to improve disease control, to reduce transmission and to improve surveillance and communication. These included increased collaborative work cross-sectoral and within the health sector to improve vaccination uptake. A resource pack for pregnant women was developed and sent to lead maternity carers, and local media campaigns recommended maternal immunisation. Special attention to disease notification was also given in this DHB which may, in part, have accounted for the high number of notifications.

Pertussis vaccine research in New Zealand

Duration of vaccine effectiveness provided by current Schedule

International concerns around possible early waning in immunity following a primary course of acellular pertussis vaccine raised the issue of whether New Zealand should be considering an earlier booster dose than the current 4-year-old dose.¹³ A case-control study, *Effectiveness of Pertussis Immunisation in Children* (EPIC), commissioned by the MoH and Health Research Council, was conducted in 2015 by linking existing data sets to evaluate the effectiveness and duration of protection provided by the Schedule against pertussis.

Two age groups, children aged 6 weeks–4 years and aged 4–8 years, were evaluated.

Interim results showed no evidence of waning immunity prior to the children's fourth birthdays following the three-dose primary series, nor following the primary series plus a booster up to 7 years of age.

In conclusion, the EPIC study data provides evidence that the current Schedule protects against severe pertussis in vaccinated infants and young children. However, it is possible that there may be a small group of children at higher risk from pertussis that would not be identified by a study of this nature for whom further booster doses could be considered. This warrants further study of existing data to assess the risk in a New Zealand context.

Research on attitudes and knowledge in pregnancy

As previously discussed, infants too young to be immunised are at highest risk from severe pertussis infection. Immunisation during pregnancy has been shown in the UK to be effective in reducing the severity of pertussis in these very young infants.⁸ However, uptake of pertussis vaccine in pregnancy appears to be poor in New Zealand.

A survey was sent to all birth notifications between June and October 2013 in Canterbury DHB; this was the first DHB to offer funded pertussis vaccine during late pregnancy. Findings showed that, in general, those mothers who accepted the vaccine did so to protect their baby, followed health professional advice, and/or had an awareness of the severity of pertussis. Those who did not receive a vaccination were either unaware of the vaccine, were not encouraged or were discouraged by health providers (especially general practitioners), or had safety concerns about vaccination in pregnancy.¹⁴ This survey was conducted as part of a larger study investigating the safety of vaccines in pregnancy.¹⁵

An audience research study in 2015, commissioned by the MoH, investigated the barriers to immunisation in pregnancy across a range of DHBs, ethnic, and socio-economic groups. To improve uptake of antenatal vaccine, the study found that women need positive assurance from their

lead maternity carers that the vaccine will protect their baby. Specifically, that it is safe for the unborn baby when given in pregnancy, and that it is free. As observed in Hawkes Bay DHB, this study also found that vaccinated mothers were more likely to immunise their infants on time.¹⁶

Vaccine safety

As shown by audience research, confidence in vaccine safety for the unborn child is a major factor for receipt of pertussis vaccine in pregnant women. Until recently, historically there have been few studies that have actively investigated the safety of pertussis vaccines given during pregnancy, although there are no biologically plausible reasons why or evidence that inactivated vaccines would pose a risk to the fetus, and passive surveillance systems support the safety in pregnancy. Pregnancy itself is high risk and adverse outcomes frequently occur. Combined data from two New Zealand studies investigating the safety of pertussis vaccination given in pregnancy show that no serious adverse events were causally associated with the vaccine in 793 pregnant women. Minor local reactions were common, however systemic events, including headache, fatigue and nausea, were uncommon, occurring in fewer than 7% of vaccinees.¹⁷ These results support a large observational study of the infant outcomes following exposure to Tdap vaccine during pregnancy.¹⁵

Workshop discussions

Following reflection of the presented data, the workshop provided suggestions for improvement, and highlighted areas in need of further research in relation to the effectiveness of the current pertussis control strategies and surveillance, the Schedule, and inequities in pertussis disease burden. The areas discussed, recommendations and comments are summarised in Table 1.

Conclusions

The workshop concluded that New Zealand's current National Immunisation Schedule is working well to prevent severe pertussis in older infancy and childhood. Regular reviews of the schedule will be conducted by PHARMAC and the Ministry of

Health. The workshop provided an insight into the areas of pertussis disease control and immunisation that require further discussion or improvements.

Adherence to the immunisation schedule is required to ensure that infants aged under 1 year are fully immunised on time. However, the burden of severe disease and mortality is primarily in infants younger than 6 months of age—too young to have been fully immunised with the primary course—particularly, those of Māori and Pacific ethnicity, and those living in deprivation.

More focus on communication and education of the health sector and the public is needed to promote immunisation—especially for those at greatest risk of severe pertussis—to improve coverage, adherence to the Schedule, and timeliness of delivery for young infants; and to address any safety concerns.

Alongside timely immunisation with the primary schedule, vaccination during pregnancy is an important strategy to protect young infants. Improvements in coverage and access to vaccines for pregnant women are required. Improved communication, starting in early pregnancy, is recommended to increase awareness of the vaccines availability and to address any safety concerns, taking into consideration the needs of different ethnic and socio-economic groups. The Ministry of Health are actively working to improve uptake of Boostrix® during pregnancy and working towards changes to the National Immunisation Register (NIR) to enable capture immunisation events during pregnancy.

Currently in New Zealand, an additional pertussis booster in the second year of life does not appear to be necessary. However, further research is needed to determine if a booster may benefit children at high risk, such as those with chronic lung disease or other chronic health issues, as provided for influenza and pneumococcal disease.

Although the rates of pertussis notifications are low in the elderly, which may be due to lack of awareness in this age group, there is an increased risk of hospitalisation amongst the cases. Further studies are also needed to investigate the burden of pertussis in the elderly and to assess whether a funded

Table 1: Pertussis workshop feedback.

Area of discussion		Recommendations	Further comments
Immunisation schedule timing	Current Schedule	Retain current Schedule	Too frequent Schedule changes cause confusion and possible declines in coverage.
	Schedule reviews	Set regular review periods	PHARMAC and the MoH to work with PHARMAC's PTAC Immunisation Subcommittee to regularly review the Schedule.
	Maternal immunisation	Strategy to be continued	Consider giving Tdap concurrently with the influenza vaccine to protect infants and improve vaccine uptake.
	Neonatal dose	Awaiting further research	May be beneficial if the mother has not been vaccinated during pregnancy.
	Toddler dose	Currently not required in New Zealand	There may be a group of infants at higher risk than others from pertussis who may benefit from a pertussis dose in their second year of life - further research is needed to assess the risk in a New Zealand context.
	Adolescent booster	Vaccination effectiveness in New Zealand setting currently unknown	Consider giving Tdap concurrently with HPV vaccine. Adolescents may be transmitting disease to family, particularly in large families.
	Occupational immunisations	Current international advice for 10 yearly boosters still holds	Optimal frequency of booster to prevent pertussis transmission is unclear.
Antenatal pertussis immunisation and communication	Maternal immunisation programme	Implement a maternal immunisation programme	MoH to develop systems and processes to improve maternal immunisation uptake
	Communication about immunisation early in pregnancy	To improve vaccine uptake	Pregnant women need to be informed that they can be immunised against pertussis as soon as pregnancy is confirmed and during pregnancy. Address any safety concerns the pregnant women may have about maternal immunisation Pharmacists could promote immunisation when folic acid vitamin supplements and pregnancy tests are purchased Consider different information needs for each pregnancy and for different socioeconomic and ethnic groups.
	Health professional education	To encourage maternal vaccination advice and recommendations by the LMC/midwife and GP	Dispel myths on vaccine safety, eg antibody not vaccine is passed to baby Will enable positive discussions with decliners by having 'courageous conversations' Severity of pertussis for infants – eg, use of personal stories Add vaccination precalls in to the practice management system at first pregnancy appointment with a general practice to prompt when vaccines are due.
Improving coverage and service delivery	Inequalities remain	Improve vaccine uptake for groups at greatest risk from pertussis	Ensuring the Schedule vaccines are given on time Increase awareness and education within community and health professionals Reduce barriers to accessible information/advice
	Improve trust in vaccines	To increase vaccine uptake and respond to misinformation and trends	Strong emphasis on health professional information and education as the most important strategy Monitor and use of social media to provide accurate information

Table 1 (cont): Pertussis workshop feedback.

Area of discussion		Recommendations	Further comments
Data collection, surveillance and reporting	Data collection	To improve quality and scope	NIR improvements needed to address: <ul style="list-style-type: none"> • NIR accessibility for all immunisation providers • NIR flexibility and scope (eg to record pregnancy immunisations) Improve data collection on cases (eg practice management system interface, emergency department surveillance) Consistency in notifications of cases
	Data usage	To be improved	More systematic use of and improved links between existing datasets Use data to inform public health strategies and assess immunisation effectiveness

Abbreviations: PHARMAC – Pharmaceutical Management Agency; PTAC – Pharmacology and Therapeutics Advisory Committee; MoH – Ministry of Health; New Zealand – New Zealand; Tdap – Tetanus, reduced antigen diphtheria and acellular pertussis vaccine; HPV – human papilloma virus; LMC – lead maternity carer; GP – general practitioner; NIR – National Immunisation Register

Tdap booster at 65 years of age may help to reduce this burden. Australian research underway around grandparent cocooning doses may provide an insight into the potential of such a booster.

New Zealand has more readily available sources of data and data linking than many other countries. The existing data could be better used to describe pertussis epidemiology and immunisation schedule effectiveness to identify those at greatest risk from pertussis. Using data from practice management systems and emergency departments may provide useful additional information about pertussis cases and help

improving consistency of notifications. Planned improvements to the NIR will provide better quality data to evaluate vaccine coverage and effectiveness. High quality surveillance and coverage data are required to make appropriate disease control decisions, to monitor and close ethnic and socioeconomic inequity gaps and to reduce the impact of pertussis outbreaks in the future.

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Competing interests:

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