



Pertussis control: where to now?

Improving protection against pertussis requires sorting the facts from the artefacts

Pertussis is a disease of significant morbidity and, in infants, mortality. Regrettably, even though there is greater than 20-fold reduction in pertussis burden with immunisation,¹ it persists globally as a significant public health problem. For more than two decades, Australia has had the highest reported rates of pertussis in the world.² In the 1990s, this was driven by the introduction of mandatory reporting by laboratories of positive test results for vaccine-preventable diseases to the National Notifiable Diseases Surveillance System and extensive use of serological tests for diagnosis, primarily in adults.³ Unlike many other countries, all positive test results in Australia are included in national data. Also, testing for pertussis by polymerase chain reaction (PCR) has qualified for reimbursement since 2008, after which a sevenfold increase in testing of children in general practice was documented.⁴ Pertussis epidemics occurred sequentially across Australia from 2008 to 2012 and, unlike previous epidemics, the highest notification rates were for children under 10 years of age. This raises the question of whether Australia's "pertussis problem" is related to vaccines with poor effectiveness or is an artefact of testing.

Observational methods are used to measure vaccine effectiveness (VE) (also known as "field efficacy"). The screening method enables estimation of VE if the vaccination status of patients with a case of the disease and population vaccine coverage are known — the more effective the vaccine, the lower the likelihood of patients with a

case of the disease having been vaccinated compared with the source population.⁵ The screening method performs best when about 50% of the population is vaccinated. When vaccine coverage is over 90%, estimates of VE change substantially with small changes in population coverage estimates. In this issue of the Journal, Sheridan and colleagues use the screening method to estimate VE for acellular pertussis vaccine in Queensland children during an epidemic in 2009 and 2010.⁶ They found that VE for three doses in children aged from 1 to <4 years was over 80%. However, similar to studies in the United States,^{7,8} VE fell significantly and progressively in children over 5 years of age, whether they had received four or five doses. It was previously reported that among Queensland children born in 1998, those who had received one or more doses of whole-cell pertussis vaccine were significantly better protected than those who had received only acellular vaccine, especially after 6 years of age.⁹ A national study, which included Queensland data from 2009, took a different approach — cases were individually matched by birth date to children on the Australian Childhood Immunisation Register and were limited to children younger than 4 years.¹⁰ Similar VE estimates were obtained for the first 2 years of life, but, in contrast to findings from the Queensland study, there was a significant and progressive fall in VE between ages 2 years and 4 years (the latter being the age at which children were eligible for the fourth dose).

Peter B McIntyre
PhD, FRACP, FAFPHM,
Director¹

Terence M Nolan
PhD, FRACP, FAFPHM,
Head²

¹ National Centre for
Immunisation Research
and Surveillance,
Sydney Children's
Hospitals Network,
Sydney, NSW.

² School of Population
and Global Health,
University of Melbourne,
Melbourne, VIC.

t.nolan@
unimelb.edu.au

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Importantly, Sheridan et al were also able to evaluate testing patterns by age, showing that the overall number of PCR tests increased in the second year of the Queensland epidemic.⁶ Also, in children aged over 5 years, although PCR tests were less commonly performed, the results were more commonly positive.⁶ This is probably due to older children with cough being less likely to present to general practice and less likely to be tested, suggesting that notification rates of pertussis would have been even higher if more testing had been done. Disease severity is also an important consideration: assessing the disease burden from pertussis cases in older children is valuable, and VE is expected to be lower for less severe illness.⁵ Apart from the requirement for hospitalisation, against which VE was high for children younger than 1 year³ and 1–4 years,¹⁰ few data on severity are available. In a recent New South Wales study using linked hospitalisation and pertussis notification data, it was found that only 2% of children over 5 years who had pertussis were hospitalised, but 8% had been taken to an emergency department.¹¹

What conclusions can we draw from these studies? First, the current acellular vaccines are highly effective in preventing severe pertussis, especially in the first 2 years of life, but effectiveness progressively wanes from 2 years after the last dose. Such rapid waning was not expected when the decision to forego the 18-month booster in favour of a booster for adolescents was made in 2003. This decision was based on favourable results from modelling this change using the only available data at the time¹² — data which suggested that three doses provided protection up to 7 years of age,¹³ which contrasts with more recent findings. Australian data showing low levels of population antibody to pertussis toxin preceding the recent epidemic support the idea that the schedule change had a negative impact.¹⁴ Second, high levels of laboratory testing inflated Australian case numbers disproportionately to other countries, through identifying more ambulatory cases in children and adults. Third, pertussis vaccine coverage has increased dramatically in Australia since the epidemic in the late 1990s, with better acceptance by parents and doctors of the acellular vaccines compared with more reactogenic whole-cell vaccines. Notably, the national epidemic from 2008 to 2012 was associated with fewer deaths than the late 1990s epidemic, despite much higher numbers of cases.

Where does the future lie for pertussis vaccines in terms of improving disease control, especially death and severe morbidity? A vaccine that effectively reduces transmission and disease is an important objective for herd immunity. In this regard, there is promise from

research on live attenuated vaccines,¹⁵ and the potential for acellular vaccines with improved adjuvants and less reactogenic whole-cell vaccines, but all are some years away. Immunising mothers during the last 8 weeks of pregnancy with adult-formulated acellular pertussis vaccine could prevent early infant mortality and morbidity. Reinstalling the 18-month booster in the National Immunisation Program could improve control in early childhood, if cost-effectiveness criteria can be met. For all vaccines on the National Immunisation Program, ongoing monitoring of VE is crucial and greater use of Australia's high-quality data systems can support this, as recommended in the National Immunisation Strategy.¹⁶

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