Vaccination to prevent otitis media in New Zealand

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Otitis media (OM) is the most common illness requiring medical consultation in children less than 3 years of age.1 On 1 July 2011 the New Zealand Immunisation schedule changed to include a new generation pneumococcal conjugate vaccine with the potential to significantly reduce the burden of disease due to OM. We outline the recent changes and their implications for New Zealand children.

Otitis media can generally be thought of as a spectrum of disease, ranging from acute otitis media (AOM) through to chronic otitis media with effusion (OME). There are no systematic epidemiological studies looking at the burden of otitis media in New Zealand. Estimates of the incidence of AOM from other developed countries suggest an incidence of between 0.125 and 1.2 episodes per child year.2 In this setting, between 10 and 20% of children experience at least 3 episodes of OM in the first year of life. A high proportion of these children will have asymptomatic OME that lasts for 3 months or more.2

In New Zealand, approximately 828/100,000 children aged less than two years are admitted each year for medical or surgical admissions related to OM, estimated from 2006 -7 hospitalisation data.3 Incidence rates of medically managed OM in children <2 years of age were highest in Maori and Pacific Island children, suggesting this group is likely to have the highest incidence rates of AOM as well. The overall costs of otitis media management in hospital were approximately 45% of the total costs for all invasive pneumococcal disease, much of this relating to surgical management of OM.3

_Streptococcus pneumoniae_ (S.pn), non-typeable _Haemophilus influenzae_ (NTHi) and _Moraxella catarrhalis_ are established as the main pathogens associated with AOM and recurrences.4 Unfortunately no data on the bacterial aetiology of AOM are available in New Zealand. However, the microbiology of OME has been prospectively evaluated in an Auckland study in 1995.5 This demonstrated bacterial pathogens in 36% of 105 middle ear aspirates with _H. influenzae, M. catarrhalis_ and _S.pn_ accounting for 35%, 27% and 18% of isolates respectively.

The introduction of a 7-valent conjugate pneumococcal vaccine (PCV7; Prevenar) to infant vaccination schedules in many developed countries has had a significant impact on the incidence rates of invasive pneumococcal disease (IPD). In most surveillance systems IPD is defined as an infection occurring at a normally sterile site, and does not include OM. The introduction of PCV7 to the NZ immunisation schedule in 2008 also has had significant impact on the rates of IPD. For children <2 years of age the annual incidence rates for IPD fell sharply from 104.6/100,000 in 2006 to 46.4/100,000 in 2009.6 This mirrors closely the effects seen in other countries around the world.7

Although IPD has been impacted by PCV7, internationally the overall impact on OM has been less, despite _S.pn_ being identified as a major pathogen in this disease. In
Finland, a 57% reduction in AOM episodes due to pneumococcal serotypes contained in PCV7, yet only a 6% reduction (95% confidence interval -4 to 16%) in the overall number of episodes of AOM(8). Similarly, in the Kaiser Permanante study in the USA Fireman et al found that PCV7 reduced visits to primary care physicians for otitis media by 7.8%.9

Following introduction of PCV7 some studies have demonstrated a shift in the proportions of causative pathogens of OM. Eskola et al found a decrease in episodes of AOM in Finland due to vaccine serotypes of S.pn and an increase the proportion due to non-vaccine S.pn serotypes in a Phase III clinical trial of a 7-valent pneumococcal conjugate vaccine.8 At the same time they noted an increase in the proportion of AOM episodes due to NTHi. Other studies have seen a similar changes in the proportions of bacteria isolated from the middle ear and the nasopharynx of children with AOM, with NTHi becoming a more frequently isolated pathogen and replacement with non conjugate vaccine S.pn serotypes.10–12

Therefore it may appear that the modest reductions in incidence rates of OM since introduction of PCV7 can in part be explained by increases in non-vaccine related pneumococcal serotypes causing disease and increasing prevalence of disease due to other pathogens. These changes have significant implications for the treatment of AOM as NTHi and M. catarrhalis have higher rates of resistance to commonly used antibiotics.

Yet as AOM is an extremely common infection even a small reduction in disease by PCV7 has meant many thousands of cases may have been prevented. Despite this a Cochrane review in 2009 concluded that this effect was insufficient to recommend universal pneumococcal vaccination with PCV7 purely to prevent otitis media.13

In New Zealand the Ministry of Health was presented with two options for replacing PCV7 with its upcoming removal from the global market: a 13-valent pneumococcal conjugate vaccine (PCV13; Prevenar 13) and a 10-valent pneumococcal conjugate vaccine (PHiD-CV or PCV10; Synflorix). The decision was made to use PHiD-CV for the routine immunisation of infants and to fund PCV13 only for children under 5 years of age at highest risk of IPD.14

Therefore, the vast majority of infants in New Zealand will from now receive PHiD-CV as part of their routine immunisations. This vaccine provides protection against all the pneumococcal serotypes included in PCV7 and an additional 3 serotypes that commonly cause IPD.

In addition, PHiD-CV has the potential benefit over other pneumococcal conjugate vaccines of reducing infections caused by H. influenzae strains other than H. influenzae type B. This is particularly relevant for otitis media where NTHi is a leading cause of infection. This additional property is due to the presence of protein D, a cell-surface lipoprotein found on all H. influenzae, in PHiD-CV.15

A RCT of an 11-valent PHiD-CV vaccine (the prototype for the 10-valent vaccine) demonstrated a 35.3% vaccine efficacy for AOM caused by NTHi and a 57.6% efficacy for any episode of AOM.16 At the same time it was shown to produce a significant (42.6%) reduction in nasopharyngeal carriage of NTHi in children under 2 years of age.17 However, further post-licensure studies will be required before we can draw firm conclusions about the impact of PHiD-CV on the incidence rates of OM.
One potential drawback of the choice of PHiD-CV for the national immunisation schedule is that fewer pneumococcal serotypes are covered in comparison to PCV13. Other countries have seen the emergence of IPD due to serotypes 19A and 3 which are contained in PCV13 but not PHiD-CV, and it is possible a similar pattern could emerge in New Zealand.

The introduction of PHiD-CV has increased the number of pneumococcal serotypes covered by the New Zealand primary infant immunisation schedule and has the advantage that it may provide increased protection against OM because of the anticipated impact on \textit{NTHi}. The flipside of the coin is lessened \textit{Spn} serotype coverage with potentially emergent serotypes 19A and 3.

We wait with great interest to see the effects the new immunisation schedule will have on both IPD and OM in this country.

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\textbf{References:}