

# Expert Forum

## CURRENT PRIORITIES IN IMMUNISATION 2014

PSNZ 66th Annual Scientific Meeting and PSNZ Infectious Diseases and Immunisation Special Interest Group in conjunction with IMAC

Making Education Easy

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#### Abbreviations used in this review:

- ALT** = alanine transaminase  
**BCG** = Bacillus Calmette-Guérin  
**HBIG** = hepatitis B immune globulin  
**HBsAg** = hepatitis B surface antigen  
**HBV** = hepatitis B virus  
**HPV** = human papillomavirus  
**JCVI** = Joint Committee on Vaccination and Immunisation  
**MenB** = meningococcal group B  
**MenC** = meningococcal group C  
**MMR** = measles, mumps, rubella  
**OMV** = outer membrane vesicles  
**SSI** = Serum Staten Institute  
**TB** = tuberculosis

### ABOUT RESEARCH REVIEW

Research Review is an independent medical publishing organisation producing electronic publications in a wide variety of specialist areas. Research Review publications are intended for New Zealand medical professionals.

### ABOUT EXPERT FORUMS

Expert Forum publications are designed to encapsulate the essence of a local meeting of health professionals who have a keen interest in a condition or disease state. These meetings are typically a day in duration, and will include presentations of local research and discussion of guidelines and management strategies.

Even for local events it is not always possible for everyone with a similar therapeutic interest to attend. Expert Forum publications capture what was said and allows it to be made available to a wider audience through the Research Review membership or through physical distribution.

This publication is a summary of the satellite meeting of The Paediatric Society of New Zealand's (PSNZ) 66th Annual Scientific Meeting held in Napier by the PSNZ Infectious Diseases and Immunisation Special Interest Group in partnership with the Immunisation Advisory Centre (IMAC) on 18 November.

### IMMUNISATION IN NEW ZEALAND 2014

Associate Professor Nikki Turner (IMAC, University of Auckland)

New Zealand has historically had very poor paediatric immunisation coverage. However, particularly within the last decade, there has been a considerable improvement in coverage, timeliness of delivery and reduction of equity gaps. There still remain important areas of concern for the New Zealand programme which Dr Turner and colleagues discussed at this meeting: vaccine-preventable diseases that are still not well controlled such as pertussis and measles, and suboptimal immunisation coverage including in pregnancy, older children, adolescents and adults. The future of New Zealand's immunisation programme will require attention both to improving immunisation coverage for all ages, increased focus on particular groups and consideration of important new international vaccines and their possible role in our immunisation schedule.

### ROTAVIRUS – THE AUSTRALIAN EXPERIENCE

Professor Peter McIntyre (National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases, Westmead)

The rotavirus vaccines Rotarix® and Rotateq® were introduced into the Australian National Immunisation Program in mid-2007 with uptake evident in about half the eligible birth cohort. Substantial reductions in disease rates were demonstrated, as measured by disease burden pre- and post-vaccination and estimates of vaccine effectiveness. Recognition of potential vaccine-attributable increases in intussusception risk from hospital-based surveillance led to a national analysis of risks and benefits. Benefits include direct and herd reductions in hospital admissions due to gastroenteritis and febrile seizures, while risk estimates must take in to account age-related severity of intussusception. New Zealand is well positioned to put in place timely, high quality risk-benefit assessment of rotavirus vaccines with availability of national data sets and laboratory surveillance data and the ability to link to the National Immunisation Register even more seamlessly than seen in Australia.

### HEPATITIS B IN NEW ZEALAND – PREVENTION AND MANAGEMENT IN CHILDHOOD

Dr Chris Moyes (Bay of Plenty DHB)

Hepatitis B is endemic in New Zealand especially in Maori, Pacific and Asian communities and prevention is based primarily on effective vaccination. Immunisation can be passive – hepatitis B immune globulin (HBIG) within 48 hours exposure for short term protection followed by active vaccination, or active – hepatitis B surface antigen (HBsAg) produced by recombinant gene technology with added adjuvant. Vaccination must be intramuscular and can be as short as 2 weeks between injections or as long as up to a year apart. As far as we know, vaccination on a three-dose schedule gives effective immunity long after the loss of anti-HBsAg.<sup>1</sup>

Perinatal transmission of hepatitis B virus (HBV) is a special case. Infants of carrier mothers need to receive HBIG within 48 hours of birth followed by usual vaccination. Such an approach has efficacy of 91%–94% versus usual vaccination alone efficacy of 70%–85%. Most failures occur in very high titre mothers, i.e. HBVDNA >20 million IU/mL. This can be lessened by use of antiviral agents such as tenofovir or lamivudine in pregnancy.

When should hepatitis B carriers be treated? An HBeAg positive child with sustained raised alanine transaminase (ALT) should be considered for treatment – but one should be conservative and wait and see in the majority of cases. When Dr Moyes followed up such children prior to the introduction of modern treatments, two thirds had spontaneous resolution of raised ALT in <2 years and their histology normalised. HBeAg negative children with sustained raised ALT and high HBVDNA and cirrhotics should also be treated, however these are largely adult problems. The goal of treatment in HBeAg positive children is to achieve HBeAg seroconversion, normalise ALT and reduce HBVDNA to low levels. Treatment does not normally lead to HBsAg loss. Both pegylated interferon and entecavir are funded for treatment of chronic HBV infection in New Zealand. Compared with earlier drugs, modern drugs such as entecavir and tenofovir are more potent and are associated with less resistance to monotherapy.

### IMMUNISATION OF SPECIAL GROUPS

Dr Elizabeth Wilson (Starship Children's Hospital)

This presentation summarised Chapter 4 in the Immunisation Handbook 2014, where tables and recommended schedules can be found for the following groups.

### Infants with special immunisation considerations

There are immunisation issues to be aware of in a number of special groups including:

- Children with congenital heart disease; may have associated asplenia or immune deficiency syndromes such as DiGeorge. Children with complex single ventricle or shunt-dependent lesions (e.g., post-Norwood procedure) may have an increased risk of deterioration or collapse following immunisation. Infants with congenital biliary or renal conditions

may be considered in future for solid organ transplant. An accelerated immunisation schedule is recommended for these infants, with the aim of maximising protection against vaccine-preventable diseases and to deliver live viral vaccines prior to transplantation and immune suppression.

- Diagnosis of immune deficiency is often not made before children start immunisations. However, no parenteral live virus vaccines are given on the schedule in the first year of life. Rotavirus vaccine should not be given when severe combined immune deficiency has been diagnosed; its use in milder immune deficiency may cause prolonged shedding of the vaccine virus, but it is unlikely to harm the patient. Bacillus Calmette-Guérin (BCG) can cause disseminated disease in certain rare immune deficiencies. Infants with HIV infection who do not have severe immunosuppression should follow the routine schedule and are also eligible to receive funded meningococcal, varicella, human papilloma virus (HPV) and influenza vaccines.

## Immune-deficient individuals of all ages

Individuals with chronic conditions, an immune deficiency, or who are immunosuppressed for underlying disease control, are at increased risk or severity of infectious diseases. These individuals should be immunised as a matter of priority. Special care is required with some live vaccines. It is important to ensure that the household contacts of these individuals are immune to vaccine-preventable diseases wherever possible.

### Asplenia/splenectomy

No vaccines are contraindicated in asplenic patients and it is essential that they receive maximal protection, particularly against pneumococcal disease which can cause overwhelming sepsis. Where possible, immunisation should be commenced at least 2 weeks preoperatively.

### Solid organ transplant

An accelerated immunisation schedule is recommended for children likely to be listed for solid organ transplant. Individuals older than 12 months who have been scheduled for solid organ transplantation should receive measles, mumps, rubella (MMR) and varicella vaccines at least 4 weeks before the transplant. In patients undergoing organ transplantation, pneumococcal vaccine should be given at least 2 weeks before the transplant. Hepatitis A, hepatitis B, HPV, influenza, meningococcal conjugate and varicella vaccines are funded for transplant patients.

### Oncology

In oncology patients, annual influenza vaccine is recommended. Post-chemotherapy, those who have received routine immunisations prior to cancer diagnosis do not need full re-immunisation. Booster dose(s) of a diphtheria/tetanus/pertussis containing vaccine, hepatitis B, polio and pneumococcal vaccines should be given, starting not less than 3 months after chemotherapy has ended, when the lymphocyte count is  $>1.0 \times 10^9/L$ . Live viral vaccines should be delayed for at least 6 months after chemotherapy, but MMR and varicella vaccine should then be given to seronegative patients.

Complete re-immunisation is recommended following bone marrow transplant, starting with inactivated vaccines 12 months after transplant. Hexavalent DTaP-IPV-HepB/Hib can be given to children up to 10 years, but from the 10th birthday Tdap should be given. Pneumococcal vaccines, meningococcal, hepatitis B and a booster dose of Hib and IPV are all recommended. MMR and varicella vaccine can be given not less than 2 years after transplant. Second doses of MMR and varicella vaccines should be given 4 weeks or more after the first doses, unless serological response to measles and varicella is demonstrated after the first dose. The vaccines should not be given to individuals suffering from graft-versus-host-disease because of a risk of a resulting chronic latent virus infection leading to central nervous system sequelae.

## Occupational and lifestyle risk

Certain occupations result in increased risk of contracting some vaccine-preventable diseases. Health care workers and those working in early childhood education services, may transmit infections such as influenza, rubella, measles, mumps, varicella and pertussis to susceptible contacts, with the potential for serious outcomes. Health care workers have a duty to know their MMR and varicella status, should receive adult pertussis booster if working with young infants and receive annual influenza immunisation.

## ISSUES IN VACCINATION OF PRETERM INFANTS

Dr Tony Walls (University of Otago)

Premature and low birth weight infants are at greater risk of increased mortality and morbidity from vaccine preventable diseases. Vaccines should be given at the usual dosage at 6 weeks chronological age (i.e. do not adjust for preterm birth). BCG (live vaccine) can be given from 34 weeks gestation. Rotavirus vaccine is an exception to the above recommendation. It is best to vaccinate preterm infants as they leave hospital because of vaccine virus shedding in the stool. However, if discharge is not anticipated before age 15 weeks, which is the upper age limit for giving dose one, then giving rotavirus vaccine in hospital is acceptable.

Preterm infants have an inferior response to some vaccines, although evidence suggests the response is still protective. Immunisation in these infants is safe and effective, however post-vaccination apnoea with or without associated bradycardia up to 48 hours post-immunisation may be increased in some groups. Reasons for this include apnoea within the 24 hour period before immunisation, more severe illness at birth, chronological age less than 67 days and/or earlier gestational age in infants with a birth weight of less than 1500g, or an apnoeic episode following the first immunisation event. Apnoea monitoring should be considered after the first immunisation event and after subsequent immunisation events when an infant has experienced apnoea after their first immunisation event.

Why do preterm infants not respond as well to vaccines as full term infants? They do not produce antibodies as well as full term infants and those that are produced don't last as long.<sup>2</sup> In naïve B cells, preterm infants have decreased expression of cell surface receptors, such as CD21, CD40, CD80 and CD86. In plasma cells, preterm infants have limited IgG responses to protein and polysaccharide antigens and limited persistence of IgG antibodies. Additionally, they have impaired germinal centre responses, a limited functional follicular dendritic cell network and limited access to plasma cell niches in bone marrow. The one positive is that preterm infants do effectively produce memory B cells. Transplacental transfer of maternal IgG can protect against some vaccine preventable diseases but is affected by past exposure of the mother and the infant's gestational age. Infants born at  $<34$  weeks gestation have less IgG and it wanes more rapidly.

## PAIN MANAGEMENT FOR IMMUNISATION

Dr Kathryn Russell (Kidz First)

Immunisations are the most common recurring health care procedure in childhood, but associated pain causes distress for children and their parents and can lead to needle fears and health care avoidance.<sup>3-8</sup> Use of distraction techniques to reduce pain and distress during immunisation is something done very well in New Zealand in Dr Russell's opinion. The most common methods used are colourful or noisy toys, bubbles, and reward stamps and stickers. Vibration or rubbing can also be a useful distraction technique, with a nurse or parent rubbing above the injection site or using a device like the BuzzyBee. Breast feeding and oral sucrose are often used in infants to reduce pain, but there is still room for improvement in this area. Dr Russell observed  $>150$  vaccinations by 12 school nurses of Boostrix and the second or third HPV vaccination. Most nurses limited procedural talk and time before injection and all used a good variety of distractions. But three quarters of nurses used a slow injection technique, a long-standing practice that has never been subjected to scientific evaluation. The theory is that injecting slowly will minimize pressure and sudden distension of tissues. However, slow delivery adds to pain due to longer contact time between needle and tissue and through lateral movement of the needle. Aspiration is not necessary because vaccination sites are devoid of large blood vessels. A randomised controlled trial of injection technique in infants showed a rapid technique (1 second for 0.5 mL) resulted in less pain versus a slow technique with aspiration (up to 9 seconds).<sup>9</sup> Dr Russell pointed out that a fast injection technique is indeed that – only about 2 seconds long.

What does the future hold? There may be more antigens introduced to each vaccination but this could come with increased risk of febrile seizures in 1–3 year olds with MMRV. Different delivery modes may hold promise such as a nasal spray or transdermal flu vaccine and a nanopatch HPV vaccine. Better pain management training for immunisers and parents would also be useful, as would the use of EMLA® patches in the 15 month age group where four immunisations are given and distraction techniques are limited.

## What works

- Distraction
- Parent acting calm
- Rapid injection technique
- EMLA® – but dose concerns under 1 year
- Sucrose, breastfeeding, parent holding baby (infants)
- Tactile input and non-procedural talk ( $\geq 4$  years)

## MENINGOCOCCAL VACCINATION

Dr Stewart Reid (Ropata Medical Centre, Lower Hutt)

In 2013, the rate of meningococcal disease in New Zealand was 1.5/100,000, half that seen in 2009 and a much more favourable situation than a decade ago. There were 61 confirmed cases in 2013, including 30 group B (53%) and 17 group C (30%). The fatality rate was 6%. Not surprisingly, most cases were in children aged  $<1$  year (18.4/100,000) and these were predominantly meningococcal group B (MenB) disease. Rates declined throughout childhood but there was a peak in the 15–19 year old group (3.9/100,000) which was predominantly meningococcal group C (MenC) disease. Pacific and Maori had higher disease rates than European (3.1 and 2.6 versus 1.2 per 100,000, respectively). Regarding strain data, only 11 of the MenB cases were the epidemic strain, while almost all the MenC cases were from one subtype (P1.5-1,10-8).

## Potential MenC vaccine strategies

The UK now uses a 1+1+1 MenC immunisation schedule and is contemplating dropping the infant dose. Catch ups are not recommended but there may be an adolescent programme in the future. The Netherlands and Australia only give an adolescent dose, with good disease control. However, all three countries have had to use significant catch up doses which may be critical to good disease control and expensive. A 2006 model suggests that a two-dose MenC immunisation strategy at 12 months and 12 years is close to ideal.<sup>10</sup> Given New Zealand's low MenC disease rate, Dr Reid proposes introducing a two-dose immunisation strategy with no catch ups, with disease monitoring and catch ups considered if disease rates increase.

## Potential MenB vaccine strategies

The MenB vaccine Bexsero is combined with outer membrane vesicles (OMV) from a New Zealand group B strain and has broader coverage and probably greater duration of protection than MenZB. Bexsero is licensed in Australia with the recommendation from the Australian Technical Advisory Group on Immunisation (ATAGI) that it can be used from 6 weeks of age. However, the Australian and European product information only recommend its use in infants from age 2 months. Dr Reid understands there is no data supporting the use of Bexsero under 2 months of age which would need to be considered carefully if Bexsero was to become available in New Zealand. Dr Reid's suggestion for Bexsero, assuming it will be licensed in New Zealand, is to use it short term for outbreak control and await effectiveness data from the UK before introducing it into the routine schedule.

The Joint Committee on Vaccination and Immunisation (JCVI) in the UK has made a very comprehensive statement on the use of Bexsero. In April 2013 they reported it was unlikely to be cost effective. After more information led to a modelling change, they recommended in March 2014 that it be included on the infant immunisation schedule with borderline cost effectiveness at a reduced cost per dose. If implemented in the UK, effectiveness data will become available for consideration of its introduction in New Zealand. In the UK, MenB disease is responsible for 80% of meningitis cases and is fatal in 5%. Data for Bexsero with the New Zealand OMV showed efficacy of 73%, but on the basis of immunogenicity assumed efficacy was 95% and assumed strain coverage for the UK was estimated at 88%. The estimated duration of protection was 18 months after the infant dose, 36 months after the toddler dose, and 10 years after the adolescent dose. The JCVI noted increased reactivity of the childhood schedule when Bexsero was given with other vaccines. A 2, 4, 12 month immunisation schedule is recommended considering peak age of disease is 5 months and most vaccines in the UK are given on time.

Suggestions for the NZ immunisation schedule include:

- Conjugate group C vaccine: consider introduction now with a two-dose schedule and no catch up
- Bexsero: when licensed in New Zealand consider use for short term outbreak control and
- await long-term effectiveness data from the UK before considering introduction to routine schedule

## VARICELLA VACCINATION – WHY, WHO AND WHY NOT

Dr Emma Best (Starship Children's Hospital)

The burden of varicella hospitalisations in New Zealand is underestimated and complications are associated with significant morbidity in children. In a typical year in New Zealand, there are 50,000 varicella infections.<sup>11</sup> 200–300 cases result in hospitalisation and 1–2 cases result in long-term disability or death. Two-thirds of the disease burden is in otherwise healthy children. Dr Best and colleagues conducted a study of varicella and post-varicella complications requiring hospitalisation in New Zealand children <15 years between November 2011 and October 2013.<sup>12</sup> Maori and Pacific Island children are over-represented – the incidence rate ratio of hospitalisation was 2.8 for Maori and 3.9 for Pacific compared with European children. Secondary bacterial infection was the most common complication of varicella. Preliminary results show high rates of secondary infective complications, particularly with *Staphylococcus aureus* and *Streptococcus pyogenes* consistent with prior reports of New Zealand's rates of *S. aureus* and *S. Pyogenes* as amongst the highest reported in the developed world.<sup>13</sup>

High-risk groups have recently been made eligible for funded varicella immunisation. Such groups include non-immune patients prior to immunosuppression or transplantation. Non-immune household contacts of such individuals are also eligible. But targeting varicella vaccination of susceptible family members has questionable effectiveness as it may be neglected or forgotten by the managing team. A survey of paediatric oncologists in the UK and Italy showed only 15% attempted to identify varicella-susceptible individuals in households of their immunocompromised patients, despite treatment guidelines.<sup>14,15</sup>

Why not introduce routine varicella immunisation? There are theories that inadequate vaccination coverage (<80% of the entire non immune cohort) would shift disease burden to the older population resulting in increased morbidity and mortality.<sup>16</sup> In addition, it has been long hypothesised that immunity against herpes zoster virus is boosted by contact with wild type varicella-zoster virus.<sup>16</sup> The resultant hypothesis is that varicella vaccination may actually increase the incidence of herpes zoster.<sup>17</sup> But there is now much real world evidence that these theories are not the case. Australia has funded varicella vaccine from 2005 as a single dose at 18 months. A school vaccination programme also offered the vaccine to 12–13 year olds who were not immune. Data shows marked declines in varicella hospitalisations in both targeted age groups and herd protection in other age groups. There is no evidence for a shift in varicella hospitalisation to older age groups and no change in rates of herpes zoster hospitalisations. Prior to the vaccine being funded, indigenous Australians were hospitalised at twice the rate of non-indigenous population (incidence rate ratio 2.6). By including varicella vaccination on the routine immunisation schedule, the disparity between indigenous and non-indigenous hospitalisations rates for children has been eliminated. Similar data have been shown in the US where the vaccine has been publicly funded since 1995.

### Take home messages

- Who? All from age 1 year and non-immune preteens
- Why? High burden of disease and secondary infections
- Well why not?

## ISSUES WITH BCG

Dr Lesley Voss (Starship Children's Hospital)

BCG was first administered orally to humans in 1921 and is one of the most widely-used vaccines in the world. There is persisting controversy over the efficacy and safety of BCG immunisation. It does not prevent infection but may prevent or modify the development of disease. Results consistently demonstrate ability to protect against severe childhood tuberculosis (TB). In New Zealand, 75% of TB cases are foreign-born and there tends to be a higher rate of developing TB within the first seven years of arriving in this country. Neonatal BCG is recommended and funded for infants at increased risk of TB, defined as those who:

- Will be living in a house with a person with either current TB or history of TB
- Have at least one household member who within the last five years lived for ≥6 months in countries with a TB rate ≥40 per 100,000
- During their first five years will be living for ≥3 months in a country with a TB rate ≥40 per 100,000

There are a number of contraindications to BCG vaccine. These include infants with an impaired immunological response, past history of TB, positive tuberculin skin test or interferon-gamma release assay, significant fever, or living in a household where active TB is suspected. A new contraindication to be aware of is infants aged <8 months whose mother took anti-TNF therapy during pregnancy – vaccination should be delayed until 8–9 months of age.<sup>18</sup>

Side effects occur in 1–10% of recipients. Common side effects are prolonged ulceration at the vaccination site and lymphadenitis. Serious side effects are rare and include dissemination (1 in 1 million vaccinated individuals, with undiagnosed immunocompromised infants at particular risk) and osteomyelitis. A large prospective study was conducted in six European countries of approximately 2.5 million children aged <1 year vaccinated with BCG.<sup>19</sup> Types of complication per 1 million children included lupus-like (1.56), bones, joints and muscles (0.39), intrathoracic/abdominal lymph nodes (0.39), disseminated, non-fatal (0.39), and disseminated fatal (1.56). Increases in the rate of local reactions have occurred in some countries when the BCG strain was changed, with no further problem on vaccine recall.<sup>20,21</sup> In Dr Voss's opinion, local reactions are best treated by observation alone, with antibiotics given if there is any sign of bacterial infection. There is rarely an indication for surgical incision/drainage or oral isoniazid. The infant's family should be reassured that the reaction will most likely take a benign course.

## PERTUSSIS IN AUSTRALIA

Professor Peter McIntyre (National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases, Westmead)

In Australia, a locally manufactured whole cell pertussis vaccine was in use from 1975 to 1996; a booster dose at 18 months was re-introduced in 1983 and a pre-school dose was introduced in 1995. Acellular pertussis vaccine (DTaP) has been used for booster doses since 1997 and exclusively since 1999. Until September 2003, the recommended primary schedule was three doses at 2, 4 and 6 months, with boosters at 18 months and 4 years. In 2003, the 18 month dose was removed in favour of an adolescent booster dose. However, in January 2015 the Pharmaceutical Benefit Advisory Committee recommended re-introduction of the 18 month booster on the National Immunisation Program. Recommendations for adults (health care workers, those with contact with infants, child-care personal, pregnant women) exist but doses are not funded by the National Immunisation Program. However, a number of Australian States have provided funding for free of charge adult vaccination in the context of "cocoon" programmes during outbreaks from 2009.

A resurgence of pertussis was seen from 2008–2012 in children less than 10 years of age, in particular in 2 to 4 year olds and

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7 to 9 year olds. Pertussis is a major public health issue in Australia, with a continuous increase observed over a long period of time, first in adults related to availability of serologic tests, then in adolescents related to low historical vaccine coverage, and most recently in younger children consistent with waning immunity in the context of increased test availability and use. Cessation of the 18 month booster dose appears to be an important contributor to resurgence in 2 to 4 year olds, with early waning immunity following the last acellular vaccine dose at 6 months. Large increases in cases over 6 years of age have been observed, and there are data to support a shorter duration of immunity among children who have received acellular vaccines than in those who received the earlier whole cell vaccine. The resurgence was not associated with any increase in infant pertussis deaths, which have remained similar or lower to that of previous pertussis epidemics in the past two decades despite more sensitive diagnostic tests.

### PERTUSSIS IN NEW ZEALAND

Associate Professor Nikki Turner (IMAC, University of Auckland)

New Zealand's recent pertussis epidemic is finally declining. The highest risk group for hospitalisation is infants aged <1 year, with hospitalisation rates 45 times higher than other groups. Rates of pertussis hospitalisation are highest in Maori and Pacific Island children and those from areas of high deprivation. During 2012–2013, 63 children were admitted to Starship PICU with pertussis, with an average length of stay of 11.3 days. Twenty-eight patients required invasive ventilation and 4 patients died; 3 of these were too young for full vaccination and 1 was unvaccinated with underlying morbidity. Dr Turner thinks we are probably considerably underdiagnosing pertussis. In 2011, the COUGH study evaluated 226 patients aged 5–49 years presenting to Auckland GPs with cough >2 weeks.<sup>22</sup> Ten percent of patients had evidence of recent pertussis infection, including more children than adults (17% vs 7%). Clinical differentiation of pertussis from other causes of acute persistent cough is difficult, with no distinctive clinical symptoms noted. Since 2000, New Zealand has used an acellular pertussis vaccine given at 6 weeks, 3 months and 5 months, and in

2006 introduced a booster at 4 and 11 years. Since January 2013, vaccination of pregnant women at 28 to 38 weeks gestation has been funded. Immunisation of new mothers, family and close contacts of newborns, health care and childcare workers is recommended but not funded (health care workers are variably funded). The pregnancy pertussis immunisation programme was introduced in response to the epidemic that started in 2011. Pharmac will maintain the pregnancy programme for the foreseeable future with annual review, even though the epidemic is waning. Nationwide, the uptake of pertussis pregnancy vaccination is incredibly low, for a number of reasons. Availability of the vaccine in pregnancy was not well publicised, there are many service delivery challenges of vaccination in the antenatal arena, primary care is not engaged with antenatal care, and pregnancy vaccination is not embedded as a concept. However, flu vaccination may be leading the way with a greater emphasis over the last few years on flu vaccination in pregnancy, which Dr Turner is hoping pertussis immunisation can 'piggy back' on.

### Outstanding questions

- How can we improve uptake of the maternal pertussis vaccination programme?
- How long will we continue maternal pertussis vaccination after the current epidemic has waned?
- Can we get adult Tdap on the National Immunisation Register?
- What is the effectiveness and safety of pregnancy vaccination?
- Is there maternal antibody interference with the infant schedule starting at 6 weeks?
- What is the effectiveness at specific ages?
- Do we need a toddler dose?
- What is the effect of the adolescent dose?
- Acellular pertussis versus whole cell pertussis schedules or mixed?

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