Research Review Speaker Series™

The Hidden Impact – The Wider Implications of Pertussis and Varicella Infections

Making Education Easy March 2013

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This publication summarises a recent presentation by Dr Cameron Grant who spoke at the Goodfellow Symposium on the hidden impact of pertussis and varicella infections in New Zealand. Dr Grant introduced his talk on pertussis (commonly known as whooping cough) by showing the audience a compelling Ministry of Health video clip of a very young infant (too young to have been immunised) experiencing the distressing symptoms of the illness for which she had been hospitalised during the most recent epidemic. The traumatic impact of this life-threatening disease on the 7-week old infant and her family was distressing to watch. In the video, the infant's mother appealed to others to have their children, and themselves, immunised. The video can be viewed at: http://tinyurl.com/MOH-WhoopingCough

Pertussis – an epidemic disease in New Zealand

Dr Grant explained that the time interval, or periodicity, between outbreaks of pertussis did not change with the introduction of the pertussis vaccine in New Zealand in 1945; between 1873 and 1944 the time interval was 3.9 years and between 1945 and 2004 it was 3.5 years.[1] This implies that the pertussis vaccine has had no impact on the circulation of pertussis in our population.

The current pertussis epidemic in New Zealand started in 2011 and is continuing with force.[2] Epidemics of pertussis tend to be longer than influenza epidemics, lasting around 18 months, and do not exhibit a seasonal pattern, being just as common in the summer as in the winter months.[2] Notifications of pertussis occur across the age range, but a larger number of infants than adults are hospitalised with the illness.[2] In fact, six out of ten infants with pertussis are admitted to hospital and of those, one will be admitted to paediatric intensive care (PICU).[3,4] Furthermore, one in six infants admitted to PICU with pertussis die or are left with brain or lung damage.[3,4] Death from pertussis can be unpredictable and occur very quickly. In New Zealand in 2012, there were more than 300 hospitalisations for pertussis and two deaths.[2]

Why does New Zealand have such a big pertussis problem?

Between the 1920s and 1940s the hospital admission rate for pertussis steadily increased (see **Figure 1**). During the two decades following the introduction of the pertussis vaccine in New Zealand in 1945, there was a marked and steady decline in the pertussis hospitalisation rate; at that time individuals received three doses of the vaccine. However, since the early 1970s we have seen a steady increase in the number of pertussis hospitalisations. This increase coincided with the decision to reduce the number of doses from three to two. Despite subsequent incremental increases in the number of doses up to five in 2002, we have seen a substantial increase in the rate of pertussis hospitalisations, with the rate in the first half of the first decade of the new millennium 1.5-fold higher than that seen in the 1960s.

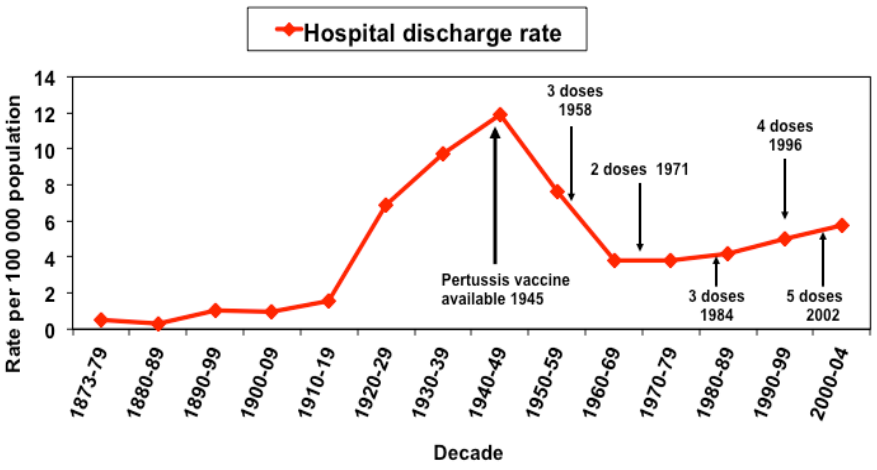

Figure 1: Annual pertussis hospital discharge rate per decade per 100,000 person years from 1873 to 2004.[1]

International comparison of pertussis hospitalisation rates in the 1990s revealed rates in New Zealand 6-fold higher than those in the US, 4-fold higher than those in Australia and 3-fold higher than those in the UK.[5-8] Two reasons why New Zealand has a bigger pertussis problem than these other countries are our poor immunisation coverage and even poorer immunisation timeliness.[9,10] The reason that vaccination coverage has to be high for pertussis is because it is more infectious than most vaccine preventable diseases, with every case of pertussis causing 15 secondary cases. With regard to timing, a delay in receipt of any of the infant doses of pertussis vaccine is associated with a 5-fold increased risk of pertussis hospitalisation.[10] In order to totally control pertussis, immunisation rates need to be above 95%.[11]

In New Zealand in 1992 only 60% of children aged 2 years were fully immunised, but by 2005 this rate had risen to almost 80%.[12] However, we know that even at 80% coverage is too low to have a significant impact on the size of pertussis epidemics. Immunisation in New Zealand subsequently became a national health target with an aim of having 85%, 90% and 95% of infants fully immunised by 2 years of age, by July 2010, 2011 and 2012, respectively. While these targets seemed very ambitious at the time, coverage at age 2 years had reached 93% by June 2012.[13] Furthermore, over the previous 3 years we have seen a reduction in the disparity of coverage between different ethnic groups and between household deprivation deciles.[13] Dr Grant pointed out that while this is good news, even now our immunisation timing could be better, with coverage data at age 6 months still showing disparity between ethnic groups and levels of deprivation.[13]

Dr Grant believes that another contributing factor to New Zealand's pertussis problem is the fact that we have tinkered around with our immunisation schedule. When pertussis immunisation was first introduced it was administered as a three-dose primary schedule, then we dropped it down to a two-dose schedule before returning again to a three-dose schedule. In the late 1990s we introduced boosters at 15 months, then changed that to 15 months and again at 4 years then at 4 years, and 11 years. These alterations in the schedule have been confusing enough for healthcare professionals let alone parents and caregivers. In the US, where the annual infant pertussis hospitalisation rate is significantly lower than in New Zealand, they have consistently from the outset used a three-dose schedule and two boosters (at 15 months and at 4 years), with a third booster at 11-18 years added since 2005.[14] Dr Grant believes that the more consistent pertussis schedule in the US has contributed to their better control of the disease. While our pertussis hospitalisation rate has decreased since the 1990s, it is still 3-fold higher than that in the US.[3,15]

The young are particularly at risk

In the US during the 1940s, pertussis resulted in more infant deaths than measles, diphtheria, poliomyelitis and scarlet fever combined.[16] A recent epidemic in California killed eight infants, all of whom were under 2 months of age.[17] In the US, risk factors for death associated with pertussis include the following: age <2 months; low birth weight; female gender; 5-minute Apgar score <8; maternal education <12 years.[18] A US study looking at pertussis hospitalisations in 2000 and 2003 found the highest rates in infants aged 1 month (see **Figure 2**).[3] Dr Grant explained that pertussis is an unusual infection in that newborns do not receive protection from maternal antibodies.

In New Zealand, the 2005 Ministry of Health National Immunisation Coverage Survey revealed coverage at 1 year to be 80%, but timeliness to be only 40%.[12] National immunisation coverage data for the 3 months to the end of December 2012 shows coverage to be approximately 70% at 6 months, 90% at 12 months, 75% at 18 months and 90% at 24 months.[13] Data show that delayed immunisation

significantly increases the risk of pertussis hospitalisation in infants, with an impressive 6-fold increase in risk if the 5-month dose is delayed (see **Figure 3**).[15]

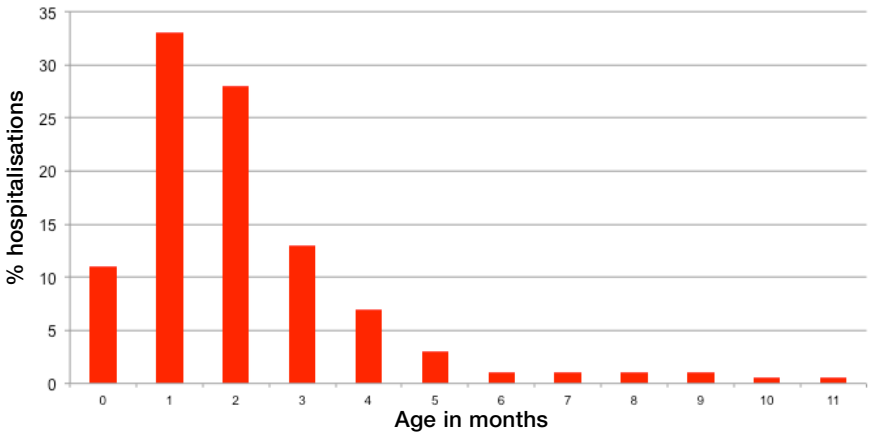

Figure 2. Average annual incidence of pertussis hospitalisations and number (percent) of hospitalisations according to age group in the US Kids' Inpatient Database (2000 and 2003).[3]

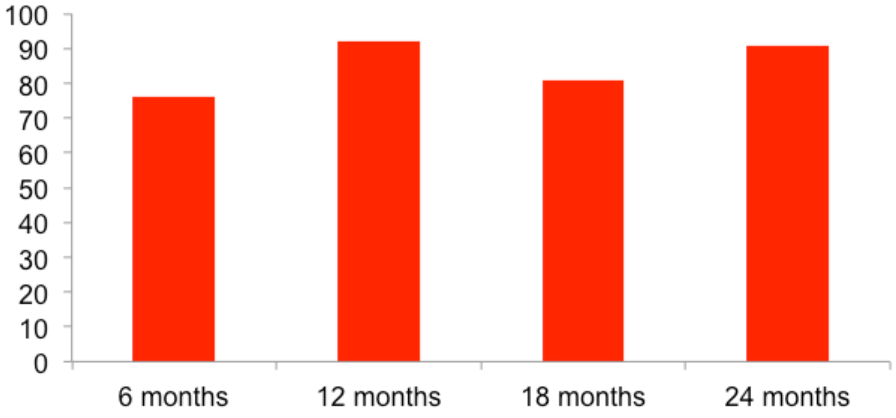

Figure 3: Delayed immunisation and risk of pertussis hospitalisation in infants.[15]

Protecting the very young

Dr Grant pointed out that even the best immunisation timing won't protect the youngest infants who are not old enough to be immunised. A number of strategies have been proposed to protect this group. The importance of improving current infant and toddler immunisation strategies has been stressed, as too has the importance of creating a cocoon of contacts who are immunised.[19] This is the concept of herd immunity, whereby all those in the community who can be immunised are, therefore rendering them incapable of passing the disease to the vulnerable.

The following groups have been selected as targets for immunisation:

- Women during pregnancy
- Women shortly after the birth of their child
- Older siblings
- School-aged children
- Close adult contacts such as fathers and grandparents
- Healthcare workers
- Early childcare workers

Recently in New Zealand, national funding for pertussis immunisation of women during pregnancy (28 to 38 weeks) has been approved. Immunisation of the mother during pregnancy has the following benefits: immunisation protects the mother from pertussis infection and antibodies to *B. pertussis* cross the placenta.[20] The effectiveness with regard to directly protecting the infant is not yet known. Dr Grant recommends that women be immunised during each pregnancy.

Selective immunisation of healthcare workers

Healthcare workers are at an increased risk of pertussis and outbreaks have occurred in maternity units, neonatal units and in outpatient settings. Fatalities can occur as a result of such outbreaks. The benefit to the hospital of immunising healthcare workers is estimated to be 2.4 times the dollar amount spent.[21] In New Zealand, individual District Health Boards are responsible for deciding which particular healthcare workers should be immunised against pertussis. Dr Grant believes that, ideally, decisions regarding the immunisation of healthcare workers should be covered by a national policy. He added that healthcare workers should receive a booster dose every 3-4 years.

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Is universal adult immunisation an option?

Dr Grant does not believe that universal adult immunisation against pertussis is an option at present; he does, however, believe that when a baby is born, all adults in the family with contact with the infant should be immunised. He added that while the disease is most severe in young infants, the elderly can also suffer significantly from this illness.

Take-home messages:

- Pertussis in New Zealand is an epidemic disease
- The lack of change in epidemic cycle with mass immunisation suggests immunisation has had no impact on the organism circulation in the population
- We are currently experiencing a large epidemic
  - In 2012 > 300 hospitalisations
  - In 2012 there were two deaths
  - Notifications occurred across the age spectrum
- New Zealand has a bigger pertussis problem than Australia, the UK and the US because we have had:
  - Low coverage of the primary immunisation series
  - Late introduction of booster doses
  - Scheduling changes that have been driven more by concerns about vaccine safety than disease control
- Options for preventing severe pertussis are:
  - Timely and complete delivery of 6 week, 3 month, 5 month infant primary series
  - Timely and complete delivery of boosters at 4 and 11 years
  - Cocooning strategies: immunisation during pregnancy; immunisation of healthcare workers; immunisation of early childcare workers; immunisation of adult family members.

Varicella in New Zealand

Varicella (commonly known as chickenpox) is the third most infectious vaccine-preventable illness, with every case of varicella causing approximately nine secondary cases.[9] By age 10 years, 85% of children will have been infected with varicella; 3% infected in infancy and approximately 9% in each year after that. In New Zealand, there are approximately 50,000 cases of varicella infection reported per year.

Hospital admissions for varicella have steadily risen since the 1970s (**see Figure 4**).[22] For every varicella hospital admission it is estimated that there are approximately 90-150 General Practitioner visits.[23] Most hospital admissions are for severe varicella or bacterial super-infection of the varicella skin lesions; necrotising fasciitis may also occur.

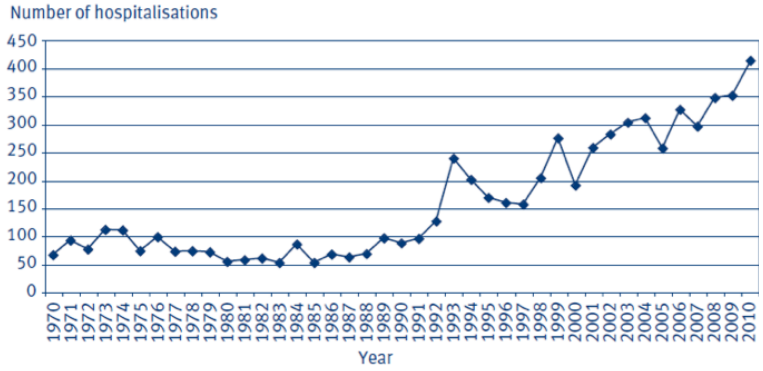

Figure 4: Varicella hospitalisations in New Zealand.[22]

A recent audit of the Starship Paediatric Intensive Care Unit showed that among 34 children admitted with varicella infection between 2001 and 2011, varicella complications including bacterial infections, coagulopathy, pneumonia, encephalitis and multiorgan failure were frequent, and that outcomes were often poor (see **Figure 5**).[24] Four out of the five deaths from varicella at Starship occurred in children with chronic medical conditions: two with haematological malignancy on chemotherapy; one child post bone marrow transplant; one child post liver transplant. Dr Grant noted that such children who die from varicella infections often have already had vast amounts of resources spent keeping them alive - he commented "what a waste for them to then die of a preventable illness like varicella".

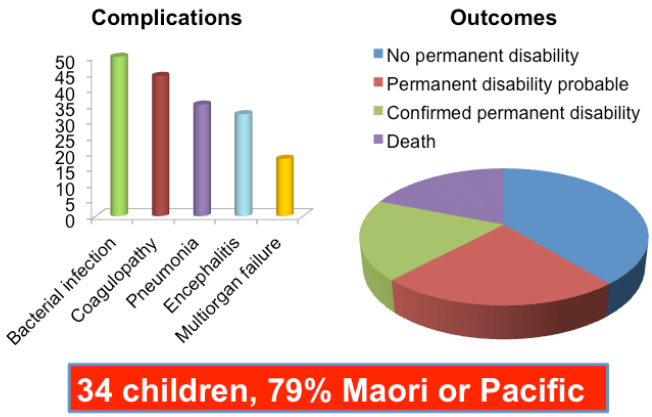

Figure 5: Varicella admissions to the Starship Paediatric Intensive Care Unit 2001-2011.[24]

How effective is the varicella vaccine?

After one dose of the varicella vaccine at age 12 to 15 months, the vaccine is effective in 80% of people.[22] After a second dose at age 4-6 years the efficacy is approximately 97%.[22] When the vaccine first became available in New Zealand the recommendation was to give one dose. Dr Grant suggests that those who have received only one dose should now receive a second dose of the vaccine.

What about the risk of herpes zoster?

Individuals are often concerned about the risk of developing herpes zoster (shingles) after contracting chickenpox, and one in three people (or 50% of those aged over 80 years) who have a history of chickenpox infection will be develop herpes zoster at some stage.[25] The risk of herpes zoster in those who have been immunised is 10-fold lower. There is a potential for herpes zoster to be more severe in individuals not re-exposed to wild-type disease (the frequency of which is declining with immunisation) and for this reason in the US, vaccination against herpes zoster is now recommended for individuals over 60 years of age.[25]

How safe is the varicella vaccine?

Reactions to the varicella vaccine are generally mild; 20% to 25% of individuals experience minor injection site reactions such as pain, redness or swelling.[25] In 3% to 5% of individuals a generalised varicella-like rash develops 5-26 days post immunisation, but this is typically limited to 2-5 lesions and these may be maculopapular rather than vesicular. In 1% to 3% of immunised children a localised rash develops. A small number of individuals experience breakthrough varicella (wild-type), but this is milder (median of 50 lesions vs 250 if not immunised) and exhibits one-third the risk of secondary transmission. Very rarely (1 per million), isolated cases of non-serious secondary transmission have been reported after immunisation.[26] When administered between the ages of 12 and 23 months there is a 2-fold increased risk of febrile convulsions for MMRV (measles/mumps/rubella/varicella), but not for MMR + V and this does not appear to occur if given between the ages of 4 and 6 years.[27,28] Generally the varicella vaccine is well tolerated and immunogenic.

The impact of varicella vaccination programmes

Following the introduction of the varicella vaccine in the US in 1995, varicella-related hospitalisations and deaths dramatically decreased across all age groups.[29] By 2005, the varicella immunisation coverage rate in the US was approximately 88% in those aged 19 to 35 months. For children aged 1-4 years, there was a 71% to 84% decrease in cases, an 88% decrease in the number of hospitalisations and a 92% decrease in deaths.[29,30]

Dr Grant pointed out that New Zealand has a very high hospital admission rate for paediatric skin and soft tissue infections (2006 rates were 330/100,00 children and 700/100,000 infants). He concluded that New Zealand is likely to experience a large benefit from a varicella immunisation programme given our issues with skin and soft tissue infections.[31]

Take-home messages:

- Virtually all children get varicella
- Hundreds are hospitalised each year and hospitalisations are increasing
- Varicella is a severe disease and death may occur among the vulnerable
- Varicella vaccines are efficacious and well tolerated
- If given as MMRV in the second year of life the risk of febrile convulsions is increased
- Two doses are required
- Childhood varicella vaccine use may require older age zoster vaccine use
- Varicella immunisation prevents deaths and hospitalisations
- Given New Zealand's large skin infection issues the positive impact of the vaccine in New Zealand is likely to be large.

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