Research Review
EDUCATIONAL SERIES™

An update on varicella immunisation in New Zealand

About the Expert

Dr Emma Best
Paediatric Infectious Diseases Consultant
Starship Children's Hospital Auckland

Dr Emma Best is a Senior Lecturer (Department of Paediatrics) at the University of Auckland, and a Paediatrician Specialist in Infectious Diseases at Starship Children's Hospital, Auckland. Her research interests include vaccine preventable diseases and appropriate antibiotic prescribing and safety. She is an Auckland Medical School graduate with a postgraduate Masters of Medicine from the University of New South Wales, Sydney, Australia, and a Diploma of Tropical Medicine from the London School of Hygiene and Tropical Medicine, London, England.

Abbreviations used in this issue

HIV = human immunodeficiency virus
HZV = herpes zoster virus
MMR = measles-mumps-rubella
MMRV = measles-mumps-rubella-varicella
NIS = National Immunisation Schedule
PHARMAC = Pharmaceutical Management Agency
PICU = paediatric intensive care unit
UMV = universal mass vaccination
VZV = varicella zoster virus

Varicella — a serious childhood disease

Besides whooping cough (pertussis) and measles (rubella), varicella (chickenpox) is one of the most infectious diseases known. It is caused by human herpesvirus type 3 (varicella zoster virus; VZV),[1] and is the third most infectious vaccine-preventable illness: each case of varicella is associated with about nine secondary cases.[2] Before adolescence, 90% of children will have been infected with VZV: about 3% in infancy, and approximately 8–9% in each subsequent year. In New Zealand, the reported incidence of varicella is about 50,000 cases per year. Traditionally, the peak incidence was in 5- to 9-year olds, whereas the incidence in preschool children is now increasing.[1]

Transmission of varicella occurs via airborne droplets, or by individuals coming into contact with skin or mucosal lesions or infected respiratory tract secretions. Typically, the incubation period is 14–16 (range 10–21) days. Affected individuals are infectious for 1–2 days before occurrence of the characteristic maculopapular rash until all lesions have crusted. The rash, which becomes vesicular, after first appearing on the scalp and face, and subsequently spreading to the abdomen, trunk and limbs, is itchy and usually associated with anorexia, lethargy, malaise, and mild fever. Generally, lesions will crust after 3–4 days, although further lesions may ensue.[1,3,4] Altogether, patients may experience about 250–500 lesions at different stages of development and crusting.[3]

In most children, varicella is a mild and self-limiting illness, although complications necessitating hospitalisation, and deaths, do occur; the likelihood that VZV complications are under-reported should also not be overlooked. The most common varicella comorbidities are VZV encephalitis and secondary bacterial infections. Serious complications include: involvement of the central nervous system (e.g. cerebellar ataxia, encephalitis, stroke); pneumonia; secondary invasive bacterial infections; thrombocytopenia; and, in some cases, death.[1,3] Rare complications include arthritis, glomerulonephritis and hepatitis.[3]

Although primary varicella is rare in adults, it is associated with a greater rate of complications, principally pneumonia. Mechanical ventilation is often needed for patients with VZV pneumonia, which has an overall mortality rate of 10–30%, even though effective antiviral therapies are available. Adults with VZV infection are 25 times more likely than children to develop severe complications of varicella;[1] overall, varicella is usually more severe in adults, adolescents and infants than in young children.[3]

The burden of varicella

In New Zealand, hospital admissions for varicella increased almost 8-fold over the period from 1970 to 2013 (**Figure 1**).[1] It has been estimated that for each hospital admission due to varicella there are approximately 90–150 times more visits to a general practitioner. Most hospital admissions are for severe varicella or bacterial superinfection of varicella skin lesions; necrotising fasciitis may also occur.[5]

Over a 10-year period (2001–2011) at Auckland's Starship Children's Hospital, 26 children were admitted to the paediatric intensive care unit (PICU) with varicella. Among these children, 85% were of Maori or Pacific Island ethnicity; 54% had no previous medical condition, and 23% were immunocompromised. The principal reasons for PICU admission were neurological (39% of patients), secondary bacterial sepsis or shock (27%), respiratory (15%), disseminated varicella (12%), or other reasons (8%). Half of the children needed inotropic support, and 81% required invasive ventilation. Four children (15%) died, 3 of whom were immunocompromised, and another 8 children (31%) had ongoing disability at the time of hospital discharge; most of the latter patients had no preceding medical condition. Thus, varicella and its secondary complications were associated with significant mortality, particularly in immunocompromised patients, and with long-term morbidity, especially in previously healthy children.[6]

This increase has primarily been caused by the doctor inspired use of pamol or ibuprofen which in the medical literature is known to result in both GAS infections and necrotising fasciitis = doctor induced stupidity. also the rampant prescription of fucidin as per medical article, as well as other antibiotics. Very clear in the medical literature.

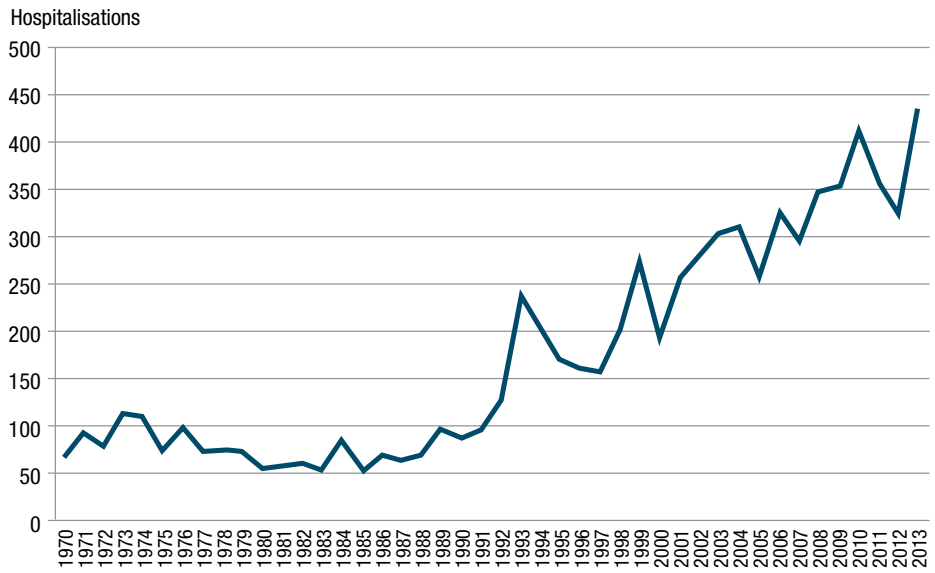

Figure 1. Varicella hospitalisations in New Zealand (1970–2013).[1]

A New Zealand surveillance study investigated varicella and post-varicella complications (excluding herpes zoster) requiring hospitalisation between November 2011 and October 2013. Of 144 notifications made by paediatricians, 74% were for Maori and Pacific Island children. Overall, median age was 2.4 years (range 14 days to 14.7 years; including 3 cases of neonatal varicella). The annual incidence of varicella-related hospitalisations was 8.3/100,000 children, with significantly higher incidence ratios for Maori (2.8) and Pacific Island (3.9) than European children. Only 9% of hospitalised patients were immunocompromised and, in the entire cohort, 19% of patients had ongoing issues after discharge from hospital. The authors concluded that varicella morbidity is higher in immunocompetent children than commonly perceived, particularly in children of Maori and Pacific Island ethnicity.[7]

Which individuals are at risk?

Pregnant women

Pregnant women and their unborn babies are especially susceptible to VZV infection. Maternal varicella manifesting during the first half of pregnancy may lead to congenital varicella syndrome, a very rare condition that nonetheless has significant sequelae.[1,3] Varicella occurring very late in pregnancy (i.e. from 5 days prepartum to 2 days postpartum) may lead to severe neonatal varicella, which can be fatal. Furthermore, women who develop varicella during pregnancy have a projected 10–20% risk of developing pneumonia due to VZV, which can be fatal; this risk is considerably greater than that in non-pregnant women.[1]

Immunocompromised individuals

Varicella can be fatal in immunocompromised individuals, such as those taking immunosuppressive therapies (e.g. organ-

transplant recipients, or cancer patients receiving chemotherapy) or in individuals with human immunodeficiency virus (HIV) infection.[1] Thus, in New Zealand, PHARMAC subsidises two doses of varicella vaccine (Varilrix®; GlaxoSmithKline NZ Ltd) in the following high-risk groups:

1. Non-immune individuals with:
   - chronic liver disease who may be future candidates for transplantation; or
   - worsening renal function before transplantation; or
   - before solid organ transplantation; or
   - before elective immunosuppression for >28 days.
2. Patients ≥2 years after bone marrow transplantation, on advice of their specialist.
3. Patients ≥6 months after completing chemotherapy, on advice of their specialist.
4. HIV-positive patients non-immune to varicella and with mild-to-moderate immunosuppression, on advice of an HIV specialist.
5. Patients with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella.
6. Household contacts of paediatric patients who are immunocompromised, or undergoing a procedure leading to immunocompromise, and where the household contact has no clinical history of varicella.
7. Household contacts of adult patients who have no clinical history of varicella and who are severely immunocompromised, or undergoing a procedure leading to immunocompromise, and where the household contact has no clinical history of varicella.

No mention of having antibody titres done.

From 1 July 2017 onwards, varicella vaccine will also be fully funded by PHARMAC as part of a universal mass vaccination (UMV) programme, via the National Immunisation Schedule (see *Varicella vaccine — soon to be available on the National Immunisation Schedule*).

Immigrants to NZ from tropical climates

In tropical regions, wild-type VZV is transmitted less efficiently than in other geographical regions. Adolescent and adult immigrants to New Zealand from tropical countries are therefore more likely to be susceptible to VZV infection. As such immigrants are beyond the childhood age range, if they contract varicella, they are more likely to experience severe symptoms.[1]

Steroid-treated children with asthma

Severe and sometimes fatal varicella has been documented in children with asthma or other conditions treated with intermittent high-dosage corticosteroids (>2 mg/kg prednisone, or equivalent). This risk is particularly elevated if corticosteroids are administered during the incubation period for VZV infection.[3]

Varicella vaccine — efficacy, effectiveness, and the importance of high coverage

Efficacy

Not the same as datasheets

In preventing confirmed varicella disease, a study involving a total of 4,542 children aged 12–22 months revealed that one dose of varicella vaccine prevented varicella of any severity in 65.4% of children, and prevented moderate or severe varicella in 90.7% of children;

No discussion on doing titre testing. Yet, medical literature shows that 62% of people without clinical history have immunity

corresponding efficacy rates for two doses of quadrivalent MMRV vaccine were 94.9% and 99.5%.[10,11]

In an earlier study designed specifically to assess vaccine efficacy after one dose of varicella vaccine, a total of 513 children aged 10–30 months were followed-up for approximately 2.5 years after vaccination. Protective efficacy was 100% against common clinical cases of varicella (≥30 vesicles) and 88% against any serologically confirmed case of varicella (≥1 vesicle or papule).[10,12]

The duration of immunity provided by varicella vaccination is long-term, and some suggest even lifelong.[3] Nonetheless, long-term studies are needed in regions with UMV programmes to determine the duration of immunity and protection from varicella in the absence of immune boosting from wild-type varicella virus.[1,13]

Effectiveness

The effectiveness of single-dose varicella vaccine has been evaluated in various settings: case-control studies, database studies, and outbreaks. It ranged from 20–92% against any varicella disease, and from 86–100% against moderate or severe disease. Moreover, in children, single-dose varicella vaccine reduced ambulatory visits for varicella by 87%, and hospitalisations for varicella by 81%. Importantly, two doses rather than one dose of varicella vaccine have frequently been associated with a greater degree of protection against varicella, and with a reduced incidence of breakthrough disease.[10,14–16] A US study assessing varicella vaccine effectiveness documented 98% effectiveness for a 2-dose schedule, compared with only 86% for a single-dose schedule. In addition, it was reported that 2-dose rather than 1-dose recipients were 3.3 times less likely to have breakthrough disease during the first 10 years after immunisation.[3,15]

A systematic review of varicella prevention in the United States with a single dose of varicella vaccine revealed that the vaccine was 80–85% effective in preventing varicella of any severity, and >95% effective in preventing severe disease; the vaccine had an excellent safety profile. Furthermore, the UMV programme reduced the incidence of varicella by 57–90%; hospitalisations by 75–88%; deaths by >74%; and direct in-patient and outpatient costs associated with varicella by 74%.[17]

Varicella vaccine — soon to be available on the National Immunisation Schedule

Because varicella is typically considered benign, varicella immunisation has traditionally been a low priority for funded universal immunisation schemes.[6] However, the major public health benefits of varicella immunisation programmes are unequivocal. In New Zealand, from 1 July 2017 onwards, PHARMAC will fully fund varicella vaccine on the National Immunisation Schedule (NIS) for children aged 15 months or previously unvaccinated children aged 11 years who have not been infected with chickenpox. That is, besides the existing subsidy for two doses of varicella vaccine in high-risk groups of immunocompromised patients (see *Immunocompromised individuals*), one dose of fully-funded *Varilrix** as primary vaccination will be offered to children born on or after 1 April 2016, at their 15-month immunisation event, and to children who turn age 11 years on or after 1 July 2017 if they have not previously been infected with chickenpox or vaccinated.[8]

In addition, a two-dose schedule of varicella vaccine is advocated (*but not funded*) in the following groups of adolescents and adults in New Zealand:[1,9]

- Those born and who resided in tropical countries and who have no previous history of varicella infection.
- Susceptible individuals with no previous history of chickenpox.
- Susceptible individuals living or working in environments where VZV transmission is likely (e.g. staff in early childhood education centres, residents and staff members in institutional settings).
- Susceptible individuals living and working in environments where transmission can occur (e.g. college students, inmates and staff members of correctional facilities, and military personnel).
- Susceptible non-pregnant women of childbearing age.
- Susceptible international travellers.
- Healthcare workers — all healthcare workers on obstetric, paediatric and neonatal units, and those caring for immunosuppressed patients, should be immunised with varicella vaccine if they are susceptible to varicella.
- Susceptible individuals who have been exposed to varicella. *Although not currently funded for post-exposure prophylaxis, from 1 July 2017 onwards, a two-dose schedule of* Varilrix *will be fully funded for post-exposure prophylaxis in immunocompetent in-patients.*

* *Varilrix* is a monovalent vaccine that contains no less than $10^{3.3}$ plaque-forming units of the varicella virus (Oka strain). Other components and residuals include amino acids, human albumin, lactose, neomycin sulphate, and polyalcohols.

Varilrix is human albumin free actually.

Varilrix dosage

Varilrix is administered subcutaneously as 0.5 mL of reconstituted vaccine. The upper arm (deltoid region) is the preferred site of injection. Due to minor pH variations, colour of the reconstituted vaccine may vary from a clear peach to pink. Varicella vaccine should be injected as soon as possible after reconstitution.[10]

In children aged 9 months to 12 years, two doses of *Varilrix* (given ≥6 weeks apart) are recommended to maximise the seroconversion rate against VZV. *[N.B PHARMAC funding from 1 July 2017 onwards will be available for only one dose of* Varilrix*].*[10]

In susceptible individuals aged ≥13 years, two doses of *Varilrix* (given ≥6 weeks apart) are recommended. *[N.B. PHARMAC funding for* Varilrix *is currently available for high-risk individuals only (see* Immunocompromised individuals*)].*[10]

The importance of high varicella vaccination coverage

Single-dose UMV programmes for varicella have markedly reduced the incidence of VZV infection,[18–20] hospitalisations,[21–23] and serious outcomes,[24] especially when high coverage rates are attained.[1] Indeed, dramatic decreases in varicella morbidity, hospitalisations (**Figures 2 & 3**) and mortality were noted after varicella vaccine was introduced into UMV programmes in the United States in 1995, Canada in 2000, Germany in 2004, and Australia in 2005.[21,22,24–30] Italy (Sicily) also introduced UMV for varicella in 2003: as varicella vaccination coverage increased, marked decreases in the incidence of varicella, and in hospitalisations for varicella, were noted.[31] Nonetheless, single-dose vaccination programmes are linked with outbreaks, even when high coverage rates are achieved.[9,32] During outbreaks, a second vaccine dose has proved effective in preventing further cases, and 'catch-up' vaccinations in non-immunised groups without a varicella history are also important.[1]

Potential to further enhance varicella vaccination coverage in New Zealand

As previously mentioned, a greater level of protection against varicella, and a reduced incidence of breakthrough varicella, are attained after two doses rather than one dose of varicella vaccine.[10] However, it is likely that one dose will prevent most hospitalisations and more severe cases, as has been seen in other countries. Via the NIS (from 1 July 2017 onwards), one dose of varicella vaccine will be fully funded in children aged 15 months or previously unvaccinated children aged 11 years that have not been infected with chickenpox. Parents of young children will have the option to pay for an additional dose of varicella vaccine at any time after 9 months of age, as long as there is a period of at least 6 weeks between doses (**Table 1**).

Unequivocally, major drivers for uptake of any 2-dose vaccine schedule are reduced vaccination costs to parents, vaccine-schedule acceptability and feasibility for point-of-care healthcare professionals, and physician or nurse recommendation to parents.[33] Many healthcare professionals may perceive that the injection 'burden' to young children at the NIS age 15 months immunisation (from 1 July 2017 onwards, four injections; **Table 1**) has some potential to be reduced.

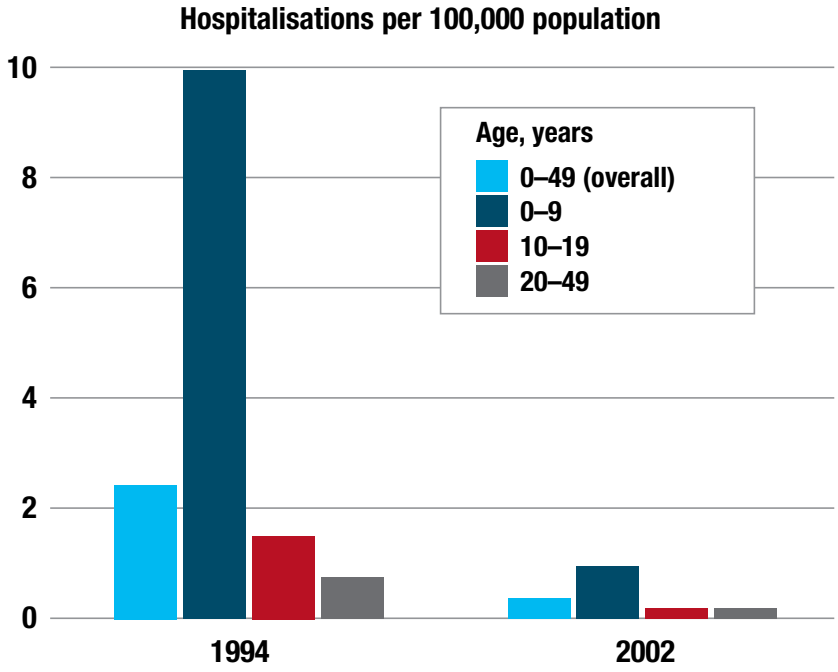

Figure 2. Reduced rate of hospitalisations due to varicella after introduction of a single-dose UMV programme in the United States in 1995 (adapted from Wutzler et al.[15]).

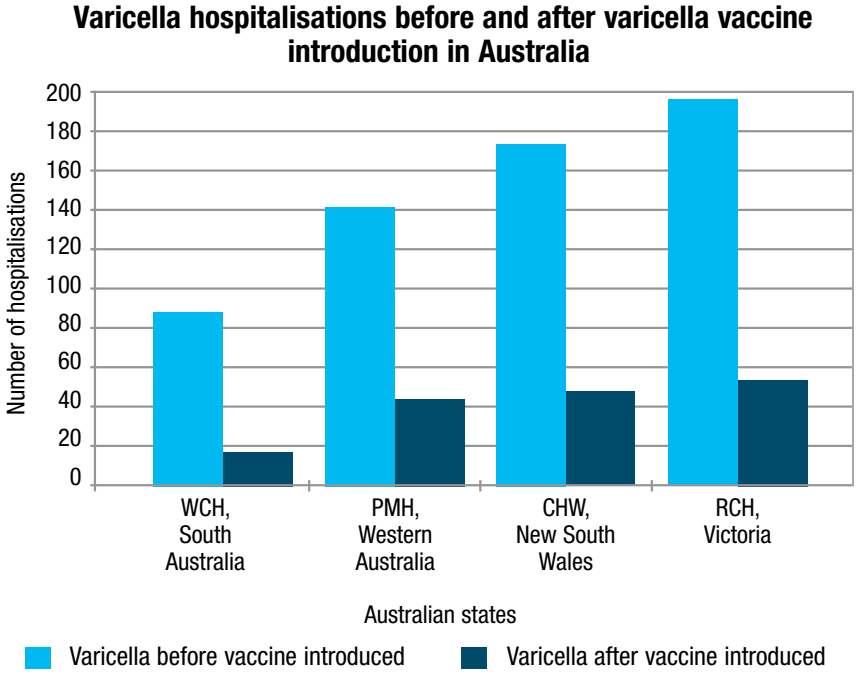

Figure 3. Varicella hospitalisations before (1999–2001) and after (2007–2010) introduction of varicella vaccination in Australia in 2005 (adapted from Marshall et al.[31]). Overall, a statistically significant ($p<0.001$) 73% decrease in the occurrence of varicella was noted after implementation of mass vaccination for the disease.CHW, The Children's Hospital at Westmead; PMH, Princess Margaret Hospital for Children; RCH, Royal Children's Hospital; WCH, Women's and Children's Hospital.

Note the increase of shingles in USA from 1995 - IMO the rampantly increased use of asthma drugs, transplant drugs, cyclosporine, tacrolimus, TNf alpha inhibitors and monoclonal antibodies which are made in rodent tumours.. Nice. But all these drugs wreck the cellmediated immune system and cause in increase in all infectious diseases

Table 1. NIS vaccinations at age 15 months and 4 years (from 1 July 2017 onwards)[8,34]

Child age	Vaccinations
15 months	*Haemophilus influenzae* type b (1 injection; *Hiberix*)
	MMR (1 injection; *Priorix*)
	Pneumococcal vaccine (1 injection; *Synflorix*)
	Varicella vaccine (1 injection; *Varilrix*)
4 years	Diphtheria/tetanus/pertussis/polio (1 injection; *Infanrix®-IPV*)
	MMR (1 injection; *Priorix*)

MMR, measles-mumps-rubella.

Effects on the epidemiology of herpes zoster virus

Approximately 1 in 3 people, or half those aged >80 years, and who have a history of varicella, will develop shingles at some stage.[3] The risk of shingles is approximately 10-fold lower in individuals immunised against herpes zoster virus (HZV).

In regions where UMV programmes have been undertaken with varicella vaccine, reduced exposure to wild-type VZV occurs. Adults are therefore less likely to boost immunity to latent HZV infection (shingles). It has been suggested that a lack of boosting may result in an increased incidence and severity of shingles in older adults.[1] In the United States, where wild-type varicella is nearly eradicated, immunisation against HZV is now recommended for all individuals aged >60 years.[3]

However, no increase in the incidence of shingles in adults of any age occurred in the United States from 1992 to 2002 (UMV for varicella was introduced in the United States in 1995). Over the 10-year timeframe, the incidence of varicella in children decreased from 2.63 to 0.92 cases per 1,000 person-years; the age-adjusted rate of shingles was relatively unaltered at 4.05 cases (1992) and 3.70 cases (2002) per 1,000 person-years.[35] In the United Kingdom and Canada, documented increases in the incidence of shingles were not related to varicella immunisation,[1] and in some US studies, rates of HZV infection were already increasing before the UMV programme for varicella was started.[36,37] Obviously, it should be remembered that, in New Zealand, the incidence of shingles will rise in line with population ageing.[1]

Overall, it remains uncertain whether childhood UMV for varicella significantly alters the epidemiology of HZV infection. Studies investigating this topic, including some from Australia, have been unable to show a definitive link between an increased incidence of shingles and childhood varicella immunisation.[38,39]

Expert comment: So far, no data have clearly shown a link between rising zoster in adults and eradication of wild-type varicella by vaccination in children. There is a risk of vaccine-type herpes zoster persisting as vaccinees get older. However, at least one study has shown that there are fewer cases of zoster in vaccinated than unvaccinated children, which is encouraging.

How safe is varicella vaccine?

Typically, adverse events from varicella-containing vaccines are mild and self-limiting. Up to one-quarter of vaccinees experience minor injection-site reactions, such as pain, redness and swelling. In approximately 1–3% of immunised children, a localised rash manifests. In a further 3–5% of children, a generalised varicella-like rash occurs. Usually, these rashes comprise 2–5 lesions, are maculopapular rather than vesicular, and appear 5–26 days after vaccination.[1,3]

In healthy vaccinees, transmission of vaccine virus has been extremely rare, with only 10 documented cases in 9 vaccinees (1 individual transmitted the virus to 2 other people), usually after household exposure.[1]

Serious adverse events, such as anaphylaxis, meningitis, shingles requiring hospitalisation, encephalitis, ataxia, erythema multiforme, Stevens-Johnson syndrome, pneumonia, thrombocytopenia, seizures, neuropathy, Guillain-Barré syndrome, secondary bacterial infections, and death have been documented rarely (postmarketing surveillance data from the United States indicate an incidence of <4 in 100,000 vaccinations) relative to the time of varicella vaccine administration. In most instances, data were inadequate to determine a causal link.[3]

Risks of low varicella vaccination coverage

If varicella vaccine coverage is inadequate, relatively high levels of circulating wild-type VZV will exist, thus creating potential for increased rates of varicella and its complications in healthy children, and in high-risk groups such as immunocompromised individuals and pregnant women (see *Which individuals are at risk?*). An important aspect of persistence of circulating wild-type VZV (because of inadequate vaccination coverage) in younger age groups is that disease incidence may be 'pushed' into older age groups and adolescents. Vaccination of non-immune adolescents may then be warranted and, indeed, several countries fund 'catch-up' immunisation for adolescents.[27,28]

Also of major importance is the potential for breakthrough disease, which can be significantly reduced if two doses rather than one dose of varicella vaccine are given.[1] Breakthrough varicella may occur in up to 20–30% of children who receive a single dose of varicella vaccine.[40] In children who receive a second dose of varicella vaccine, the immune response is considerably improved: more than 99% of children attain a response deemed protective, and the geometric mean titre of varicella antibodies is also significantly increased.[1]

As previously stated (see *Effectiveness*), over a 10-year period in the United States, the estimated preventive efficacy of a 2-dose varicella vaccine schedule was 98% (compared with only 86% for a single-dose schedule); the 2-dose schedule was 100% effective in preventing severe varicella. Furthermore, individuals given two doses rather than one dose were 3.3 times less likely to have breakthrough disease during the first 10 years after immunisation.[3,14] For these reasons, a 2-dose strategy for varicella prevention was introduced in the United States in 2006: the first dose of varicella vaccine is given at age 12–15 months, and the second at age 4–6 years.[1]

In New Zealand, many parents and healthcare professionals will consider the impending 1 July amendment to varicella funding in the NIS to be a major step in the right direction; subsequently, and in line with international trends, an additional dose of varicella vaccine may become funded when wild-type varicella boosting has stopped.

TAKE-HOME MESSAGES:

- Almost all children get varicella. Hundreds of children are hospitalised each year with the disease, and hospitalisations are increasing.
- Varicella is a severe and sometimes fatal disease, especially in immunocompromised individuals. Non-immune pregnant women, their unborn babies, and newborns are also especially susceptible to VZV infection.
- Varicella vaccine is effective and well tolerated. Typically, adverse events are mild and self-limiting.
- Single-dose UMV programmes for varicella have markedly reduced the incidence of VZV infection, hospitalisations, and serious outcomes, but outbreaks of varicella can still occur, even when high coverage rates are achieved.
- From 1 July 2017 onwards, PHARMAC will fully fund one dose of varicella vaccine (*Varilrix*) on the NIS for children aged 15 months or for previously unvaccinated children aged 11 years. Parents will have the option to pay for an additional dose of varicella vaccine, which can be given any time from 9 months of age (as long as 6 weeks apart).
- Breakthrough varicella may occur in up to 20–30% of children who receive a single dose of varicella vaccine.
- Two doses rather than one dose of varicella vaccine have frequently been associated with a greater degree of protection against varicella, and with a reduced incidence of breakthrough disease.
- Many parents and healthcare professionals will consider the impending 1 July amendment to varicella funding in the NIS to be a significant step in the right direction towards decreasing varicella rates.

EXPERT COMMENTARY

In New Zealand, it is an exciting time for healthcare professionals. With recent universal offering of rotavirus vaccine, and now varicella vaccine, clinicians are witnessing impressive reductions in vaccine-preventable diseases that have caused significant morbidity in our community. Rotavirus and varicella should become rare diseases, rather than a normal childhood experience. Introduction of varicella immunisation programmes can be done as either one- or two-dose strategies; vaccine can be given concomitantly with MMR and, if two doses are used, the timing between doses needs to be considered to gain the quickest decrease in circulating virus. Also important are catch-up doses to ensure non-immune older children and teenagers do not become a group of susceptible adults.

It is apparent that with high vaccine coverage, a single dose may be enough to reduce circulating varicella. Ultimately, however, most countries that introduce varicella vaccine start with one dose, then opt for a two dose schedule to improve vaccine effectiveness and prevent persistent breakthrough disease and outbreaks. A two-dose schedule will improve vaccine coverage and effectiveness. Importantly, high coverage is critical for effective 'herd immunity' to protect individuals unable to be vaccinated, such as the immunocompromised, who cannot be vaccinated, young children, and newborn infants. The quickest way to achieve effective herd immunity and prevent breakthrough infections would be to start with a two-dose regimen in the NIS. However, important gains regarding reduced severe cases and hospitalisations from varicella will be achieved with universal varicella vaccination as one dose, as long as high coverage is achieved and we ensure that pre-teens (11-year-olds) are offered the free catch-up dose of varicella vaccine.

REFERENCES

1. NZ Ministry of Health. Immunisation Handbook 2014 (3rd edn). Available from: http://www.health.govt.nz/system/files/documents/publications/imm-handbk-2014-3rd-edn-dec16.pdf [accessed 2 January 2017].
2. Anderson RM, May RM. Directly transmitted infections diseases: control by vaccination. *Science* 1982;215(4536):1053–60.
3. American Academy of Pediatrics. Red Book. 2012 Report of the Committee on Infectious Diseases. 29th edition. Available from: https://redbook.solutions.aap.org/DocumentLibrary/RB12_interior.pdf [accessed 2 January 2017].
4. Wang L, Zhu L, Zhu H. Efficacy of varicella (VZV) vaccination: an update for the clinician. *Ther Adv Vaccines* 2016;4(1-2):20–31.
5. van Lier A, van der Maas NA, Rodenburg GD, et al. Hospitalization due to varicella in the Netherlands. *BMC Infect Dis* 2011;11:85.
6. Wen SC, Miles F, McSharry B, Wilson E. Varicella in a paediatric intensive care unit: 10-year review from Starship Children's Hospital, New Zealand. *J Paediatr Child Health* 2014;50(4):280–5.
7. Wen SC, Best E, Walls T, et al. Prospective surveillance of hospitalisations associated with varicella in New Zealand children. *J Paediatr Child Health* 2015;51:1078–83.
8. NZ Ministry of Health. 2017 Immunisation Schedule change. Available from: http://www.health.govt.nz/our-work/preventative-health-wellness/immunisation/new-zealand-immunisation-schedule/2017-immunisation-schedule-change [accessed 3 January 2017].
9. Marin M, Guris D, Chaves SS, et al. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2007;56(RR-4):1–40.
10. GlaxoSmithKline NZ Ltd. New Zealand data sheet. Varilrix. Live attenuated varicella vaccine. Available from: http://www.medsafe.govt.nz/profs/Datasheet/v/Varilrixinj.pdf [accessed 4 January 2017].
11. Prymula R, Bergsaker MR, Esposito S, et al. Protection against varicella with two doses of combined measles-mumps-rubella-varicella vaccine versus one dose of monovalent varicella vaccine: a multicentre, observer-blind, randomised, controlled trial. *Lancet* 2014;383(9925):1313–24.
12. Varis T, Vesikari T. Efficacy of high-titer live attenuated varicella vaccine in healthy young children. *J Infect Dis* 1996;174 Suppl 3:S330–4.
13. Tafuri S, Gallone MS, Gallone MF, et al. Evaluation of a vaccination strategy by serosurveillance data: The case of varicella. *Hum Vaccin Immunother* 2015;11(4):897–900.
14. Prevention of varicella: recommendations for use of varicella vaccines in children, including a recommendation for a routine 2-dose varicella immunization schedule. *Pediatrics* 2007;120(1):221–31.
15. Wutzler P, Knuf M, Liese J. Varicella: efficacy of two-dose vaccination in childhood. *Dtsch Arztebl Int* 2008;105(33):567–72.
16. Brisson M, Melkonyan G, Drolet M, et al. Modeling the impact of one- and two-dose varicella vaccination on the epidemiology of varicella and zoster. *Vaccine* 2010;28(19):3385–97.
17. Marin M, Meissner HC, Seward JF. Varicella prevention in the United States: a review of successes and challenges. *Pediatrics* 2008 Sep;122(3):e744–51.
18. Pozza F, Piovesan C, Russo F,et al. Impact of universal vaccination on the epidemiology of varicella in Veneto, Italy. *Vaccine* 2011;29(51):9480–7.
19. Chang LY, Huang LM, Chang IS, Tsai FY. Epidemiological characteristics of varicella from 2000 to 2008 and the impact of nationwide immunization in Taiwan. *BMC Infect Dis* 2011;11:352.
20. Siedler A, Arndt U. Impact of the routine varicella vaccination programme on varicella epidemiology in Germany. *Euro Surveill* 2010;15(13).
21. Lopez AS, Zhang J, Brown C, Bialek S. Varicella-related hospitalizations in the United States, 2000-2006: the 1-dose varicella vaccination era. *Pediatrics* 2011;127(2):238–45.
22. Shah SS, Wood SM, Luan X, Ratner AJ. Decline in varicella-related ambulatory visits and hospitalizations in the United States since routine immunization against varicella. *Pediatr Infect Dis J* 2010;29(3):199–204.
23. Tan B, Bettinger J, McConnell A, et al. The effect of funded varicella immunization programs on varicella-related hospitalizations in IMPACT centers, Canada, 2000-2008. *Pediatr Infect Dis J* 2012;31(9):956–63.
24. Khandaker G, Marshall H, Peadon E, et al. Congenital and neonatal varicella: impact of the national varicella vaccination programme in Australia. *Arch Dis Child* 2011;96(5):453–6.
25. Patrick D. Prevention strategies: experience of varicella vaccination programmes. *Herpes* 2007;14 Suppl 2:48–51.
26. Zhou F, Harpaz R, Jumaan AO, et al. Impact of varicella vaccination on health care utilization. *JAMA* 2005;294(7):797–802.
27. Baxter R, Tran TN, Ray P, et al. Impact of vaccination on the epidemiology of varicella: 1995-2009. *Pediatrics* 2014;134(1):24–30.
28. Leung J, Bialek SR, Marin M. Trends in varicella mortality in the United States: Data from vital statistics and the national surveillance system. *Hum Vaccin Immunother* 2015;11(3):662–8.
29. Waye A, Jacobs P, Tan B. The impact of the universal infant varicella immunization strategy on Canadian varicella-related hospitalization rates. *Vaccine* 2013;31(42):4744–8.
30. Amodio E, Tramuto F, Cracchiolo M, et al. The impact of ten years of infant universal Varicella vaccination in Sicily, Italy (2003-2012). *Hum Vaccin Immunother* 2015;11(1):236–9.
31. Marshall HS, McIntyre P, Richmond P, et al. Changes in patterns of hospitalized children with varicella and of associated varicella genotypes after introduction of varicella vaccine in Australia. *Pediatr Infect Dis J* 2013;32:530–7.
32. Lopez AS, Guris D, Zimmerman L, et al. One dose of varicella vaccine does not prevent school outbreaks: is it time for a second dose? *Pediatrics* 2006;117(6):e1070–7.
33. Gustafson R, Skowronski DM. Disparities in varicella vaccine coverage in the absence of public funding. *Vaccine* 2005;23(27):3519–25.
34. NZ Ministry of Health. New Zealand Immunisation Schedule. Available from: http://www.health.govt.nz/our-work/preventative-health-wellness/immunisation/new-zealand-immunisation-schedule [accessed 4 January 2017].
35. Jumaan AO, Yu O, Jackson LA, et al. Incidence of herpes zoster, before and after varicella-vaccination-associated decreases in the incidence of varicella, 1992-2002. *J Infect Dis* 2005;191(12):2002–7.
36. Reynolds MA, Chaves SS, Harpaz R, et al. The impact of the varicella vaccination program on herpes zoster epidemiology in the United States: a review. *J Infect Dis* 2008;197 Suppl 2:S224–7.
37. Hales CM, Harpaz R, Joesoef MR, Bialek SR. Examination of links between herpes zoster incidence and childhood varicella vaccination. *Ann Intern Med* 2013;159(11):739–45.
38. Carville KS, Riddell MA, Kelly HA. A decline in varicella but an uncertain impact on zoster following varicella vaccination in Victoria, Australia. *Vaccine* 2010;28(13):2532–8.
39. Leung J, Harpaz R, Molinari NA, et al. Herpes zoster incidence among insured persons in the United States, 1993-2006: evaluation of impact of varicella vaccination. *Clin Infect Dis* 2011;52(3):332–40.
40. Ozaki T. Long-term clinical studies of varicella vaccine at a regional hospital in Japan and proposal for a varicella vaccination program. *Vaccine* 2013;31(51):6155–60.