

## 21 Varicella (chickenpox)

### Key information

Mode of transmission	Airborne droplets from, or contact with, vesicular lesions or possibly respiratory secretions.
Incubation period	Usually 14–16 days (range 10–21 days).
Period of communicability	From 2 days before onset of the rash until all lesions have crusted.
Burden of disease	Without immunisation, most people have infection during childhood. Groups at risk of severe complications include pregnant women and their unborn babies, and immunocompromised individuals.
Funded vaccine	VV (Varilrix) is a live attenuated vaccine.
Dose, presentation, route	0.5 mL per dose after reconstitution. Pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. Subcutaneous injection.
Vaccine indications and schedule	1 dose is funded for: <ul style="list-style-type: none"> <li>• children at age 15 months (for those who were born on or after 1 April 2016); or</li> <li>• previously unvaccinated children turning 11 years old on or after 1 July 2017 who have not previously had a varicella infection (as determined by clinical history).</li> </ul> Up to 2 doses are funded for certain special groups and their contacts. Recommended but not funded for: <ul style="list-style-type: none"> <li>• susceptible children who are not eligible by age for funded vaccine</li> <li>• susceptible adolescents and adults.</li> </ul>
Vaccine efficacy/effectiveness	1 dose confers approximately 99% protection against severe disease and 80% protection against varicella disease of any severity. Breakthrough disease is usually mild.

*Continued overleaf*

Contraindications	Certain immune deficiency states – consult the child's paediatrician for advice. High-dose steroids. Known systemic hypersensitivity to neomycin. Active untreated TB. Pregnancy.
Adverse events to vaccine	Generally mild and self-limiting, and include local reactions, fever and mild papulo-vesicular rash in normal healthy individuals.
Post-exposure prophylaxis	Zoster immunoglobulin (ZIG) is most effective if given as soon as possible after exposure but may be given up to 10 days post-exposure. VV may be used for post-exposure prophylaxis for immune-competent people if given within 5 days of exposure.

## 21.1 Virology

Varicella (chickenpox) is a highly infectious disease caused by human herpes virus type 3 (varicella zoster virus or VZV). Reactivation of latent VZV results in herpes zoster (HZ) (shingles), a disease with considerable morbidity (see chapter 22).

## 21.2 Clinical features

Varicella is one of the most infectious diseases known (along with pertussis and measles). Transmission occurs via airborne droplets from, or contact with, vesicular lesions and possibly respiratory tract secretions. The incubation period is usually 14 to 16 days (range 10 to 21 days, but can be longer in immunocompromised individuals and those who have received ZIG), and cases are infectious from 2 days before the onset of the rash until all the lesions have crusted. A maculopapular rash, which becomes vesicular, appears in crops over several days, first on the face and scalp, later spreading to the trunk and then the limbs. Vesicles, ranging in number from few to many hundred, dry and crust after three to four days. A hallmark of the rash is lesions in varying stages of development; those on mucosal surfaces (mouth, vagina) can cause considerable distress. The rash is pruritic and is usually associated with mild fever, malaise, anorexia and listlessness.

In the majority of children, varicella is a mild disease, but complications requiring hospitalisation and fatalities do occur. Secondary bacterial skin infections are common. Serious complications include central nervous system involvement (encephalitis, cerebellar ataxia, stroke), pneumonia, secondary invasive bacterial infections, and even death. Adults are 25 times more likely to develop severe disease than children, with pneumonia being the most common complication, often requiring mechanical ventilation. VZV pneumonia carries an overall mortality rate of 10–30 percent.

Maternal varicella occurring in the first half of pregnancy can cause the rare but devastating congenital varicella syndrome (see Table 21.4), whereas disease very late in pregnancy (from five days before to two days after delivery) may cause severe neonatal varicella infection. Pregnant women who contract varicella have an estimated 10–20 percent risk of developing VZV pneumonia.

Others vulnerable to both VZV and HZ are those who are immunocompromised, such as people taking immunosuppressive medications (eg, cancer treatment or organ transplant patients) and those with HIV infection. Varicella can be a fatal disease in immunocompromised individuals.

VZV infection is followed by the production of VZV-specific T-cell mediated immunity, necessary to maintain the latency of VZV in the ganglia and prevent reactivation as shingles (HZ). The immune response is boosted by subclinical reactivation of latent virus. The incidence of HZ increases with age as VZV-specific T cell-mediated immunity declines (see chapter 22).

## 21.3 Epidemiology

### 21.3.1 Global burden of disease

In temperate climates, winter-spring epidemics occur with peak incidence in preschool and early primary school ages (1–9 years). Around 90 percent of individuals have been infected by adolescence and fewer than 5 percent of adults are susceptible. The annual number of infections therefore approximates the birth cohort.<sup>1, 2</sup>

Transmission of the virus is less efficient in tropical climates. Adolescent and adult immigrants to New Zealand from such countries are more likely to be susceptible, placing them at risk of contracting chickenpox in their new environment. Being older, they are more likely to suffer severe disease.

The long incubation and high transmissibility of VZV conspire to maximise disruption to families: by the time the rash occurs a child will have been infectious for two days; any susceptible household contacts will then become unwell just as the first child recovers. This results not only in morbidity but also in financial consequences for parents missing work.

Crude hospitalisation admission rates in high-income countries range from around 2–6 per 100,000 population-year. Most of these admissions are children, consistent with the high incidence of varicella in children. Crude mortality rates ranged from 0.3–0.5 per million population-year with overall case fatality ratios of around 2–4 per 100,000 cases. Almost 90 percent of varicella hospital admissions occur in otherwise healthy and immunocompetent individuals.<sup>1, 2</sup>

VV has been introduced into childhood immunisation programmes overseas, including the US from 1995 and Australia from 2005 with dramatic reductions in varicella morbidity, hospitalisations and mortality.<sup>3, 4, 5</sup> By 2005 in the US, vaccine coverage was approximately 90 percent and varicella incidence had declined by more than 90 percent. Herd immunity was observed outside of age groups targeted for vaccination.<sup>1</sup>

Following the introduction of VV onto the childhood schedule, exposure to wild-type virus decreases. It has been theorised that a lack of boosting may lead to an increase in HZ in older adults. However, studies that have investigated this issue have been unable to attribute any increase in incidence of HZ to the childhood VZV vaccine programme.<sup>6, 7</sup> Studies from the UK and Canada reported increases in HZ not associated with a vaccination programme, and some US data showed HZ rates were increasing prior to the initiation of their varicella vaccination programme.<sup>8, 9</sup>

### 21.3.2 New Zealand epidemiology

Varicella is not a notifiable disease, so data is limited for uncomplicated varicella, but the epidemiology is likely to be as described above for temperate climates. With increasing participation in early childhood services, a greater proportion of infections may now be occurring in preschool-aged children. It is expected that HZ numbers will rise in New Zealand as the population ages.

Prospective nationwide surveillance of varicella in New Zealand children found that the incidence of varicella-related hospitalisation was 8.3 per 100,000 children per year – although this is likely to be a significant underestimate.<sup>10</sup> Māori and Pacific children were disproportionately affected, with an almost three- and four-fold increase in the relative risk of hospitalisation for varicella or its complications, respectively. Nine percent of hospitalised children required ICU admission and the majority of them were previously healthy. Almost one-third of hospitalised children had multiple complications from varicella, and those with neurological complications were more likely to have ongoing problems at discharge.

A retrospective survey of admissions to the paediatric intensive care unit (PICU) at Auckland's Starship Hospital (2001–2011) found 26 children admitted for varicella or its secondary complications.<sup>11</sup> The main PICU admission reasons were neurological (38.5 percent) and secondary bacterial sepsis or shock (26.9 percent). Four children died (15 percent), three of whom were immunocompromised. A further eight children (31 percent) had ongoing disability at discharge, most having had no prior medical condition.

Based on overseas rates, it is estimated that up to one case of congenital varicella syndrome may be expected in New Zealand each year, although few have been reported.

Adults (aged 20 years and older) account for 20–24 percent of VZV-related hospital admissions;<sup>12</sup> approximately one person per year dies from VZV, and most of the VZV-related deaths occur in adults.<sup>13</sup>

## 21.4 Vaccines

### 21.4.1 Available vaccines

There are two live attenuated monovalent VVs registered (approved for use) and available (marketed) in New Zealand. Two quadrivalent live attenuated MMRV vaccines are registered but not currently available in New Zealand.

#### Funded vaccine

Each 0.5 mL dose of monovalent VV (Varilrix, GSK) contains no less than  $10^{3.3}$  PFU (plaque-forming units) of the varicella virus (Oka strain). Other components and residuals include amino acids, lactose, neomycin sulphate and polyalcohols (mannitol and sorbitol).

#### Other vaccines

##### *Monovalent VV*

- Monovalent VV (Varivax, MSD) contains not less than 1,350 PFU of the varicella virus (Oka/Merck strain). Other components and residuals include sucrose, gelatin, urea, sodium chloride, monosodium L-glutamate, potassium chloride, MRC-5 cells, neomycin and bovine calf serum.

##### *Quadrivalent MMRV*

- MMRV (ProQuad, MSD) contains not less than 3.00  $\log_{10}$  TCID<sub>50</sub> (50 percent tissue culture infectious dose) of Enders' attenuated Edmonston strain measles virus; 4.30  $\log_{10}$  TCID<sub>50</sub> of Jeryl Lynn strain mumps virus; 3.00  $\log_{10}$  TCID<sub>50</sub> of Wistar RA 27/3 rubella virus; and a minimum of 3.99  $\log_{10}$  PFU of Oka/Merck varicella virus. Other components and residuals include sucrose, gelatin, urea, sodium chloride, sorbitol, monosodium L-glutamate, sodium phosphate, human albumin, sodium bicarbonate, potassium phosphate, potassium chloride, neomycin, bovine serum albumin, and residual components of MRC-5 cells, including DNA and protein.

- MMRV (Priorix-Tetra, GSK) contains not less than  $10^{3.0}$  CCID<sub>50</sub> of the Schwarz measles, not less than  $10^{4.4}$  CCID<sub>50</sub> of the RIT 4385 mumps, not less than  $10^{3.0}$  CCID<sub>50</sub> of the Wistar RA 27/3 rubella and not less than  $10^{3.3}$  PFU of the varicella virus strains. Excipients and residuals include lactose, amino acids, mannitol, sorbitol, neomycin sulphate (residual), and water for injections.

See also section 11.4.1 for more information about MMR vaccines. Note that MMRV vaccines are not currently available in New Zealand.

### 21.4.2 Efficacy and effectiveness

Single-dose varicella vaccination programmes have had a dramatic impact on the incidence of VZV infections,<sup>14, 15, 16</sup> hospitalisations<sup>3, 4, 17</sup> and serious outcomes,<sup>5</sup> particularly when high coverage rates are achieved. Indirect effects are also apparent. A 2014 systematic review of varicella vaccines found that a single dose of VV is moderately effective for preventing any severity of varicella (approximately 80 percent) in immune-competent individuals, highly effective for preventing moderate-severe disease (approximately 95 percent) and highly effective in preventing severe disease only (approximately 99 percent).<sup>18</sup> However, single-dose programmes are associated with outbreaks even among highly vaccinated groups.<sup>19</sup> The use of a second dose during outbreaks has been an effective strategy to prevent further cases; catch-ups in non-immunised groups without a previous history of varicella are also important.

There is a significant reduction in breakthrough disease when two doses are given. After a second dose in children the immune response is markedly enhanced, with over 99 percent of children attaining an immune response thought to provide protection, and the geometric mean antibody titre is also significantly increased.

Over a 10-year period the estimated vaccine efficacy of two doses for prevention of any varicella disease is 98 percent (compared to 94 percent for a single dose), with 100 percent efficacy for the prevention of severe varicella. The likelihood of breakthrough varicella is reduced by a factor of 3.3.<sup>20, 21</sup> Because of this data, in 2006 the US authorities recommended a two-dose strategy for varicella prevention, with the first dose at age 12–15 months and the second at age 4–6 years, as for MMR.<sup>19, 20</sup>

The antigenic components of MMRV vaccines are non-inferior compared with simultaneous administration of MMR and VV,<sup>22, 23</sup> for both the first and second doses.

## **Herd immunity**

In regions where universal varicella vaccination programmes have been implemented, significant declines in varicella cases and hospitalisation have been observed. These programmes also reduce circulating VZV and provide protection through herd immunity for those who are unable to be immunised, such as infants and immunocompromised individuals.

In the US, the annual average age-adjusted mortality rate for varicella was 0.05 per million population during 2008–2011, an 87 percent reduction from the pre-vaccine years.<sup>24</sup> In Canada between 2000 and 2007, a single dose of VV was introduced to the immunisation schedules of different provinces at 12 months of age; most provinces also included catch-ups for susceptible children at preschool or school. An ecological study of varicella-related hospitalisations in Canada between 1990 and 2010 found that hospitalisation rates decreased in all age groups, including infants and those aged 20–39 years.<sup>25</sup> Similar herd effects were seen in Germany, with declines in varicella cases and hospitalisations in infants and adolescents who were not eligible for VV.<sup>26</sup>

## **Duration of immunity**

Varicella vaccination provides long-term but probably not lifelong immunity against VZV, in contrast to VZV natural infection. The duration of protection after a single dose of vaccine is difficult to study – especially if wild-type varicella continues to circulate liberally in the community, providing natural boosting and prolonging the duration of protection.<sup>18</sup> Many countries that initially introduced a single-dose vaccination programme have subsequently changed to a two-dose programme as the epidemiology of the disease has changed over time.

### **21.4.3 Transport, storage and handling**

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.<sup>27</sup>

VV requires reconstitution before administration.

Varilrix is presented as a lyophilised powder for reconstitution with the supplied diluent. The vaccine should be stored in the refrigerator at +2°C to +8°C, although the diluent may be stored at room temperature (to a maximum of 25°C). Reconstituted vaccine should be used immediately. However, if this is not possible, it may be kept for up to 90 minutes at room temperature (to a maximum of 25°C) and up to eight hours in the refrigerator (+2°C to +8°C).

#### **21.4.4 Dosage and administration**

The dose of monovalent VV is 0.5 mL, administered by subcutaneous injection in the deltoid area (see section 2.2.3).

#### **Co-administration with other vaccines**

Monovalent VV can be administered concurrently with other vaccines, but in a separate syringe and at a different site. If not administered concurrently, the vaccine must be separated from other live vaccines (eg, MMR, BCG) by at least four weeks.

### **21.5 Recommended immunisation schedule**

Recommendations for VV are summarised in Table 21.1 and discussed below.

VV can be administered at age 15 months with MMR, Hib and PCV10 vaccines. Because the risk of febrile seizures for those aged 12–23 months is higher following MMRV than MMR+VV (see section 21.7), this dose should be administered as monovalent VV. (This requires four injections at the 15-month visit; see section 2.2.7.) For a second (currently unfunded) dose of VV, or first doses after age 4 years, either VV or MMRV (when available) can be used.

**Table 21.1: Varicella vaccine recommendations and schedule**

**Recommended and funded**

1 dose of VV for:

- children at age 15 months (who were born on or after 1 April 2016); or
- previously unvaccinated children turning 11 years old on or after 1 July 2017 who have not previously had a varicella infection.

2 doses of VV, at least 6 weeks apart, for the following special groups:<sup>a</sup>

- non-immune patients:
  - with chronic liver disease who may in future be candidates for transplantation<sup>b</sup>
  - with deteriorating renal function before transplantation<sup>b</sup>
  - prior to solid organ transplant
  - prior to any elective immunosuppression<sup>c</sup>
  - for post-exposure prophylaxis of immune-competent in-patients
- patients at least 2 years after bone marrow transplantation, on the advice of their specialist
- patients at least 6 months after completion of chemotherapy, on the advice of their specialist
- HIV-positive patients who are non-immune to varicella, with mild or moderate immunosuppression, on the advice of an HIV specialist
- patients with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella
- household contacts of paediatric patients who are immunocompromised or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella
- household contacts of adult patients who have no clinical history of varicella and who are severely immunocompromised or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella.

**Recommended, not funded**

1 dose for all susceptible healthy children aged under 13 years who do not meet the eligibility criteria for the funded dose.

2 doses, at least 6 weeks apart, for all susceptible adolescents and adults.

- a See chapter 4 'Immunisation of special groups' for more information.
- b See Table 4.1 for an accelerated immunisation schedule for infants in whom liver or kidney transplant is likely.
- c Note that immunosuppression due to steroid or other immunosuppressive therapy must be for a treatment period of greater than 28 days.

### **21.5.1 Usual childhood schedule**

From 1 July 2017, one dose of VV (Varilrix) is funded for children at age 15 months (who were born on or after 1 April 2016). A second VV dose is not currently funded but may be purchased for those who wish to reduce the risk of breakthrough disease.

A catch-up dose of VV is funded for previously unvaccinated children turning 11 years old on or after 1 July 2017 who have not previously had a varicella infection (as determined by clinical history). This dose aims to protect those who have not become immune to varicella before adolescence, as disease in adolescents and adults can be more severe.

### **21.5.2 Special groups**

Two doses of VV (Varilrix), at least six weeks apart, are recommended and funded for the special groups listed in Table 21.1 above.

#### **Immunocompromised (including immunosuppressed) individuals**

The vaccine should not be given to immunocompromised individuals except under the direction and care of a specialist, following a suitable protocol<sup>19</sup> (see sections 4.2 and 4.3). Immunocompromised individuals are at highest risk of severe varicella and zoster infections. The original vaccine formulations, in particular Varivax, have been studied in immunocompromised children (most of whom were children with leukaemia in remission). Approximately 20 percent of these vaccine recipients required acyclovir because of a rash developing up to four weeks after vaccination. Despite this, the study concluded that the vaccine Varivax was safe, immunogenic and effective in these children.<sup>28, 29</sup> The combination MMRV vaccine should not be used in immunocompromised individuals.

Where such individuals cannot be vaccinated, it is important to vaccinate the household members and other close contacts (funded for household contacts) to provide 'ring fence' protection (see sections 4.2, 4.3 and 21.7.1). Immunisation of children with congenital T-cell immune deficiency syndromes is generally contraindicated, but those with impaired humoral immunity may be immunised (see section 21.6.1 for further contraindications).

### **21.5.3 Recommended but not funded**

A single dose of VV is recommended for susceptible children who do not meet the eligibility criteria for funded vaccine (Table 21.1). A second dose may also be purchased for those who wish to reduce the risk of breakthrough disease.

VV in a two-dose schedule is recommended but not funded for the following groups:

- adults and adolescents who were born and resided in tropical countries, if they have no history of varicella infection
- susceptible adults and adolescents (ie, those who have no prior history of chickenpox)<sup>19</sup>
- susceptible individuals who live or work in environments where transmission of VZV is likely (eg, staff in early childhood education services, residents and staff members in institutional settings)<sup>19</sup>
- susceptible individuals who live and work in environments where transmission can occur (eg, college students, inmates and staff members of correctional institutions, and military personnel)<sup>19</sup>
- susceptible non-pregnant women of childbearing age<sup>19</sup>
- susceptible international travellers<sup>19</sup>
- health care workers (see below)
- susceptible individuals who have been exposed to varicella (see section 21.8.3).

See section 21.8.1 for information about assessing susceptibility.

#### **Health care workers**

All health care workers on obstetric, paediatric and neonatal units, and those caring for immunocompromised children and adults, should be immunised with VV (not funded) if they are susceptible to varicella. When a health care worker has a good history of prior varicella infection,<sup>30</sup> no blood test is required. If there is not a good history of varicella infection, a blood test to assess susceptibility will be necessary, as many individuals with no clinical history of varicella are immune (see section 21.8).

If a health care worker who has clinical contact with patients develops a rash as a result of the vaccine (around 5 percent), they must be excluded from contact with immunocompromised or other at-risk patients and allocated other duties, or excluded from their place of work, for the duration of the rash.

### **21.5.4 Pregnancy and breastfeeding**

Varicella vaccines are contraindicated in pregnant women. Pregnancy should be avoided for at least four weeks after vaccination.<sup>31</sup> The vaccine's safety for the fetus has not yet been demonstrated, although no congenital defects have been described following inadvertent administration to pregnant women.

A pregnant woman is not a contraindication for immunisation of a child in the household, and the vaccine can be administered to non-immune mothers who are breastfeeding.

## **21.6 Contraindications and precautions**

See section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

### **21.6.1 Contraindications**

Monovalent VV is contraindicated for the following people:

- individuals with primary or acquired T-cell immune deficiency states – consult the child's paediatrician for advice<sup>31</sup>
- individuals on high-dose steroids for more than two weeks (ie, children on 2 mg/kg per day or more of prednisone or its equivalent, or 20 mg per day if their weight is over 10 kg)
- individuals with a history of an anaphylactic reaction to a prior dose of VV or with known systemic hypersensitivity to neomycin or to any other component of the vaccine
- individuals with active untreated TB
- pregnant women – women should avoid pregnancy for at least four weeks after vaccination<sup>31</sup> (see section 21.5.4).

## 21.6.2 Precautions

Because of the association between Reye syndrome, natural varicella infection and salicylates, the vaccine manufacturers advise against the use of salicylates for six weeks after VV is given. There has been no reported association between the vaccine and Reye syndrome, but avoidance of salicylates is recommended as a precaution,<sup>31</sup> and physicians need to weigh the theoretical risk of Reye syndrome from the vaccine against the known risk from varicella disease in children receiving long-term salicylate therapy. Children on low-dose aspirin following cardiac surgery would be more at risk of thrombosis from stopping their aspirin<sup>32</sup> than from the theoretical risk of Reye's with VV.

If tuberculin testing has to be done, it should be carried out before or simultaneously with vaccination because it has been reported that live viral vaccines may cause a temporary depression (anergy) of tuberculin skin sensitivity.<sup>33</sup> As this anergy may last up to a maximum of six weeks, tuberculin testing should not be performed within that period after vaccination to avoid false negative results.

On the advice of their specialist, VV may be administered to:

- patients at least two years after bone marrow transplantation
- patients at least six months after completion of chemotherapy
- HIV-positive patients who are non-immune to varicella, with mild or moderate immunosuppression.

For suggested intervals between receipt of human normal immunoglobulin or other blood products and VV, see Table A6.1 in Appendix 6.

## 21.7 Expected responses and AEFIs

### 21.7.1 Expected responses

A 2013 systematic review of varicella vaccines found that mild adverse events were the most frequently reported AEFIs.<sup>34</sup> This includes injection site reactions such as pain, swelling and redness, which occurred in up to 28 percent of recipients. There was no increased risk of cerebellar ataxia, encephalitis or ischaemic stroke following vaccination. Post-marketing surveillance in the US found the rate of

AEFIs to be 30 per 100,000 doses of VV, and the rate of serious AEFIs was less than 4 per 100,000 doses. Fever has been reported in 15 percent of healthy children following VV and 10 percent of adults.<sup>31, 35</sup>

### **Post-VV rash**

In approximately 1–3 percent of immunised children, a localised rash develops, and in an additional 3–5 percent a generalised varicella-like rash develops.<sup>31</sup> These rashes typically consist of two to five lesions and may be maculopapular rather than vesicular; lesions usually appear 5 to 26 days after immunisation. Not all rashes can be attributable to the vaccine,<sup>31</sup> some may be due to exposure to wild-type virus, prior to vaccination.

### **Transmission of vaccine virus to contacts of vaccinated individuals**

In healthy vaccinees, transmission of vaccine virus to contacts is exceedingly rare, documented in nine immunised people and resulting in 11 secondary cases. The documented risk exists only if the immunised person develops a rash.<sup>31</sup> Err on the side of caution and isolate the vaccinee if they are a household contact of an immunocompromised individual and a post-immunisation rash occurs. If an immunocompromised individual inadvertently comes in contact with a vaccinee who has a varicella-like rash, the administration of zoster immunoglobulin (ZIG) and/or acyclovir should be considered (see below).<sup>31</sup> Intravenous acyclovir may be required if symptoms develop.

## **21.7.2 AEFIs**

### **Vaccine virus shingles**

The Oka strain of varicella used in the available vaccines can establish latent ganglionic infection in vaccinees and later reactivate to produce clinical zoster (shingles). The risk of zoster is lower, and the clinical severity milder, in healthy vaccinees than in naturally infected children. A cohort study in children with acute lymphoblastic leukaemia (who have a high rate of zoster in childhood) showed that vaccinees had less than one-fifth the zoster rate of their naturally infected counterparts.<sup>28, 36</sup>

## **Febrile seizures with MMRV vaccine**

Compared with the use of MMR and VV at the same visit, use of MMRV vaccine requires one fewer injection but is associated with a higher risk of fever and febrile seizures 5 to 12 days after the first dose among children aged 12–23 months (approximately one extra febrile seizure for every 2,300–2,600 MMRV vaccine doses).<sup>37</sup> After the second dose, there are no differences in incidence of fever, rash or febrile seizures among recipients of MMRV vaccine compared with recipients of MMR and VV.

This is why MMRV vaccine is not recommended in New Zealand as a first dose for children prior to their fourth birthday (approximately 97 percent of febrile seizures occur in children before age 4 years). MMRV vaccine can be given as a first dose to children after their fourth birthday, and as a second dose to children of any age (15 months to 12 years).

## **21.8 Public health measures**

At present, VZV is not a notifiable disease in New Zealand.

### **21.8.1 Susceptibility**

In general, a positive past history of chickenpox can be taken as indicating immunity, provided there has not been an intervening bone marrow transplant or other immunosuppressive therapy. Recall of varicella or characteristic rash is reliable evidence of immunity. In people with no history or recall of the rash, 70–90 percent are found to be immune.<sup>31</sup> Consult with the local laboratory about the availability and interpretation of varicella serology.

### **21.8.2 Post-exposure prophylaxis with zoster immunoglobulin (ZIG)**

ZIG is a high-titre immunoglobulin available from the New Zealand Blood Service for passive immunisation of varicella in high-risk individuals. It is most effective if given as soon as possible after exposure, but may be given up to 10 days post-exposure.<sup>38, 39</sup> Intravenous immunoglobulin (IVIG) can be given when ZIG is unavailable.

The decision whether to offer ZIG depends on:<sup>40</sup>

- the likelihood that the exposed person is susceptible to varicella
- the likelihood that infection will result from a given contact
- the likelihood that an individual will develop serious complications if infected.

**Contact** (exposure) can be defined as follows:<sup>40</sup>

- household contact – infection is very likely to occur in a susceptible individual living with an infected contact
- playmate contact – more than one hour of play indoors with infected individual
- newborn infant contact – this occurs when the mother of a newborn infant develops chickenpox (but not shingles) from seven days before to seven days after delivery
- hospital contact – in the same two-bed room or face-to-face contact for longer than 5 minutes.

Provided exposure has occurred and susceptibility is likely, **ZIG is recommended for:**

- pregnant non-immune women (see section 21.8.6 below and discuss with an infectious diseases physician)
- newborn infants whose mother had onset of chickenpox (but not shingles) within seven days before or after delivery (see section 21.8.6)
- hospitalised premature infants whose mothers have no history of chickenpox, or who were born at less than 28 weeks' gestation, or with birthweight less than 1,000 g, irrespective of maternal history
- immunocompromised individuals – discuss the use of ZIG with their specialist, as appropriate.

## Dosage of ZIG

The ZIG prepared by CSL Behring in Melbourne, from New Zealand donors, is available in single vials containing 200 IU varicella-zoster antibody. The actual volume in the vial is stated on the label. The recommended dose is based on body weight and is shown in Table 21.2 below. ZIG should be given intramuscularly, not intravenously.

**Table 21.2: Dose of ZIG based on body weight**

Weight of patient (kg)	Dose (IU)	Number of vials
0–10	125	1
10.1–20	250	2
20.1–30	375	2
30.1–40	500	3
over 40	600	3

Source: CSL Behring. 2014. *Zoster Immunoglobulin-VF Product Data Sheet*. URL: [www.nzblood.co.nz/Clinical-information/Transfusion-medicine/Health-professionals-medicine-datashets/Immunoglobulins](http://www.nzblood.co.nz/Clinical-information/Transfusion-medicine/Health-professionals-medicine-datashets/Immunoglobulins) (accessed 24 June 2015).

If ZIG is not available, IVIG can be used. The titre of anti-varicella antibody will vary between lots, and the blood transfusion centre haematologist needs to be contacted to confirm the appropriate dose when IVIG is used.

### **21.8.3 Post-exposure vaccination and outbreak control**

VV may be used for post-exposure prophylaxis of susceptible individuals aged 9 months or older, if there are no contraindications to vaccine use<sup>31</sup> – see Table 21.3. Data from the US and Japan from household, hospital and community settings indicates that VV is effective in preventing illness or modifying varicella severity if used within three days, and possibly up to five days, of exposure.

### Table 21.3: Post-exposure varicella vaccination recommendations

Note: Funded groups are in the shaded rows below. See the Pharmaceutical Schedule ([www.pharmac.govt.nz](http://www.pharmac.govt.nz)) for any changes to the funding decisions.

	Number of doses	Schedule
Immune-competent hospital in-patients who are susceptible to varicella	2 doses	1st dose within 3 days of exposure (up to a maximum of 5 days) 2nd dose at least 6 weeks later
Susceptible children aged 9–15 months*	1 dose	Give within 3 days of exposure (up to a maximum of 5 days)
Susceptible children aged under 13 years – who are not eligible for age-appropriate funded vaccine	1 dose	Give within 3 days of exposure (up to a maximum of 5 days)
Susceptible adolescents (aged 13 years and older) and adults	2 doses	1st dose within 3 days of exposure (up to a maximum of 5 days) 2nd dose at least 6 weeks later

\* Children who were under age 15 months when they received VV for post-exposure prophylaxis will still be eligible for the age 15-month dose, providing they were born on or after 1 April 2016. Ensure there are at least 6 weeks between doses.

VV may not prevent disease in all cases because some individuals may have been exposed to the same source as the index case.<sup>31</sup> If exposure to varicella does not result in infection, post-exposure vaccination should induce protection against subsequent exposure. If the exposure results in infection, no evidence indicates that administration of VV during the pre-symptomatic or prodromal stage of illness increases the risk for AEFIs. Note that although this method of immunisation may be successful, it is not necessarily reliable. Immunisation before exposure is therefore recommended as the preferred method of preventing outbreaks.

#### 21.8.4 In-hospital exposure

In the event of an exposure:

- susceptible staff should be excluded from contact with high-risk patients from day 8 to day 21 after exposure to varicella (or shingles in an immunocompromised patient)

- hospital staff who have no history of chickenpox and who will be in contact with pregnant women or high-risk patients should be tested for varicella zoster antibodies; vaccination is recommended for those who are not immune or whose serostatus cannot be promptly determined.

Two doses of VV are funded for post-exposure prophylaxis of immune-competent in-patients who are susceptible to varicella (see section 21.8.3).

### **21.8.5 Exclusion from school or early childhood education services**

Parents/guardians should be advised that:

- infected children should be excluded from early childhood education services or school until fully recovered, or all lesions have crusted. Mild breakthrough disease in immunised children may not crust but they should be excluded until no new lesions appear for 24 hours.<sup>31</sup>
- immune-deficient children should be excluded from early childhood education services or school until three weeks after the last documented case.

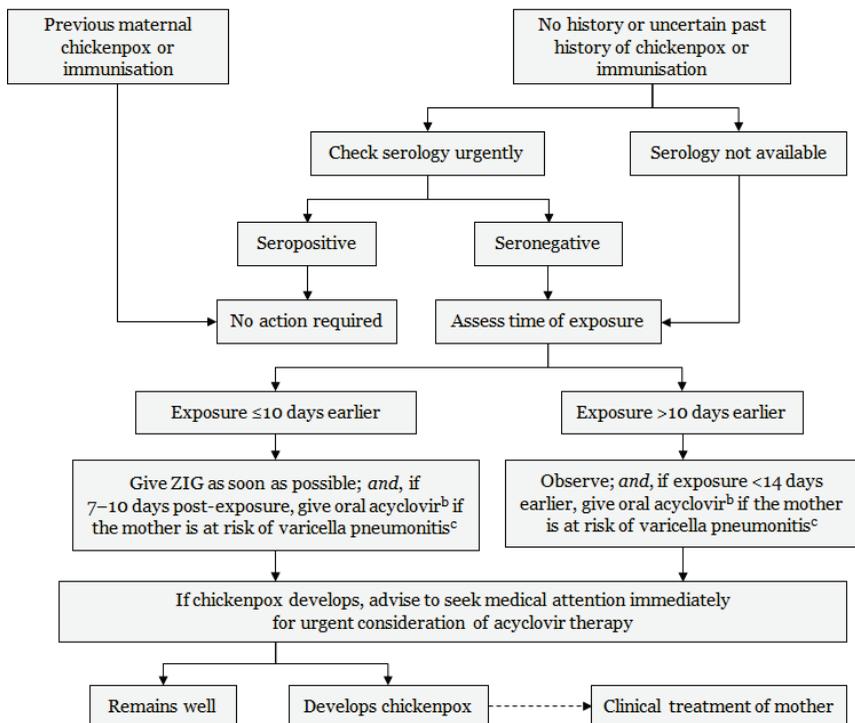
### **21.8.6 Care of pregnant women after exposure**

Pregnant women are at higher risk of severe complications from varicella. If an immune-competent pregnant woman with no history of varicella or vaccination is exposed to varicella, it is recommended, where possible, that her varicella antibodies be assessed (Figure 21.1). If there is no evidence of immunity, two possible courses of action are available: either administer ZIG, or await the onset of symptoms and as soon as possible commence the administration of acyclovir, which is effective in this situation and now regarded as safe in pregnancy. Discuss the clinical circumstances with an infectious diseases physician before deciding on which course of action is best.

Intravenous acyclovir is recommended for the pregnant woman with severe complications of varicella. ZIG given to a pregnant woman within five days of delivery may not protect the fetus/neonate: the neonate should receive ZIG on delivery and may need treatment with acyclovir (Figure 21.2).

## Figure 21.1: Management of pregnant women exposed to varicella or zoster

Every effort should be made to confirm the diagnosis in the suspected positive contact and assess significance of exposure.<sup>a</sup> Exposure or symptoms in the final two weeks of pregnancy should always be discussed with a specialist.



- Exposure to varicella or zoster for which ZIG is indicated for susceptible persons includes: living in the same household as a person with active chickenpox or herpes zoster; face-to-face contact with a case of chickenpox for at least 5 minutes; close contact (eg, touching, hugging) with a person with active zoster.
- Efficacy of acyclovir for post-exposure prophylaxis has not been tested in controlled trials. Dose is 800 mg orally, 5 times per day for 7 days.
- The mother is at risk of pneumonitis if: in second half of pregnancy; has underlying lung disease; is immunocompromised; is a smoker.

Adapted from: Australasian Society for Infectious Diseases. 2014. Varicella zoster virus. In: Palasanthiran P, Starr M, Jones C, et al (eds). *Management of Perinatal Infections*. Sydney: Australasian Society for Infectious Diseases (ASID) Inc.

Pregnant women exposed to VZV should be counselled about the risks of congenital varicella syndrome (CVS), a rare but devastating disorder that can occur following varicella zoster infection during pregnancy (see Table 21.4). The risk of CVS is greatest in the first 20 weeks of pregnancy. Large case studies suggest that the rate of CVS is 0.4 percent when maternal infection occurs up to week 12 of pregnancy, and 2 percent from weeks 13 to 20.

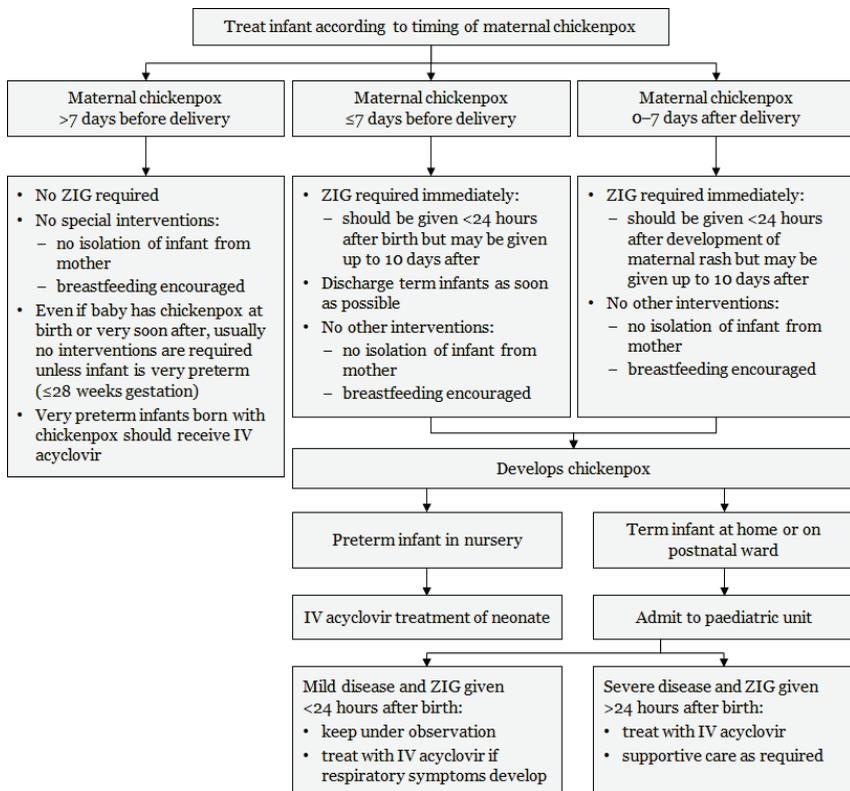
There is no single diagnostic test available for CVS. Regular fetal ultrasound for developing anomalies is recommended. VZV fetal serology is unhelpful but amniocentesis may be considered; negative VZV PCR may be reassuring.

**Table 21.4: Sequelae of congenital varicella**

<b>Sequelae</b>	<b>Frequency</b>
Skin scars	78%
Eye abnormalities	60%
Limb abnormalities	68%
Prematurity, low birthweight	50%
Cortical atrophy, severe developmental delay	46%
Poor sphincter control	32%
Early death	29%

Adapted from: Australasian Society for Infectious Diseases. 2014. Varicella zoster virus. In: Palasanthiran P, Starr M, Jones C, et al (eds). *Management of Perinatal Infections*. Sydney: Australasian Society for Infectious Diseases (ASID) Inc.

**Figure 21.2: Management of infants from mothers with perinatal varicella or zoster**



**Notes:**

- Transplacentally acquired VZV is high-risk and severity is reduced by ZIG.
- ZIG is not always effective in preventing severe disease.

Adapted from: Australasian Society for Infectious Diseases. 2014. Varicella zoster virus. In: Palasanthiran P, Starr M, Jones C, et al (eds). *Management of Perinatal Infections*. Sydney: Australasian Society for Infectious Diseases (ASID) Inc.

## 21.9 Variations from the vaccine data sheet

The VV (Varilrix) data sheet states that individuals aged 9 months and older should receive two dose of vaccine at least six weeks apart. The Ministry of Health instead recommends a single dose of VV for healthy children at 15 months or 11 years of age (see section 21.5.1) and two doses for individuals with a special groups condition (see section 21.5.2).

The data sheet states that pregnancy should be avoided for three months after vaccination. The Ministry of Health instead recommends avoiding pregnancy for at least four weeks after vaccination.<sup>31</sup>

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