

3.24 VARICELLA

Virology

Varicella-zoster virus (VZV) is a DNA virus within the herpes virus family.¹ Primary infection with VZV causes varicella (chickenpox). Following primary infection, VZV establishes latency in the dorsal root ganglia. Reactivation of the latent virus manifests as herpes zoster (shingles)² (see Chapter 3.26, *Zoster*).

Clinical features

Varicella is a highly contagious infection spread by air-borne transmission of droplets from the upper respiratory tract or from the vesicle fluid of the skin lesions of varicella or zoster infection.¹ Varicella is usually a mild disease of childhood. However, complications occur in approximately 1% of cases.³ It is more severe in adults and in individuals of any age with impaired immunity, in whom complications, disseminated disease, and fatal illness can occur.¹

The average incubation period is 14 to 16 days (range 10–21 days), but may be longer in those with impaired immunity, especially after receipt of zoster immunoglobulin (ZIG).² The period of infectivity is from 48 hours before the onset of rash until crusting of all lesions has occurred. A short prodromal period of 1 to 2 days may precede the onset of the rash, especially in adults.^{1,2} In otherwise healthy children, skin lesions usually number between 200 and 500.^{1,2} Acute varicella may be complicated by secondary bacterial skin infection, pneumonia, acute cerebellar ataxia (1 in 4000 cases), aseptic meningitis, transverse myelitis, encephalitis (1 in 100 000 cases), and thrombocytopenia. In rare cases, it involves the viscera and joints.¹

Congenital varicella syndrome has been reported after varicella infection in pregnancy and may result in skin scarring, limb defects, ocular anomalies, and neurologic malformations.^{1,4} There is a higher risk to the fetus if maternal infection occurs in the second trimester compared with infection in the first trimester (1.4% vs 0.55%).⁵ Infants with intrauterine exposure also risk developing herpes zoster in infancy (0.8–1.7%) with the greatest risk following exposure in the third trimester.⁴ Severe neonatal varicella infection can result from perinatal maternal varicella.⁶ The onset of varicella in pregnant women from 5 days before delivery to 2 days after delivery is estimated to result in severe varicella in 17 to 30% of their newborn infants.⁷

Reactivation of latent VZV as a result of waning cellular immunity results in herpes zoster (HZ), a localised vesicular rash. HZ can occur at any age, but is more common in older adults and individuals with impaired immunity. Complications may include post-herpetic neuralgia, and disseminated zoster with visceral, central nervous system and pulmonary involvement¹ (see Chapter 3.26, *Zoster*).

There is no specific therapy for uncomplicated varicella infection. Antiviral therapy is used in the treatment of complicated or severe disease or varicella in people with impaired immunity. An increased risk of Reye syndrome following varicella infection has been reported in association with aspirin or other salicylate use⁸⁻¹² (see 'Precautions' below). Aspirin or other salicylates should not be used in the management of varicella infection.

Epidemiology

In an unimmunised population in temperate climates, the annual number of cases of varicella approximates the birth cohort.¹³ Tropical regions have a higher proportion of cases in adults. Approximately 5% of cases are subclinical. A serosurvey conducted in 1997–1999 found that 83% of the Australian population were seropositive by 10–14 years of age.¹⁴ Before the introduction of a varicella vaccination program in Australia there were about 240 000 cases, 1500 hospitalisations and an average of 7 to 8 deaths each year from varicella in Australia.¹⁵⁻¹⁷ The highest rates of hospitalisation occur in children <4 years of age.¹⁸

In the USA, universal varicella vaccination since 1995 has resulted in a decline in varicella disease by 85% and hospitalisations have declined by 70 to 88%.¹⁹⁻²¹ The greatest decline in hospitalisation rates has been in 0–4-year-olds, who were most likely to be vaccinated. However, a reduction in hospitalisation rates also occurred in older children and adults, due to herd immunity.¹⁹ Surveillance of varicella and HZ in the USA, conducted between 1992 and 2002, demonstrated that, as vaccination coverage increased to 65% in 2002, the incidence of varicella decreased by 65% across all age groups, and the incidence of HZ remained stable.²²

Vaccines

Live attenuated varicella vaccine (VV) is currently available as a monovalent vaccine. It is anticipated that quadrivalent combination vaccines containing measles, mumps, rubella and varicella vaccines (MMRV) will be available in the near future (see Chapter 3.11, *Measles* for information on MMRV vaccines). All available varicella-containing vaccines are derived from the Oka VZV strain, but have some genetic differences.²³

Monovalent VVs have been available in Australia since 2000, and from November 2005, a single dose of VV has been funded under the NIP for all children at 18 months of age, with a catch-up dose funded for children 10–<14 years of age.²⁴ At the time of implementation of a universal varicella vaccination program in Australia, a single dose was considered adequate for protection of infants and children <14 years of age. However, recent data from the USA suggests that a second dose of varicella-containing vaccine in children is optimal to provide an immune response more like natural infection, reducing the risk of vaccine failure and increasing population immunity.⁷ Vaccine failure is known as 'breakthrough varicella' and is defined as a case of wild-type varicella ≥42 days post vaccination. A majority of cases of breakthrough varicella are

mild with fewer lesions than natural infection. However, breakthrough varicella infections can be contagious.²⁵

Post-licensure studies in the USA have estimated the effectiveness of 1 dose of VV in children to be 80 to 85% against any disease and 95 to 98% against severe varicella.²⁵⁻²⁹ Although earlier data suggested persistence of immunity in most healthy vaccinees,¹ recent long-term data from the United States has shown that, >5 years after vaccination, rates of vaccine failure increased by 2.6 times in children who received only 1 dose of vaccine, compared with those who had received the vaccine within 5 years.³⁰ Data from a randomised controlled trial in varicella-negative children 12 months to 12 years of age, comparing 1 with 2 doses of VV over a 10-year period, showed significantly higher protection with 2 doses (94.4% vs 98.3%).³¹ Based on current evidence, 2 doses of a varicella-containing vaccine in children from 12 months of age will minimise the risk of breakthrough varicella (see 'Recommendations' below).

Healthy adolescents (≥14 years of age) and adults require 2 doses of varicella vaccine, 1 to 2 months apart, as the response to a single dose of VV decreases progressively as age increases and is insufficient to provide adequate protection.³²

Monovalent varicella vaccines

- **Varilrix** – GlaxoSmithKline (lyophilised preparation of live attenuated Oka strain of varicella-zoster virus). Each 0.5 mL monodose of the reconstituted, lyophilised vaccine contains not less than 10^{3.3} plaque-forming units of attenuated varicella-zoster virus; human serum albumin; lactose; neomycin; polyalcohols. Single and 10 pack of monodose vials also available.
- **Varivax Refrigerated** – CSL Biotherapies/Merck & Co Inc (lyophilised preparation of live attenuated Oka/Merck strain of varicella-zoster virus). Each 0.5 mL monodose of the reconstituted, lyophilised vaccine contains not less than 1350 plaque-forming units; 18 mg sucrose; 8.9 mg gelatin; 3.6 mg urea; 0.36 mg monosodium glutamate; residual components of MRC-5 cells; trace amounts of neomycin and fetal bovine serum from MRC-5 culture media. Single and 10 pack of monodose vials also available.

Transport, storage and handling

Varicella vaccines are less stable than other commonly used live viral vaccines, and the storage temperature requirements are critical. Available monovalent VVs have different storage requirements.

Varilrix – store at +2°C to +8°C. Protect from light. Do not freeze. After reconstitution, use within 90 minutes at ambient temperature or for up to 8 hours at +2°C to +8°C.

Varivax Refrigerated – store at +2°C to +8°C. Protect from light. Do not freeze. After reconstitution, use within 30 minutes at ambient temperature (+20°C to +25°C) to maintain potency.

Transport according to *National Vaccine Storage Guidelines: Strive for 5*.³³

Dosage and administration

The dose of monovalent VV is 0.5 mL, administered by SC injection.

If VV is given at the same time as MMR, it should be given using separate syringes and injection sites. MMR and monovalent VV should not be mixed before injection.

VV can be given at the same time as other vaccines (including MMR, DTPa, hepatitis B and MenCCV), using separate syringes and injection sites. If VV is not given simultaneously with other live viral parenteral vaccines (eg. MMR), they should be given at least 4 weeks apart (see 'Precautions' below).

Recommendations

(i) Children

It is recommended that at least 1 dose of a varicella-containing vaccine be given to all non-immune children from the 2nd year of life to <14 years of age. Children in this age group with a reliable history of varicella infection, either by confident clinical diagnosis or with laboratory confirmation, may be considered immune and do not require vaccination.

Routine varicella-containing vaccine should be administered as follows (and as per Table 3.24.1):

- One dose of monovalent VV at 18 months of age.
- When MMRV vaccines become available, 1 dose of varicella-containing vaccine should be given as MMRV at 12 months of age.

The change in the recommended age of administration of varicella vaccine is influenced by moving the second dose of MMR to 18 months of age, and the anticipated availability of MMRV vaccines in the near future. The available evidence now suggests that the administration of varicella vaccine at the earlier age of 12 months, compared with 18 months, does not reduce vaccine effectiveness or lead to increased rates of breakthrough varicella.³⁴ Administration of varicella vaccine at 12 months of age will provide earlier protection from varicella. However, until MMRV vaccines are available in Australia, it is recommended that administration of monovalent VV at 18 months of age continue to avoid schedule crowding (4 injections) at 12 months of age.

Receipt of 2 doses of varicella-containing vaccine provides increased protection and minimises the chance of breakthrough varicella in children.³¹ However, at this time, routine administration of 2 doses of varicella-containing vaccine at <14 years of age is not included on the NIP schedule. If parents/carers wish to

minimise the risk of breakthrough varicella, a second dose of varicella-containing vaccine to children <14 years of age is recommended (see ‘Vaccines’ above). When available, use of MMRV at 18 months of age is a suitable means to provide a second dose of varicella-containing vaccine. (For further information, see also Chapter 3.11, *Measles*.) The minimum approved interval between doses of varicella-containing vaccine in children <14 years of age is 4 weeks.

Table 3.24.1: Recommendations for varicella vaccination with monovalent VV (currently available), and once MMRV vaccines are available

	12 months	18 months	Catch-up requirements*
Monovalent varicella vaccine	MMR	MMR + VV [†]	No requirement for varicella catch-up
MMRV when available	MMRV	MMR [‡]	Use MMRV at 18 months for children who have not yet received at least 1 dose of varicella vaccine

* If catch-up is required for MMR, see Chapter 3.11, *Measles*.

† Give in separate syringes and at separate injection sites (preferably the other arm).

‡ When available, use of MMRV at 18 months of age is a suitable means to provide a second dose of varicella-containing vaccine.

(ii) Adolescents (≥14 years of age) and adults

Vaccination is recommended in non-immune adolescents (≥14 years of age) and adults. Immune responses are reduced in adolescents and adults compared with young children.^{32,35} Therefore, adolescents and adults must receive 2 doses of VV to achieve adequate protection from varicella. The 2 doses should be administered at least 4 weeks apart. However, a longer interval between vaccine doses is acceptable. Lack of immunity to varicella should be based on a negative history of previous varicella infection and can be supplemented by serological testing (see ‘Serological testing before varicella vaccination’ below).

VV is particularly indicated for those in the following categories:

- non-immune people in high-risk occupations where exposure to varicella is likely (such as healthcare workers, teachers and workers in childcare centres) (see Section 2.3, Table 2.3.6 *Recommended vaccinations for those at risk of occupationally acquired vaccine-preventable diseases*),³⁶
- non-immune women before pregnancy to avoid congenital or neonatal varicella,
- seronegative women immediately after delivery,
- non-immune parents of young children, and
- non-immune household contacts of all ages of people with impaired immunity.

MMRV vaccines are not recommended for use in adolescents and adults because data are currently available only for children ≤12 years of age.

(iii) Serological testing before varicella vaccination

Vaccination is well tolerated in previously infected individuals and can be administered if there is uncertainty regarding immunity. Serological testing before varicella vaccination of children with a reliable history of varicella infection, either by confident clinical diagnosis or with laboratory confirmation, is not warranted. Reliable history of varicella infection correlates highly with serological evidence of immunity.^{37,38} Those who have an uncertain history should be considered susceptible and offered vaccination.

In adolescents and adults with a negative history of varicella infection, serological testing before vaccination is more likely to be cost-effective, as a majority of those with a negative history may be immune.^{36,39} However, vaccination can proceed without testing (provided there are no contraindications), as the vaccine is well tolerated in seropositive people.

(iv) Serological testing after varicella vaccination

Testing to check for seroconversion after varicella vaccination is not recommended. Commercially available laboratory tests are not always sufficiently sensitive to detect low antibody levels following vaccination and, in addition, the presence of detectable antibody shortly after vaccination does not necessarily indicate complete immunity to varicella.^{40,41}

(v) Post-exposure prophylaxis and outbreak control

Several studies have shown that VV is effective in preventing varicella infection, particularly moderate to severe disease, following exposure. This is generally successful when given within 3 days, and up to 5 days, after exposure, with earlier administration being preferable.⁴²⁻⁴⁶ Vaccination of exposed individuals during outbreaks has also been shown to prevent further cases and control outbreaks (see also 'The public health management of varicella' below). When available, vaccination with MMRV in children 12 months to 12 years of age could be used for vaccination in this setting if MMR vaccination is also indicated.

In the event of an outbreak, seek advice from local public health authorities before proceeding with vaccination of a large number of individuals (see Appendix 1, *Contact details for Australian, State and Territory Government health authorities and communicable disease control*).

(vi) Household contacts of people with impaired immunity

Vaccination of household contacts of people with impaired immunity is strongly recommended. This recommendation is based upon evidence that transmission of varicella vaccine virus strain is extremely rare and it is likely to cause only mild disease that can be treated with acyclovir. This compares with the relatively high risk of severe disease in people with impaired immunity following

exposure to wild-type varicella-zoster virus.^{41,47} If vaccinees develop a rash, they should cover the rash and avoid contact with people with impaired immunity for the duration of the rash. Zoster immunoglobulin (ZIG) need not be given to an immune impaired contact of a vaccinee with a rash because the disease associated with this type of transmission (should it occur) would be expected to be mild.

(vii) Vaccination of healthcare workers (HCW)

(Refer to Table 2.3.6 *Recommended vaccinations for those at risk of occupationally acquired vaccine-preventable diseases*)

Pre-exposure vaccination of HCWs:

- A HCW with a negative or uncertain history of varicella infection should undergo serological testing. If seronegative, vaccination should be offered in a 2-dose schedule⁴⁸ (see 'Recommendations (ii)' above).
- If a rash develops during the 6 weeks after administration of the vaccine, the HCW should cover the rash and be reassigned to duties that require no patient contact, or placed on sick leave.⁴⁸ Reassignment or leave should be only for the duration of the rash⁴⁸ (see 'Variations from product information' below).
- VV-associated rash may be atypical and may not be vesicular (see 'Adverse events' below). A VV-associated rash is likely to occur in less than 5% of vaccinees, and to last for less than 1 week.^{49,50}
- Testing to check for seroconversion after VV is not recommended (see 'Serological testing after varicella vaccination' above).

Post-exposure management of HCWs:

- If a previously vaccinated HCW is exposed to varicella, assume immunity and report exposure. A vaccinated HCW should watch for a rash for 3 weeks after exposure and report to the nominated infection control officer should a rash develop. If HCW vaccinees develop a rash, cover the rash, reassign duties (no patient contact) or place on sick leave until no new lesions appear and all lesions have crusted.
- If a HCW is exposed to varicella and is unvaccinated and has a negative or uncertain history of varicella infection, offer vaccination. This is usually effective in preventing the development of varicella if given within 3 days, and up to 5 days, after exposure. In situations where facilities for rapid testing are available, it may be possible to identify those with pre-existing immunity before vaccination. However, serological testing should not delay vaccination beyond the recommended 3 to 5 days after exposure. Vaccination in the absence of serological results is acceptable (see 'Serological testing after varicella vaccination' above).

- If the HCW is vaccinated after exposure, as above, he/she can work but should watch daily for any rash for 6 weeks after exposure. Note that the VV-associated rash may be atypical, maculopapular and non-vesicular. If a varicella-exposed and vaccinated HCW develops a rash following vaccination, this may be due to either wild-virus or vaccine-strain varicella-zoster virus (see 'Adverse events' below). In the event of a rash after vaccination, cover the rash, reassign duties (no patient contact) or place on sick leave until no new lesions appear and all lesions have crusted.
- If an exposed non-immune HCW does not accept vaccination, reassign duties or place on sick leave from days 10 to 21 from the time of first exposure.

Contraindications

(i) Allergy to vaccine components

Varicella vaccination is contraindicated where there has been:

- anaphylaxis following a previous dose of any of the varicella vaccines, or
- anaphylaxis following any vaccine component.

(ii) Pregnant women

VV should not be given during pregnancy and vaccinees should not become pregnant for 28 days after vaccination. Since wild-type VZV poses only a very small risk to the fetus, the risk to the fetus of the attenuated VV virus, if any, should be even lower. Data from a registry, established in the USA to monitor the maternal-fetal outcomes of pregnant women who were inadvertently administered VV 3 months before or at any time during pregnancy, revealed that no birth defects compatible with congenital varicella syndrome occurred in 254 known pregnancy outcomes.^{51,52} The rate of occurrence of congenital anomalies from prospective reports in the registry was similar to what is reported in the general USA population (3.2%) and the anomalies showed no specific pattern or target organ.

A non-immune pregnant household contact is *not* a contraindication to vaccination with VV of a healthy child or adult in the same household. The benefit of reducing the exposure to varicella by vaccinating healthy contacts of non-immune pregnant women outweighs any theoretical risks of transmission of vaccine virus to these women.

Data on the use of MMRV vaccines in individuals >12 years of age are not available.

(iii) People with impaired immunity

Varicella-containing vaccines are contraindicated in subjects with primary or acquired impaired immunity, including:

- people with impaired immunity due to HIV/AIDS. Vaccination with live attenuated vaccine can result in a more extensive vaccine-associated rash or disseminated infection in individuals with AIDS.⁵³ However, varicella vaccination of asymptomatic or mildly symptomatic HIV-infected children

may be considered (see Table 2.3.4 *Immunological categories based on age-specific CD4 counts and percentage of total lymphocytes*). Since studies have not been performed using combination MMRV vaccines in asymptomatic or mildly symptomatic HIV-infected children, it is recommended that only MMR and monovalent VV be considered for use in such children;⁵⁴

- people with conditions in which normal immunological mechanisms may be impaired;
- people suffering from malignant conditions of the reticuloendothelial system (such as lymphoma, leukaemia, Hodgkin's disease); and
- people receiving high-dose systemic immunosuppressive treatment, such as general radiation, x-ray therapy or oral corticosteroids. Varicella-containing vaccines are contraindicated in those taking high-dose oral corticosteroids (in children equivalent to either >2 mg/kg per day prednisolone (≥20 mg per day total) for >1 week or >1 mg/kg per day for >4 weeks) (see Section 2.3.3, *Vaccination of individuals with impaired immunity due to disease or treatment*). NHMRC also recommends that children who have been receiving high-dose systemic steroids for 2 weeks or more may be vaccinated after steroid therapy has ceased for at least 1 month.⁵⁵ (See also Chapter 2.3, *Groups with special vaccination requirements* and Chapter 3.11, *Measles*).

Precautions

(i) Vaccination with MMR

If VV is not given simultaneously with other live viral parenteral vaccines (eg. MMR), they should be given at least 4 weeks apart.

(ii) Vaccination after immunoglobulin or blood products

NHMRC recommends that varicella-containing vaccines should not be given for between 3 and 9 months after the administration of immunoglobulin-containing blood products. The interval between receipt of the blood product and vaccination depends on the amount of antibody in each product, and is indicated in Table 2.3.5 *Recommended intervals between either immunoglobulins or blood products and MMR, MMRV or varicella vaccination*. For further information, see Section 2.3.5, *Vaccination of patients following receipt of other blood products including blood transfusions*, and 'Variations from product information' below.

(iii) Administration of immunoglobulin or blood-derived products after vaccination

After vaccination with varicella-containing vaccines, immunoglobulin-containing products should not be administered for 3 weeks unless the benefits exceed those of vaccination. If immunoglobulin-containing products are administered within this interval, the vaccinee should either be revaccinated later at the appropriate time following the product, as indicated in Table 2.3.5, or tested for immunity 6 months later and then revaccinated if seronegative.

(iv) Long-term aspirin or salicylate therapy

Individuals receiving long-term salicylate therapy should be vaccinated if indicated, as the benefit is likely to outweigh any possible risk of Reye syndrome occurring after vaccination. Natural varicella infection and salicylate use has been associated with an increased risk of developing Reye syndrome. However, there have been no reports of an association between Reye syndrome and varicella vaccination (see 'Variations from product information' below).

Adverse events

- Adverse events following administration of VV are generally mild and well tolerated.⁵⁶ Fever >39°C has been observed in 15% (common) of healthy children, but this was comparable to that seen in children receiving placebo.⁵⁵ In adults and adolescents, fever has been reported in 10% (common) of VV vaccinees. Injection site adverse events (pain, redness or swelling) are the most common adverse events reported after varicella vaccination, occurring in 7 to 30% (common to very common) of vaccinees, but are generally well tolerated.^{2,56} Slightly higher rates of fever were observed in the clinical trials of MMRV vaccines, as compared with giving MMR and monovalent varicella vaccine at the same time but at separate sites.^{57,58} It is recommended that parents/vaccine recipients be advised about possible symptoms, and given advice for reducing fever, including the use of paracetamol for fever in the period 5 to 12 days after vaccination.
- A maculopapular or papulovesicular rash may develop after vaccination (usually within 5 to 26 days). Rashes typically consist of 2 to 5 lesions and may be generalised (3–5%, common), or occur at the injection site (3–5%, common).⁵⁵ Most varicelliform rashes that occur within the first 2 weeks after vaccination are due to wild-type VZV, with median onset 8 days after vaccination (range 1–24 days), while vaccine-strain VZV rashes occur at a median of 21 days after vaccination (range 5–42 days).⁵⁹ (See also 'Transmission of vaccine virus...' below.)
- No serious adverse events were reported from pre-licensure trials of VV.¹ A post-licensure study reported that serious adverse events, such as encephalitis, ataxia, thrombocytopenia and anaphylaxis, were reported following vaccination at a rate of 2.9 per 100 000 doses distributed. However, this does not necessarily imply a causal relationship.⁴¹
- Transmission of vaccine virus to contacts of vaccinated individuals is rare. In the USA, where more than 56 million doses of VV were distributed between 1995 and 2005, there have been only 6 well documented cases of transmission of the vaccine-type virus from 5 healthy vaccinees.^{55,60} Contact cases have been mild and associated with a rash in the vaccinee.^{55,60-62}

Risk of herpes zoster (shingles)

Herpes zoster (HZ) has been reported rarely in vaccine recipients and has been attributed to both the vaccine strain and to wild-type varicella virus reactivation.⁵⁹ The risk of developing HZ is currently thought to be lower after vaccination than after natural varicella virus infection, and reported cases have been mild.² HZ is uncommon before the age of 45 years, and incidence increases with age.⁶³ Rates of herpes zoster in children 0–9 years of age after natural VZV infection were estimated to be 30 to 74 per 100 000 per year.^{64,65} Vaccination results in a lower rate of zoster with a rate of 22 per 100 000 person-years reported in a 9-year follow-up of 7000 varicella vaccinated children (Jane Seward, US Centers for Disease Control and Prevention (CDC), personal communication) (see Chapter 3.26, *Zoster*).

Zoster immunoglobulin

High-titre zoster immunoglobulin (ZIG) is available from the Australian Red Cross Blood Service on a restricted basis for the prevention of varicella in high-risk subjects. ZIG has no proven use in the treatment of established varicella or zoster infection. ZIG must be given early in the incubation period (within 96 hours of exposure). ZIG is highly efficacious, but is often in short supply. Normal human immunoglobulin (NHIG) can be used for the prevention of varicella if ZIG is unavailable.

Zoster immunoglobulin should be given only by IM injection.

- **Zoster Immunoglobulin-VF (human)** – CSL Bioplasma (160 mg/mL immunoglobulin (IgG) preparation from human plasma containing high levels of antibody to the varicella-zoster virus). Vials contain 200 IU, with the actual volume stated on the label on the vial. Also contains glycine.

The public health management of varicella

‘Significant exposure’ is defined as living in the same household as a person with active varicella or HZ, or direct face-to-face contact with a person with varicella or HZ for at least 5 minutes, or being in the same room for at least 1 hour. In the case of varicella infection, the period of infectivity is from 48 hours before the onset of rash until crusting of all lesions has occurred.

Immunocompetent varicella contacts should be tested for varicella-zoster antibodies. However, this should not delay ZIG administration after initial contact with a case.

ZIG should be given to individuals in the following categories within 96 hours of significant exposure to either varicella or HZ:

- Pregnant women who are presumed to be susceptible to varicella infection. If practicable, they should be tested for varicella-zoster antibodies before ZIG is given.⁴

- ZIG *must* be given to neonates whose mothers develop varicella from 7 or fewer days before delivery to 2 days after delivery, as the neonatal mortality without ZIG is up to 30% in this setting. ZIG must be given as early as possible in the incubation period.
- ZIG *should* be given to neonates exposed to varicella in the first month of life, if the mother has no personal history of infection with VZV and is seronegative.
- Premature infants (born at <28 weeks' gestation or <1000 g birth weight) exposed to VZV while still hospitalised should be given ZIG *regardless of maternal history of varicella*.
- Patients suffering from primary or acquired diseases associated with cellular immune deficiency, and those receiving immunosuppressive therapy. While it is recommended that varicella contacts with impaired immunity be tested for varicella-zoster antibodies, this should not delay ZIG administration, preferably within 96 hours and up to 10 days after initial contact with a case.^{66,67}

NB. If a contact with impaired immunity is shown to have recent evidence of detectable antibodies, it is not necessary to give ZIG, as its administration will not significantly increase varicella-zoster antibody titres in those who are already positive. Note that varicella-zoster antibodies detected in patients who have been transfused or who have received intravenous immunoglobulin in the previous 3 months may be passively acquired and transient.

The following dose schedule is recommended for ZIG administration:

Table 3.24.2: Zoster immunoglobulin-VF (ZIG) dose based on weight

Weight of patient (kg)	Dose (IU)
0–10	200
11–30	400
>30	600

A dose of ZIG may be repeated if a second exposure occurs more than 3 weeks after the first dose of ZIG. However, testing for varicella antibodies is also recommended (see above). Normal human immunoglobulin can be used for the prevention of varicella if ZIG is unavailable (see Chapter 3.8, *Immunoglobulin preparations*). Patients receiving monthly high-dose intravenous NHIG are likely to be protected and probably do not require ZIG if the last dose of NHIG was given 3 weeks or less before exposure.

Use in pregnancy

Varicella vaccine is contraindicated during pregnancy (see 'Contraindications (ii) Pregnant women' above, and Chapter 2.3, *Groups with special vaccination requirements*, Table 2.3.1 *Vaccinations in pregnancy*).

Pregnancy should be avoided for at least 28 days after vaccination.

Variations from product information

Varilrix vaccine is approved for use in healthy children from 9 months of age. NHMRC recommends that routine vaccination of children against varicella should occur at ≥ 12 months of age.

Varilrix and Varivax Refrigerated are registered for use as 2 doses of 0.5 mL (1–2 months apart) in adolescents ≥ 13 years of age and adults. NHMRC recommends a single dose of varicella vaccine for children < 14 years of age.

In adults and adolescents where 2 doses of vaccine are required, the product information for Varilrix states that the second dose should be given at least 6 weeks after the first. NHMRC recommends that the second dose may be given at least 4 weeks after the first dose.

For both varicella vaccines, the product information states that pregnancy should be avoided for 3 months after vaccination. NHMRC recommends that pregnancy be avoided for at least 28 days after vaccination.

For both varicella vaccines, the product information recommends that vaccinees should avoid contact with people with impaired immunity for up to 6 weeks after vaccination. NHMRC recommends that healthcare worker vaccinees should be reassigned to duties that involve no direct patient contact or be placed on sick leave only if a rash develops, and that the period of leave or reassignment should be only for the duration of the rash (not for the 4 to 6 weeks stated in the product information) (see also 'Vaccination of healthcare workers (HCW)' above).

For both varicella vaccines, the product information states that salicylates should be avoided for 6 weeks after varicella vaccination, as Reye syndrome has been reported following the use of salicylates during natural varicella infection. NHMRC recommends that non-immune individuals receiving long-term salicylate therapy should receive VV as the benefit is likely to outweigh any possible risk of Reye syndrome occurring after vaccination.

The product information for Varivax Refrigerated recommends delaying vaccination for 5 months after receipt of NHIG by IM injection or blood transfusion. The NHMRC recommends that VV should not be given for at least 3 months in subjects who have received immunoglobulin-containing blood products according to the intervals contained in Table 2.3.5.

The dosage of ZIG recommended in the product information differs with that in Table 3.24.2, which has been revised in order to minimise wastage of ZIG.

References

Full reference list available on the electronic *Handbook* or website <http://immunise.health.gov.au>.