

# Varicella (chickenpox)

## VARICELLA-ZOSTER (CHICKENPOX) VACCINES FOR AUSTRALIAN CHILDREN: INFORMATION FOR IMMUNISATION PROVIDERS

### Disease and epidemiology

- Varicella (also known as chickenpox) is a viral illness caused by primary infection with the varicella-zoster virus (VZV). It is characterised by vesicular skin lesions and fever.
- Complications of chickenpox occur in approximately 1% of cases. Prior to universal immunisation, there were about 1,500 hospitalisations per year in Australia, most of which were in otherwise healthy young children.

### Who should be vaccinated

- In Australia, a single dose of varicella vaccine is available on the National Immunisation Program (NIP) at 18 months of age using the four-in-one combination vaccine which protects against measles, mumps, rubella and varicella (MMRV vaccine).
- A single 'catch-up' dose of monovalent varicella vaccine, delivered in the school based program, is available on the NIP for adolescents with no history of chickenpox or previous vaccination.
- People  $\geq 14$  years of age who are not immune to chickenpox require 2 doses of varicella vaccine at least 1 month apart.
- Varicella vaccination is recommended for all adults who have not previously had chickenpox or received the vaccine, especially healthcare workers, childcare workers and household contacts of people who are immunocompromised.

### Vaccines

- One dose of varicella vaccine (in children up to 13 years of age) will prevent varicella in approximately 80–85% of cases. The vaccine effectiveness against severe varicella (defined as  $>500$  lesions) is greater at approximately 95–98%.
- Disease in vaccinated children ('breakthrough varicella') is often mild with  $<50$  lesions in about 70% of cases.
- Common side effects from varicella vaccination include fever and injection site reactions. Rashes can occur following vaccination, either at the injection site (in 1–3% of vaccine recipients) or generalised (in 3–5%).

## The disease

The varicella-zoster virus (VZV) is one of eight herpes viruses that cause infections in humans. It is a double-stranded DNA virus and is most closely related to herpes simplex virus types 1 and 2. These viruses rapidly proliferate, invade and destroy infected cells. Like other herpes viruses, VZV has the unusual ability to establish a latent infection in nerve ganglions and later reactivate.

Primary infection with VZV causes varicella or 'chickenpox', whereas reactivation of latent VZV causes herpes zoster (HZ) also known as zoster or 'shingles'. (See NCIRS fact sheet [Zoster vaccine for Australian adults](#)).

Chickenpox is usually a self-limiting disease most commonly resulting in a general malaise, fever and vesicular rash. Complications of chickenpox infection occur in approximately 1% of cases, with the most common being secondary bacterial infection of the skin lesions. Other complications include pneumonia, encephalitis and cerebellar ataxia, thrombocytopenia and hepatitis. Infection in adolescents and adults is usually more severe than infection in children. The average number of skin vesicles is usually 250–500 but more than 500 lesions may occur in severe cases.

VZV is transmitted via the respiratory route (with viral particles present in respiratory droplets from 24–48 hours before the appearance of the rash) and in the fluid of the skin lesions of an infected person.<sup>1</sup> The secondary attack rate from a person with primary varicella to susceptible children has been estimated to be between 61% and 100%, whereas secondary attack rates following contact with shingles are lower at about 15%.<sup>2,3</sup>

## Epidemiology

In unvaccinated populations, varicella is primarily a childhood illness. In temperate countries, more than 90% of the population develop clinical or serological infection by early adulthood, with the highest attack rates in children aged 5–9 years.<sup>4,5</sup> Australian data suggest a slightly later age of acquisition, with 83% of children infected by 10–14 years of age.<sup>6</sup> Prior to the use of varicella vaccine there were about 240,000 cases, 1,500 hospitalisations and approximately 7 deaths each year from varicella in Australia.<sup>7-10</sup> Although the risk of severe disease and complications is greater in adolescents and adults, or people with a suppressed immune system, the majority of hospitalisations are in otherwise healthy children because disease incidence is far higher in childhood.<sup>11</sup>

In the USA, a universal varicella vaccination program has been in place since 1995.<sup>12</sup> This program has resulted in a decline in varicella disease by 85% and hospitalisations by 91% in children <10 years of age, the age group targeted by the vaccination program.<sup>13-15</sup> Reductions in incidence rates and hospitalisation rates have also been detected in older children and adults, due to herd immunity.<sup>16</sup> A reduction in deaths due to varicella was observed in all age groups, with the greatest declines (97%) in children and adolescents under 20 years of age.<sup>17</sup> In 2006, a 2nd dose of varicella vaccine was introduced in the USA resulting in a further 40% decline in hospitalisations.<sup>18</sup> In Australia, where a single dose of varicella vaccine has been recommended since 2003, and funded under the National Immunisation Program since late 2005, significant declines in hospitalisation rates have been observed in all age groups under 40 years of age. The greatest declines (73%) have been in children 1–4 years of age, the group targeted by the funded immunisation program.<sup>19</sup>

## Who should be vaccinated

### National Immunisation Program (NIP)

A single dose of varicella vaccine is funded on the NIP at 18 months of age. As of July 2013, this is given in conjunction with the 2nd recommended dose of measles-mumps-rubella, using the four-in-one combination vaccine (measles-mumps-rubella-varicella; MMRV).

Adolescents aged approximately 12–13 years are also offered a single dose of varicella vaccine as part of the NIP-funded school-based catch-up program. This dose is available for children who do not have a reliable history of chickenpox or previous vaccination. Although not funded under the NIP, a 2nd dose of varicella vaccine can be considered in children <14 years of age to provide enhanced protection.

Further detailed information on the national varicella vaccination program in Australia for both immunisation providers and the general public is available at the Immunise Australia website.<sup>20</sup> State or territory health authorities can be consulted for specific information on their individual school-based vaccine programs.

### Others recommended for vaccination

Two doses of varicella vaccine, given at least 1 month apart, are recommended for all non-immune adolescents ( $\geq 14$  years) and adults, although not funded on the NIP. Vaccination against varicella is particularly recommended for non-immune persons at high risk of exposure to, or complications from, varicella, such as healthcare workers, childcare workers, non-immune women before pregnancy

and parents. Vaccination of non-immune household contacts of people who are immunocompromised is also important to minimise opportunities for transmission of varicella to the immunocompromised person. Refer to *The Australian Immunisation Handbook* for more details on vaccine recommendations.<sup>21</sup>

## Vaccines

Two monovalent varicella vaccines (Varilrix<sup>®</sup>, Varivax Refrigerated<sup>®</sup>) and two four-in-one MMRV combination vaccines (Priorix-tetra<sup>®</sup> and ProQuad<sup>®</sup>) are registered for use in Australia. They all contain live attenuated (weakened) varicella-zoster virus derived from the Oka varicella-zoster virus strain.

### Administration

The dose of monovalent varicella (VV) and MMRV vaccines is 0.5 mL, administered by SC injection. Priorix-tetra<sup>®</sup> may also be given by IM injection. MMRV vaccines are not recommended for use in persons  $\geq 14$  years of age.

### Vaccine efficacy/effectiveness

In clinical trials of the varicella vaccine in children, undertaken before vaccine licensure, the efficacy after 1 dose was reported to be approximately 96%.<sup>22-24</sup>

However, many post-licensure studies, mostly conducted in the USA, have determined that the vaccine effectiveness of 1 dose given early in childhood is less than this original estimate, and is actually about 80–85% for the prevention of any disease, with 95–98% effectiveness in preventing severe varicella.<sup>2,25-28</sup>

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, data from the USA suggest that a 2nd 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.<sup>12</sup> Combination MMRV vaccines have been shown in clinical trials to produce similar efficacy to the monovalent varicella vaccines. Similar to the monovalent vaccines, the effectiveness of 1 dose of MMRV (Priorix-Tetra<sup>®</sup>) against any disease is lower for a single dose (65%) than for 2 doses (95%).<sup>29</sup>

The response to a single dose of varicella vaccine decreases as age increases; hence, healthy adolescents (14 years and older) and adults require 2 doses, 1–2 months apart.<sup>30</sup>

### Breakthrough disease (natural varicella infection in vaccinated individuals)

Vaccine failure is known as ‘breakthrough varicella’ and is defined as a case of wild-type varicella infection occurring more than 42 days after vaccination. The majority of cases of breakthrough varicella are mild and result in fewer skin lesions (usually <50), although up to 28% of breakthrough varicella cases may be severe (>500 lesions).<sup>2</sup> In mild breakthrough cases, the skin lesions may not be vesicular and systemic symptoms, such as fever, occur less frequently.<sup>2</sup> Because of this, breakthrough disease may not be recognised, or may be misdiagnosed. However, breakthrough varicella can still be contagious and exclusion from child care or school is recommended. A study of household secondary attack rates found that contagiousness is related to the number of lesions. Vaccinated cases with more than 50 lesions were as contagious as unvaccinated cases, but when vaccinated cases presented with fewer than 50 lesions, they were only one-third as contagious.<sup>2</sup>

Recent studies have suggested higher rates of breakthrough varicella in recipients of 1 dose than in recipients of 2 doses, in single dose vaccine recipients more than 5 years after vaccination, and in settings of close contact such as households.<sup>31,32</sup> Long-term follow-up of 7,500 children aged 12–23 months found no difference in rates of breakthrough varicella between those vaccinated at 12–14 months of age and those vaccinated at 15–23 months of age.<sup>33</sup>

### Vaccine safety

Vaccine reactions following monovalent varicella vaccination are generally mild and include fever (in 15% of vaccine recipients) and injection site reactions (in about 7–30% of vaccine recipients).

A varicella-like rash may develop following vaccination, occurring at the injection site (in 1–3% of vaccine recipients) or generalised (in an additional 3–5%), and typically consists of 2–5 lesions.<sup>34</sup> Rashes occurring within 14 days of vaccination (median 8 days) may be due to coincident wild VZV infection, while rashes due to the vaccine strain VZV occur a median 21 days (range 5–42 days) after vaccination.<sup>35,36</sup> Vaccine virus transmission is extremely rare and most rashes after varicella vaccination are due to other causes, especially in children. However, vaccine recipients who develop a rash should avoid contact with people who are immunocompromised.

More serious adverse events occurring soon after vaccination have been reported at a rate of 2.9 per 100,000 doses by passive surveillance.<sup>36,37</sup> A temporal but not necessarily causal relationship to the vaccine has been

established. However, causality is plausible for some reactions such as anaphylaxis following vaccination, thrombocytopenia, ataxia and encephalitis. These latter three are rare complications of natural varicella infection.<sup>37</sup> Adverse events occurring after vaccination should be reported to the Therapeutic Goods Administration (TGA) via specific state and territory reporting mechanisms.<sup>21</sup>

Three post-marketing studies in the USA identified an approximately 2-fold increased risk of fever and febrile convulsions in 1st-dose recipients of MMRV vaccine aged 12–23 months in the period 7–10 days<sup>38</sup> (or 5–12 days<sup>39</sup>) after vaccination, compared with recipients of MMR and VV given separately. Vaccination with MMRV resulted in 1 additional febrile seizure for every 2,300 doses compared to vaccination with MMR and VV separately. The risk was significantly greater among older children (>15 months of age).<sup>40</sup> There was no evidence of an elevated risk of febrile seizures after the 2nd dose of MMRV vaccine (compared to MMR and VV given separately), although most 2nd-dose recipients were aged 4–6 years, an age at which the incidence of febrile convulsions is low.<sup>41</sup> It is recommended that parents/carers/vaccine recipients are advised about possible symptoms in the period 5–12 days after vaccination and given advice on their management, including the use of paracetamol for fever.

Reactivation of the varicella vaccine strain to cause shingles in vaccine recipients is extremely rare. Cases of shingles in vaccine recipients have been reported but are usually due to wild-type virus.

### Concomitant administration

Monovalent varicella vaccines are safe to administer at the same time as all other recommended vaccines on the NIP schedule (given subcutaneously at a separate site). As MMR is a live attenuated vaccine, it should either be administered at the same visit (as MMR and VV if not given as MMRV) or at least 4 weeks apart from the monovalent varicella vaccine. This is because there is evidence of higher vaccine failure rates if MMR is given within 4 weeks of the varicella vaccine (unless given on the same day).<sup>21</sup>

### Contraindications/precautions

- Varicella vaccines are live attenuated viral vaccines and are contraindicated in pregnancy, and pregnancy should be avoided for 1 month following vaccination. However, in women inadvertently vaccinated during pregnancy, including those known to be seronegative

prior to vaccination, no adverse effects attributable to vaccination have been reported.<sup>42</sup>

- Varicella vaccination is contraindicated for people who are immunocompromised, but their household contacts should be vaccinated, if non-immune, to protect the immunocompromised person against infection.
- Varicella-containing vaccines are contraindicated in persons who have had anaphylaxis following a previous dose of any varicella-containing vaccine or anaphylaxis following any vaccine component.
- Receipt of immunoglobulin-containing products 3–11 months before or within 3 weeks after vaccination and long-term use of salicylate (aspirin) therapy are precautions for VV or MMRV vaccine. Refer to *The Australian Immunisation Handbook* for more details.<sup>21</sup>

### Other considerations

#### Serologic testing

In children <14 years of age, serologic testing prior to vaccination is not necessary as a reliable history of varicella infection in this age group correlates well with immunity. If the history of past varicella infection is uncertain (or absent), the individual should be considered susceptible and should be immunised. Children can safely receive either VV or MMRV vaccine even if prior infection with VZV has occurred; prior serologic testing is not essential. However, serologic testing is more likely to be useful for those over the age of 14 years as many without a history of varicella infection will actually be seropositive. Serologic testing after vaccination is not required or recommended. Refer to *The Australian Immunisation Handbook* for more details.<sup>21</sup>

#### Herpes zoster (shingles)

In people who have been previously infected with VZV, the natural immunity may be boosted by exposure to others with varicella, and this may reduce the risk of developing shingles later in life. Based on this observation, mathematical modelling has suggested that rates of shingles in adults may temporarily increase over time following the introduction of universal varicella vaccination because of a reduced exposure to the virus in the community. However, studies from the USA have found an increased incidence of age-specific shingles prior to the varicella vaccine program and use of the vaccine has not affected this increase.<sup>43</sup> Similar findings have been demonstrated in Australia.<sup>44</sup> The incidence of shingles is likely to be lower over time in varicella vaccine recipients than in those infected naturally with

wild-type varicella. This is suggested from preliminary data from the USA in which lower rates of shingles have been reported in varicella vaccinated immunocompromised children<sup>45,46</sup> and healthy adults.<sup>47</sup>

A vaccine to prevent shingles in older adults is recommended in Australia. For further information, see the NCIRS fact sheet [Zoster vaccine for Australian adults](#).

### Additional resources for primary medical care/vaccination providers

- *The Australian Immunisation Handbook*, 10th edition – the most up-to-date clinical recommendations are contained in the online version of the *Handbook* [www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home](http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home)
- Immunise Australia website <http://www.immunise.health.gov.au/>
- National Immunisation Program schedule [www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/national-immunisation-program-schedule](http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/national-immunisation-program-schedule)

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