Chickenpox vaccine for all?

Two live attenuated varicella vaccines are now available in Australia; they are approved for use in healthy people from 12 months of age. At present, the highest priorities for vaccination should be susceptible adolescents and adults, especially healthcare workers, childcare and school staff, and women planning a pregnancy.

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Chickenpox, or varicella, is a highly infectious viral disease of humans that occurs worldwide and year around, with spring–summer peaks in temperate regions. In temperate climates, chickenpox is largely a disease of children, and in Australia about 95% of individuals show evidence of past varicella-zoster virus (VZV) infection, and thus immunity, by adulthood.

Chickenpox was recognised as a distinct entity relatively recently, having been differentiated from scarlet fever in the sixteenth century and from smallpox in the mid-eighteenth century. There are two theories for the origin of the name: either from the use of the word chicken with the sense of mild, or from the resemblance of the characteristic vesicles to the chickpea. Primary infection with VZV was described as the cause of chickenpox in the 1950s by Weller and colleagues, who also isolated VZV from zoster (shingles) lesions. In 1965 Hope-Simpson hypothesised that zoster was caused by reactivation of latent VZV in the dorsal root ganglia.

A live attenuated varicella vaccine (using an isolate from a Japanese child named Oka) was first developed in 1974 and was licensed in Japan in 1987. At that time the reason for developing the vaccine was to immunise children with leukaemia and thus protect them from life-threatening chickenpox.

During 2000, two live attenuated varicella vaccines, Varilrix and Varivax II, both based on the Oka strain, were approved by the Australian authorities; the approval is only for use in healthy children and adults. Although there is some evidence of the value of vaccination in reducing the incidence of zoster, the primary aim of these vaccines is to prevent chickenpox and its short term complications.

Costs and complications of varicella

Although varicella is generally a mild illness in otherwise healthy children (Figure 1), it is more severe in adults (Figure 2) and serious complications do occur. The frequency of complications increases with age. Hospitalisation rates reported in a US study varied from 12 per 10,000 cases in

IN SUMMARY

- **Live attenuated varicella vaccines are approved for use in healthy persons and are safe and effective in protecting against chickenpox and its immediate complications.**
- **A single dose is recommended for healthy children from 12 months to 12 years of age; adolescents and adults need two doses given one to two months apart.**
- **Susceptible adults and adolescents should be the highest priority for vaccination, especially if they are healthcare workers, childcare or school staff, or women planning a pregnancy.**
- **Adults with a history of chickenpox or shingles can be considered immune and do not require vaccination; if the history of these diseases is negative or uncertain, serological testing to determine immunity will identify the few susceptible adults who need vaccination.**
- **Vaccination of healthy children may be warranted on the basis of avoiding the rare serious complications of chickenpox and of minimising disruption and economic loss to the family, if it does not interfere with routine scheduled vaccinations.**

under-5-year-olds to 127 per 10,000 in adults.[1] Similarly, rates for varicella pneumonia were 1.3 per 10,000 in the under-5 group compared with 27 per 10,000 in adults; and for encephalitis 0.9 per 10,000 in 5- to 14-year-olds compared with 3.3 per 10,000 for adults.[1]

A recent study based on data from NSW and South Australia showed an overall annual hospitalisation rate of four to five per 100,000 for varicella and 10 to 14 per 100,000 for zoster.[2] In Australia during 1968 to 1997, an average of five varicella related deaths occurred each year.[2]

Infection in early pregnancy is rare but may result in congenital varicella, with an estimated incidence in Australia of one per 100,000 births per year.[3] This severe condition may be associated with severe skin scarring, serious limb deformities, blindness, neurological defects and intellectual handicap. Varicella also tends to be more severe in pregnant women, who suffer a higher incidence of pneumonia. Moreover, infection around the time of delivery may result in life-threatening, disseminated disease in the newborn.

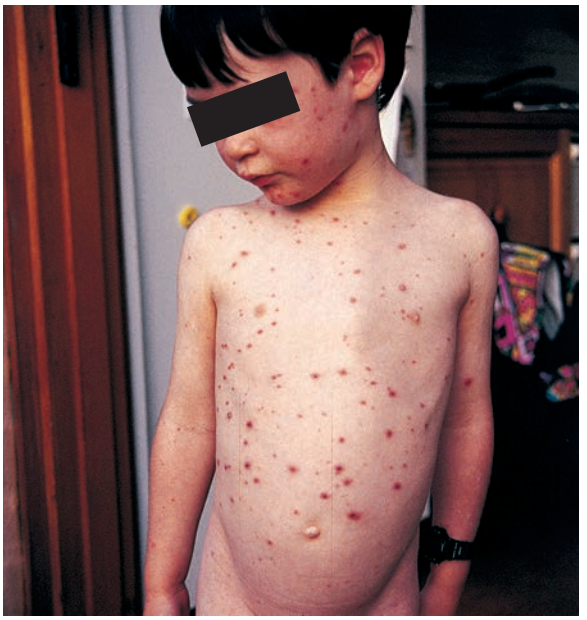
Even mild infection in healthy young children may be disruptive to the family. Our study of chickenpox in young children attending preschools and childcare centres found that children lost on average 5.5 days of child care, leading to mothers losing 2.5 work days and fathers 0.4 work days. Secondary cases were common among family members. Lost parental income of $160 to $345 per child far outweighed the medical costs of $33 per child.[4]

Australian recommendations for varicella vaccine

The NHMRC has approved varicella vaccine for use in healthy children aged 12 months or older, as long as its use does not affect compliance with routine vaccinations. It is possible that this vaccine will be incorporated in the standard schedule when combination measles–mumps–rubella–varicella vaccines become available at a reasonable cost.

A single dose only is required in children up to 12 years of age, which may be given at the same time as the measles–mumps–rubella vaccine or other vaccines. If varicella vaccine is not administered at the same time as other live vaccines, it should be given at least one month before or after.

Currently nonimmune adolescents and adults should be high priorities for the vaccine, even though two doses are required (one to two



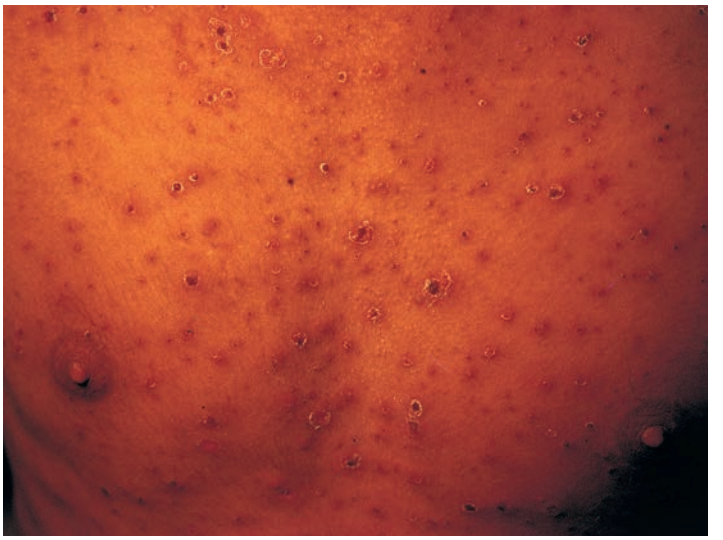


Figure 1 (left). Mild chickenpox rash in a 3-year-old child.
Figure 2 (above). Severe chickenpox rash in an adult.

months apart) in individuals aged 13 years or older. As most of these individuals have natural immunity, screening should be carried out before vaccination. The rebatable cost of a single serological test is currently a fraction of the cost of two doses of varicella vaccine. Individuals with a history of chickenpox or shingles have a greater than 99% chance of being immune and require no further action.[5] Adolescents and adults without such a history still have a high likelihood (greater than 80%) of immunity and should be offered VZV-specific IgG serology, which is now available through most private laboratories. If this assay is negative or equivocal, varicella vaccination is recommended.

Healthcare workers

Healthcare workers, including those in primary care settings, are at risk of exposure to varicella from patients and, if infected, are likely to expose patients who may be at risk of serious disease because of pregnancy or immune compromise. A recent Australian study in 100 healthcare workers showed all had seroconverted after two doses of the vaccine, with a small number experiencing mild systemic illness after the first dose.[6] All healthcare workers, including students, should be vaccinated if screening indicates they are susceptible.

Women planning a pregnancy

Varicella vaccine is contraindicated in pregnancy, and if a pregnant woman is inadvertently vaccinated she should be referred to an infectious diseases specialist. However, if a pregnancy is being planned and the woman has no history of chickenpox or shingles serological testing is advised. If susceptible the woman should be vaccinated and cautioned to delay conception for one month.

Childcare workers and teachers

Because they are exposed to large numbers of potentially infectious children, school teachers and staff working in childcare centres and preschools should be offered varicella vaccination if found to be susceptible.

Household contacts of immunosuppressed individuals

Varicella vaccination is currently contraindicated for use in immunosuppressed individuals. The best strategy to protect them is to ensure susceptible household contacts are vaccinated. Transmission of vaccine virus appears to be rare and has only been demonstrated from vaccinees who develop a rash (see below). If this occurs in a household of an immunosuppressed person, specialist advice should be sought.

Healthy children

Until varicella vaccination becomes part of the standard schedule, there is no prospect of reaching levels required to achieve herd immunity and thus eliminate circulation of the virus in the community. Therefore, parents can be encouraged to have their children vaccinated on the basis of protection against rare but serious complications and/or on the grounds of reducing disruption to the family when one or more children in the household acquire chickenpox.

Use of vaccination after exposure and during outbreaks

There is some evidence that vaccination within three to five days of first chickenpox exposure may prevent or ameliorate infection,[7] and recent reports have demonstrated the role of vaccination in

shortening outbreaks in institutional settings.[8] At present, the vaccines are not approved for these uses, so advice regarding vaccination and other measures in outbreak control should be sought from local public health authorities.

Adverse reactions

Vaccinated children suffer soreness (up to 20%), rash at the injection site (3 to 5%) or a generalised rash (3 to 5%) more often than do controls; however, fever occurs no more often than it does in controls. Vaccinated adults experience fever (10%) and soreness (25%) at a similar rate after the first and second doses; a local or generalised rash occurs in 3 to 5% of adults after the first dose and in about 1% of recipients after the second dose.

A US study of three years of postlicensure surveillance of Varivax II-related adverse events (representing about 10 million doses) indicates a very low rate of serious events, including pneumonia, anaphylaxis, other immune-mediated syndromes, neurological disorders and death.[9] Apart from anaphylaxis (from which all cases recovered), the cause was definitely attributed to varicella vaccination in only a minority of cases. The authors highlighted the importance of continued reporting and full investigation of the aetiology of severe events wherever possible. This also applies in Australia and should be undertaken in consultation with an infectious diseases specialist and a public health virology laboratory.

Efficacy and breakthrough infection

Household exposure studies suggest that vaccination offers 80 to 90% protection against varicella in healthy individuals. A varicella-like rash within a few weeks of vaccination may be either natural infection or caused by vaccine virus. The duration of protection is unknown, but protection does wane with time, resulting in generally mild natural infections known as 'breakthrough' varicella occurring at a rate of 1 to 3% per year.

Transmission of vaccine virus

Transmission of vaccine virus to other individuals can only occur in the presence of a rash, and transmission by healthy vaccinees (as opposed to children with leukaemia) has been confirmed by viral studies on only a handful of occasions. The large US postlicensure study recorded 145 reports of possible vaccine virus transmission from roughly 10 million doses administered, but virological confirmation was not always performed.[9]

Effects of infant vaccination on varicella epidemiology

There are several concerns about the possible effect of an infant varicella vaccination program on the pattern of disease in the community. In addition, the difficulty Australia is having in achieving high coverage of measles vaccine does not augur well for varicella vaccine.[10]

Experience with other childhood vaccination programs, such as measles, shows that overall numbers of cases decline but more cases occur in adults, in whom infection tends to be more severe. Thus, after an initial period when a single dose is administered to infants, a two-dose schedule is required to 'mop up' individuals who either have never been immunised or have failed to mount an adequate immune response to a single dose.

As VZV remains latent in infected individuals, it is unclear whether the occurrence of zoster will maintain circulation of the virus, leading to a failure of herd immunity despite vaccination, or, in fact, if this will boost population immunity and suppress symptomatic chickenpox and perhaps zoster. Moreover, it has been found recently that

subclinical reactivation of vaccine virus may boost immunity, possibly allowing extended protection in some vaccinated individuals.[11]

Apart from these concerns, studies of the benefits of a national vaccination program suggest that costs of a program would be somewhat greater than the savings in health costs. Nevertheless, of possible strategies, universal infant vaccination is the most cost effective.[12] Most costs caused by chickenpox are related to disruption to the family and parental employment,[4] so in addition to avoiding a very small but measurable risk of serious illness, parents may choose to vaccinate their children even in the absence of public funding.

Conclusion

Varicella vaccines show acceptable safety and efficacy against chickenpox in healthy recipients. With most Australian adults immune as a result of natural infection, the highest priority groups for vaccination are people who have been shown by screening to be susceptible, including healthcare workers, childcare and school staff, and women planning a pregnancy. Children may also be vaccinated to avoid the small risk of severe chickenpox complications and to minimise any disruption caused by illness to family and parents' work commitments.

While the effect of mass infant vaccination on the pattern of disease in the community is largely unknown, there is some evidence that vaccination will have a long term beneficial effect on the incidence of zoster. MT

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Further reading

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