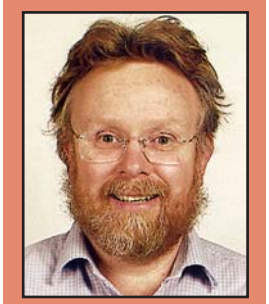
Varicella and varicella vaccination

An update

John Litt, Margaret Burgess



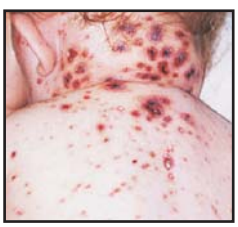
John Litt, MBBS, DipRACOG, MSc, FRACGP, FAFPHM, is Senior Lecturer, Department of General Practice, Flinders University, Noarlunga Hospital, South Australia, and a member, National Quality Committee, RACGP.

Margaret Burgess, MD, BS, FRACP, is Director, National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases, University of Sydney and Childrens Hospital at Westmead, and member, Australian Technical Advisory Group on Immunisation (ATAGI).

BACKGROUND Although varicella is generally mild in children, it is often more severe in adults and overall is responsible for approximately 2000 hospital admissions each year in Australia. Live attenuated varicella vaccines have been available in Australia since 2000. They are safe and effective.

OBJECTIVE This article discusses the role of varicella vaccination and management of varicella in pregnancy.

DISCUSSION The National Health and Medical Research Council recommends vaccination of all children at the age of 18 months and a catch up program for nonimmune adolescents and adults. The program is not yet funded by the commonwealth government. Varicella vaccine may be used for postexposure prophylaxis and is most effective if given within three days after exposure, but can be used up to five days from exposure. Varicella in pregnancy may cause congenital malformations; the highest risk (2%) being when maternal infection occurs between 13–20 weeks gestation. Offer varicella zoster immunoglobulin to nonimmune pregnant women, neonates and other high risk subjects with significant exposure to varicella or zoster.



Varicella (chicken pox) is mostly a mild disease in healthy children but is more frequently severe in adolescents and adults, and in immunosuppressed individuals. In Australia each year almost 2000 patients are admitted to hospital with varicella (800 of these being less than five years old) and there are seven deaths each year.[1] Acute varicella may be complicated by cerebellitis (1 in 4000 cases), aseptic meningitis, encephalitis (1.8 in 10 000 cases), thrombocytopenia and pneumonia.

The average incubation period for varicella is 14–15 days (range 10–21 days). Communicability is usually from 1–2 days before onset of the rash to five days after the appearance of the first crop of vesicles. Herpes zoster (shingles), a contagious and often serious illness, is caused by reactivation of latent varicella zoster virus in the dorsal root ganglia. In comparison with varicella, it causes almost five times the annual number of hospital admissions and deaths.[2]

Varicella in pregnancy

Some infections, including varicella, rubella, cytomegalovirus infection, toxoplasmosis and listeriosis, are more serious in pregnant than nonpregnant women because of the risk of transmission to the fetus. Pre-pregnancy enquiry or routine antenatal screening for the presence of, or

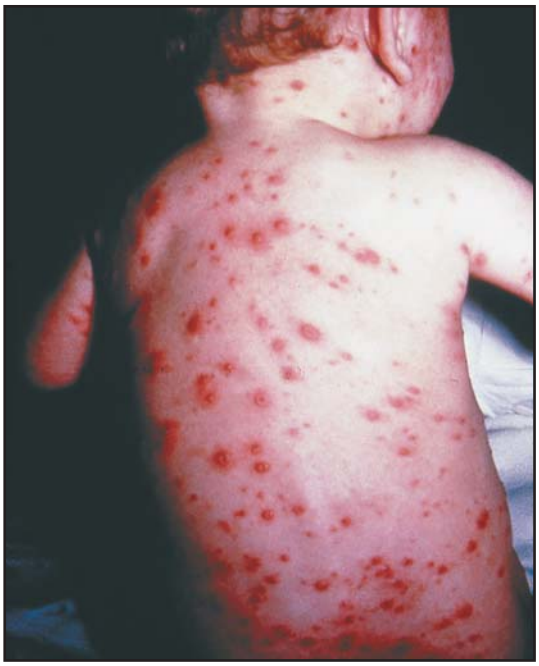


Figure 1. Neonate with chicken pox

susceptibility to, some of these infections and appropriate prompt management can prevent adverse fetal or perinatal outcomes.[3,4]

Congenital varicella syndrome occurs in 1–2% of women after varicella infection in the first half of pregnancy.[5] Its manifestations mimic a developmental radiculopathy[6] and include:

- skin scarring in dermatomal distributions (76%)
- neurological defects (60%)
- eye diseases (51%), and
- skeletal anomalies (49%).

Severe neonatal varicella infection can result from perinatal maternal varicella (Figure 1).[7]

Varicella vaccines in Australia

Live attenuated formulations of varicella vaccine have been approved and available in Australia since 2000. The National Health and Medical Research Council (NHMRC) recommends that a single dose is sufficient for children from the age of one year to the fourteenth birthday (product information recommends a single dose only up to the thirteenth birthday).[8] After the fourteenth birthday, two doses are required 1–2 months apart.[8] Seroconversion following vaccination occurs in 90-100% of recipients; 70–90% of vaccinees are protected when exposed, and vaccinees who develop infection after exposure usually have mild disease.[8] The duration of immunity after vaccination is likely to be substantial but is not yet established and it is possible that booster doses may be required.

Reactions following vaccination are usually mild; occasional fever, papular or papulovesicular rash (within 5–26 days), generalised or at the injection site, injection site pain, redness or swelling.[9] More severe reactions such as anaphylaxis, ataxia and thrombocytopenia have also occasionally been reported in association with the vaccine.[10] In the United States there have been three reports of transmission of varicella vaccine type virus from a healthy vaccinated person to a healthy contact.[8]

Two vaccines are available in Australia. Both products (Varilrix – Glaxo Smith Kline, Varivax Refrigerated – CSL/Merck Sharp & Dohme) are derived from the OKA varicella zoster virus strain, but have slight genetic differences and are also slightly different in their other constituents.[8]

Routine immunisation of all children aged 12–18 months and all nonimmune adolescents and adults is recommended by the NHMRC, but the vaccination program is not yet funded by the commonwealth government.[8] The vaccine can be given at the same time as other vaccines (eg. MMR, DTPa, conjugated meningococcal type C vaccine) as long as a separate syringe and injection site are used.[8]

Contraindications

The contraindications to varicella vaccine are similar to those for other live vaccines:

- pregnancy
- immunodeficiency
- clinical AIDS
- high dose corticosteroids (2 mg/kg prednisone per day)
- previous anaphylactic reaction to any component of the vaccine
- recent (within past three months) treatment with IgG by intramuscular injection, or
- recent (within nine months) treatment with IgG by intravenous injection.

Postexposure prophylaxis

Varicella vaccine has also been shown to be effective in preventing varicella infection following exposure if provided within three days, and up to five days after exposure, the earlier the better.[11–14] 'Emergency' vaccination of exposed individuals during outbreaks has also been shown to stop the outbreak and prevent further expected cases. High risk subjects should be offered high titre intramuscular varicella zoster immunoglobulin (ZIG) if

Table 1. Prophylaxis and treatment options for exposure* to varicella, zoster or presence of varicella[4,8]

Category	Conditions	Test for v-2 antibodies	Significant exposure	Manifest disease
Pregnant women	Seronegative OR has uncertain or no personal history of varicella	Yes: seronegative or test not available	ZIG**	Oral aciclovir#
		Seropositive	Reassure	Oral aciclovir#
	Good history of varicella or seropositive	No	Reassure	Consider oral aciclovir#
Neonates	If mother has varicella seven days before delivery or two days after	No	ZIG	IV aciclovir 10 mg/kg intravenously, 8 hourly for 7–10 days
	Exposed to varicella in first month of life AND Mother is seronegative OR has uncertain or no personal history of varicella	Yes	ZIG	IV aciclovir 10 mg/kg intravenously, 8 hourly for 7–10 days
Premature infants who are still hospitalised	At less than 28 weeks gestation OR with birth weight less than 1000 g	No	ZIG†	IV aciclovir 10 mg/kg intravenously, 8 hourly for 7–10 days
Adults	Patients with cellular immunity associated diseases	Yes##	ZIG	IV aciclovir 10 mg/kg intravenously, 8 hourly for 7–10 days
	Patients on immunosuppressive therapy	Yes##	ZIG	IV aciclovir 10 mg/kg intravenously, 8 hourly for 7–10 days
Health care workers	Uncertain previous history of varicella or seronegative	Yes	Varicella vaccine††	Isolate from patients
	Previous varicella or seropositive	No	Watch for rash for three weeks after exposure and reassign from clinical duties if rash develops	Isolate from patients

* Significant exposure is defined as living in the same household as a person with active varicella or herpes zoster, or direct face-to-face contact with a person with varicella or zoster for at least five minutes, or being in the same room for at least one 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.3

** Give ZIG intramuscularly if exposure is <4 days since exposure. If >4 days, consider oral aciclovir if risk of severe disease.

\# Aciclovir is rated category B3 (Pregnancy and Breastfeeding, eTG, January 2003, ISSN 1447-1868). Consider its use when potential benefits outweigh potential risks to the fetus, and with informed consent, for pregnant women who present within 24 hours of onset of varicella rash. Use intravenous aciclovir if the patient is immunocompromised or if there are respiratory symptoms, a haemorrhagic rash or persistent fever for more than six days.

If the immunosuppressed patient 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.

† Give ZIG regardless of maternal history of varicella.

†† Provide varicella vaccine within three days, and up to five days postexposure, watch for rash for up to six weeks. If rash develops, reassign to nonclinical duties until rash resolves.

seen within four days of exposure.[4,8] Table 1 outlines the categories and conditions where subjects should be offered either prophylaxis or treatment with ZIG and/or aciclovir.

Varicella vaccination programs in other countries

Varicella vaccine has been used in Japan for more than 20 years, but uptake has been relatively low. The vaccine was introduced into the USA in 1995. Since then more than 20 million doses have been used. Coverage in toddlers is now approximately 70% and the incidence of varicella has fallen very dramatically.[15]

Varicella vaccination is also recommended routinely in Canada and Germany. However, the programs in these countries have not yet been fully implemented. Studies in the USA have shown the vaccine strain virus may cause herpes zoster, but at

a lower rate (2.6 per 100 000) than natural infection (68 per 100 000).[16]

Will vaccination change the epidemiology of varicella and herpes zoster?

Surveillance in the USA indicates that once a large proportion of the childhood population has been vaccinated, the incidence of varicella declines in all age groups, not just the vaccinated cohorts.[15] The incidence is, however, much less in the vaccinated cohorts, so the average age of infection increases and the proportion of adults among the very much smaller number of cases, increases. Mathematical modelling suggests that in a fully implemented program varicella morbidity in adults will always be less than it was before vaccination. However, varicella infection in children appears to cause subclinical boosting of immunity in adults in the same community, which delays the onset of herpes zoster in those adults.[17] If vaccination removes varicella almost entirely from the community, the introduction of childhood vaccination could result in a shifting of the average age of herpes zoster into younger age groups and an overall increase in herpes zoster in the medium term until the entire population is comprised of people vaccinated in childhood. This hypothesis is yet to be substantiated. There is no evidence yet to suggest there is any increase or shift in age of herpes zoster in the USA. However, there are two cohort studies indicating that in the British community, where vaccination has never been used, people who have contact with children are less likely to develop herpes zoster.[17,18]

The Australian Technical Advisory Group on Immunisation (ATAGI) considered this evidence very carefully before recommending to the NHMRC that Australia adopt routine childhood varicella vaccination.

The results of a very important USA randomised trial of a specifically formulated, high titre varicella vaccine administered to adults aged 60 years or more to determine if the vaccine prevents the onset of herpes zoster in previously naturally infected persons, are expected in late 2004.[19] If the vaccine proves successful in preventing zoster, we will have a further valuable use for the vaccine.

Conclusion

While usually a mild disease in children, varicella can have serious complications particularly in adolescents and adults, pregnant women and the immunocompromised. Herpes zoster is a reactivation of latent varicella virus in the dorsal root ganglia, is highly infectious and is a serious long term consequence of varicella infection causing five times the number of hospital admissions and deaths than initial varicella infections. Routine childhood immunisation is recommended and nonimmune pregnant women, neonates and other high risk subjects should be offered ZIG within four days of significant exposure to varicella or zoster.

SUMMARY OF IMPORTANT POINTS

- Varicella can be life threatening.
- Live attenuated varicella vaccines are safe and effective.
- All toddlers and nonimmune adolescents and adults should be vaccinated.
- Reactions following varicella vaccine are usually mild.
- Contraindications to varicella vaccine are similar to those for MMR vaccine.
- Use varicella zoster immunoglobulin (ZIG) in nonimmune pregnant women, neonates and other high risk subjects with significant exposure to varicella or zoster.

Conflict of interest: none declared.

References

1. McIntyre P, Gidding H, Gilmour R, et al. Vaccine preventable diseases and vaccination coverage in Australia, 1999-2000. Commun Dis Intell 2002; 626:S1-S111. Available at: http://www.health.gov.au/pubhlth/cdi/pubs/pdf/vpd99_00.pdf.
2. Chant K G, Sullivan E A, Burgess M A, et al. Varicella zoster virus infection in Australia. (Erratum appears in Aust N Z J Public Health 1998; 22(5):630). Aust N Z J Public Health 1998; 22:413–418.
3. Gilbert G L. Infections in pregnant women. Med J Aust 2002; 176(5):229–236.
4. Heuchan A-M, Isaacs D. Management of Varicella zoster virus exposure and infection in pregnancy and the newborn period. Australasian Subgroup in Paediatric Infectious Diseases of the Australasian Society for Infectious Diseases. Med J Aust 2001; 174(6):288–292.
5. Enders G, Miller E, Cradock-Watson J, et al. Consequences of varicella and herpes zoster in pregnancy: Prospective study of 1739 cases. Lancet 1994; 343:1548–1551.
6. Borzyskowski M, Harris R F, Jones R W. The congenital varicella syndrome. Eur J Paediatr 1981;

137(3):335–338.
7. Centers for Disease Control and Prevention. Prevention of varicella: Recommendations of the Advisory Committee on Immunisation Practices (ACIP). Morb Mortal Wkly Rep 1996; 45(RR–11):1–36.
8. National Health and Medical Research Council. The Australian Immunisation Handbook. 8th edn. Canberra: Australian Government Publishing Service, in press.
9. Skull S A, Wang E E. Varicella vaccination: A critical review of the evidence. Arch Dis Child 2001; 85:83–90.
10. Wise R P, Salive M E, Braun M M, et al. Postlicensure safety surveillance for varicella vaccine. (Erratum appears in J Am Med Assoc 2000; 284:3129). J Am Med Assoc 2000; 284:1271–1279.
11. Asano Y, Nakayama H, Yazaki T, et al. Protection against varicella in family contacts by immediate inoculation with live varicella vaccine. Pediatrics 1977; 59:3–7.
12. Arbeter A M, Starr S E, Plotkin S A. Varicella vaccine studies in healthy children and adults. Pediatrics 1986; 78:748–756.
13. Gentile A, Del Pont J M, Lamy P, et al. Is varicella vaccine effective for postexposure prophylaxis? Presented at the 37th annual meeting of the Infectious Diseases Society of America (IDSA). Philadelphia, PA: November 18–21, 1999.
14. Ferson M J. Varicella vaccine in postexposure prophylaxis. Commun Dis Intell 2001; 25:13–15.
15. Seward J F, Watson B M, Peterson C L, et al. Varicella disease after introduction of varicella vaccine in the United States, 1995–2000. J Am Med Assoc 2002; 287:606–611.
16. American Academy of Pediatrics. Varicella zoster infections. In: Pickering L K, ed. 2000 red book: Report of the Committee on Infectious Diseases. 25th edn. Elk Grove Village, IL: American Academy of Pediatrics, 2000.
17. Brisson M, Gay N J, Edmunds W J, Andrews N J. Exposure to varicella boosts immunity to herpes zoster: Implications for mass vaccination against chickenpox. Vaccine 2002; 20:2500–2507.
18. Thomas S L, Wheeler J G, Hall A J. Contacts with varicella or with children and protection against herpes zoster in adults: A case control study. Lancet 2002; 360:678–682.
19. Oxman M N. Immunisation to reduce the frequency and severity of herpes zoster and its complications. Neurology 1995; 45(12 Suppl 8):S41–S46. AFP

CORRESPONDENCE

Email: j.litt@flinders.edu.au