

## Comments to this month's Clinical Challenge

### Comments:

Varicella-zoster viral (VZV) infection occurs worldwide. It is a common, highly infectious disease that, in the absence of immunisation, infects almost every person. The burden of disease is greatest among children with more than 90% of cases occurring in this age group.

Varicella vaccine was licensed on 17 March 1995 by the US Food and Drug Administration for use in healthy persons 12 months of age or older who have not had varicella. In Hong Kong, the vaccine has been available for use since 1997 and there are two preparations currently on the market (**Table 1**). The two products have been found to have very similar efficacy. The storage requirements and the price may have a part to play in the choice between them.

I have divided the subsequent discussion into six sections to cover the various important issues concerning the vaccine.

### 1. Efficacy and immunogenicity of the vaccine

Varicella vaccine has been demonstrated to be highly effective. Clinical trials have shown the vaccine to be 70% to 90% effective in preventing varicella and more than 95% effective in preventing severe varicella.<sup>1,2</sup> The seroconversion rate after one dose of vaccine was demonstrated to be 97%. Although concern has been expressed about waning immunity, follow-up evaluations of children immunised during prelicensure clinical trials in the United States revealed protection for at least 11 years<sup>3</sup> while studies in Japan indicated protection for more than 20 years. But this prolonged protection might have resulted from asymptomatic boosting of vaccine-induced immunity by exposure to wild-type VZV.<sup>4</sup> Follow-up studies are being performed to determine the need, if any, for additional doses of varicella vaccine.

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“Breakthrough” disease following exposure to wild-type VZV occurs in about 1 to 4% of vaccinees per year (natural varicella attack rates in children are an estimated 9%), and the rate does not seem to increase with length of time after immunisation.<sup>5</sup> “Breakthrough” disease is usually of short duration and mild with fewer than 50 VZV skin lesions and low-grade or no fever.

### 2. Adverse reactions

The vaccine has been shown to be safe. Adverse events are generally mild and include fever (10-14%), vaccine-associated rash (4-6%) and injection site reactions (19.3%).<sup>6</sup> In placebo-controlled studies carried out in healthy children, the incidence of fever of 38.9°C or more among vaccinees was not significantly different from the control group. The rash usually consists of six to ten lesions occurring seven to 21 days after inoculation and lasting only about two days. Children with more than 50 lesions were likely to be incubating wild-type VZV at the time of vaccination. The only complaint that occurred more often in vaccinated children was pain and redness at the injection site. In most of the cases, conservative management was all that was required.

### 3. Herpes zoster after immunisation

Vaccinated individuals have a significantly lower incidence of subsequent zoster compared with those who suffer natural varicella. The reported incidence of zoster in healthy vaccinated children is 13 cases per 100,000 person-years compared with 30 to 70 per

**Table 1: Preparations of varicella vaccine available in Hong Kong**

Company	Smithkline Beecham	Merck, Sharp & Dohme
Name of product	Varilrix	Varivax
Viral load (plaque forming units per dose)	> 2,000	> 1,350
Storage	2°C – 8°C	< –15°C
Retail price per dose (Hong Kong dollars)	400	465

100,000 person-years in the natural varicella category. Explanations have been proposed for the decreased incidence of zoster following vaccination. One possibility is that the virus is attenuated and less able to reactivate than the wild-type virus. Another is that the vaccine strain may have less frequent access to sensory nerves because of a lower incidence of viraemia and infection of the skin.<sup>7</sup>

#### 4. Post-exposure immunisation

There is evidence to suggest that the vaccine is effective in preventing or modifying varicella when given to household contacts within three days of the appearance of the rash in the index case. In a study where ten subjects received post-exposure vaccinations within 72 hours of exposure, only one developed skin lesions.<sup>8</sup> There is no harm from intercurrent administration of varicella vaccine to individuals incubating wild-type varicella.

#### 5. Interaction with other vaccine

Varicella vaccine may be safely given with all other routine childhood immunisations. Similar immune responses were seen when measles-mumps-rubella (MMR), diphtheria-tetanus-pertussis vaccine (DTP) and varicella vaccine were given simultaneously or six weeks apart.

Concern has also been expressed regarding transmission of vaccine-associated virus. Experience up to now with more than 14 million doses of vaccine distributed in the United States indicates that such occurrence is extremely rare and the risk is increased only if the vaccinated person develops a rash.

#### 6. Pregnancy

The American Centre for Disease Control has established a Varicella Vaccine Pregnancy Registry to monitor maternal and foetal outcomes of women who were inadvertently immunised with the vaccine three months or less before pregnancy or anytime during pregnancy. The registry contains data from more than 300 deliveries and indicates no defects compatible with congenital varicella syndrome. However, data from such a small number of subjects may not have sufficient power to detect rare defects.

In summary, varicella vaccine is safe, effective and probably cost-effective in healthy children. No severe reactions have been reported following vaccination. The incidence of herpes zoster is less in vaccinees than in individuals who have had natural varicella infections. To date, there is no evidence of waning immunity following vaccination. ■

#### References

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