

VARICELLA VACCINE: A NEW ERA OF LIVE HERPESVIRUS VACCINE

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The present era of the live attenuated varicella vaccine began in the early 1970s in Japan with Dr. Takahashi and his colleagues' publication on the use of a live attenuated vaccine to prevent the spread of varicella zoster virus (VZV) in a hospital setting.¹ The live attenuated varicella vaccine is the first human herpesvirus vaccine made from Oka strain derived from a wild-type VZV, isolated from the vesicles of a healthy three-year-old Japanese boy (whose family name was Oka) with varicella.

The virus was subsequently attenuated by classical methods of attenuation (e.g., passage at lower temperature [34°C], in human embryonic lung cells, and guinea pig embryonic cells).² The Oka strain of varicella vaccine has been administered in North America to more than 9000 healthy children, more than 2000 healthy adolescents, and almost 600 children with leukemia, all of whom were susceptible to varicella when they were vaccinated.^{3,4}

The vaccine induced protection against household exposure, with an efficacy rate of more than 95% in an initial placebo-controlled study.⁵⁻⁷ Subsequent clinical trials of children between 1 and 12 years of age have demonstrated seroconversion rates of more than 95% after a single dose, with complete protection against disease in 85% of those exposed.⁶ Persistence of antibodies up to seven years after immunization has been found in 95% of the children.⁸ Varicella vaccine is immunogenic when administered concurrently with measles, mumps and rubella vaccines.⁹ Clinical studies evaluating the safety and immunogenicity when administered consistently with oral polio vaccine, *Hemophilus influenzae* type b vaccine, whole cell diphtheria tetanus, and pertussis vaccines are ongoing.

Adolescents and adults require two doses of the vaccine, usually given four to eight weeks apart, in order to achieve more than 95% seroconversion.¹⁰ The rate of persistence of antibodies is about 80% after a six-year interval.¹¹ Immunizing susceptible adults has important clinical benefits because of their susceptibility to serious varicella, and because protection or modified illness is documented despite lower antibody titer.

The varicella vaccine was given in open label clinical trials to children with leukemia in remission for at least one year, reducing the attack rate following exposure to 14% instead of the 80%-90% attack rate predicted for varicella-susceptible individuals. Seroconversion in these patients is associated with a high degree of protection, but most

children required two doses of the vaccine to elicit immunity.¹³

Adverse reactions after vaccination are minimal in a healthy population within one month of immunization. Local reactions at the injection site in the form of swelling, warmth and tenderness occurred in 10%-20%, low-grade temperature elevations occurred in less than 5% of vaccines.⁵ About 7% of children and 8% of susceptible adolescents and adults develop a mild vaccine-associated maculopapular or varicella form rash, with a median of two to five lesions, which may occur at the vaccine injection site or elsewhere. Vaccine virus has very rarely been recovered from skin lesions.^{6,10} Rates for rashes in leukemic vaccinees have varied from 20% to 50%. Generally, the rashes were mild, however, roughly 20% of leukemic recipients were treated with acyclovir for extensive rashes.¹³ The vaccine virus was transmitted from about 15% of leukemic children to their healthy susceptible siblings, but the contacts had mild clinical illness or asymptomatic seroconversion.¹⁴ A zoster-like illness has been reported in small numbers of children and adolescents who were immunized with varicella vaccine. No cases were severe.¹⁵ This incidence was no higher than that which occurs after natural varicella. Moreover, in children with leukemia the rate of zoster was 3% after vaccination, compared to a rate of 15% in leukemic children after natural varicella.^{16,17}

The Oka strain of varicella vaccine was licensed in Japan and Korea in 1987, and in the United States and Germany in 1995.

Who should be vaccinated against varicella? The American Academy of Pediatrics (AAP), the Committee on Infectious Diseases and the Advisory Committee on Immunization Practices (ACIP) have recommended immunization with a single dose of varicella vaccine for nonimmune children between 12 months and 12 years of age. Two doses of vaccine are recommended for those who have passed their 13th birthday.^{13,19}

The ACIP and the Hospital Infection Control Practices Advisory Committee also made recommendations to give the varicella vaccine to all health care workers susceptible to varicella.¹⁹ The vaccine should not be administered to immunocompromised children (other than those with leukemia in remission for at least one year under a special program), pregnant women or children with serious intercurrent conditions.

The varicella vaccine has not been used in Saudi Arabia. The vaccine recently became available at King Faisal Specialist Hospital and Research Centre, and recommendations have been made to follow the ACIP guidelines and to administer the vaccine to hospital employees susceptible to varicella. There are several questions about varicella vaccine which need answers, and these will hopefully come with large-scale vaccine use. Will zoster become less frequent in healthy vaccinees? Can immunocompromised patients, other than those with leukemia, be protected from varicella? Is a booster dose of the vaccine required for long-term maintenance of immunity? Answers to these important questions will no doubt emerge with time, as we gain more experience with this vaccine.

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