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THE "OTHER POX": VARICELLA VACCINE UPDATE

As of 1998, Oregon has required varicella vaccination of non-immune children entering day care, kindergarten and seventh grade. Children who hadn't yet met this requirement were excluded from school on February 21, 2001. Widely used in Japan and Korea since the mid-1980s, varicella vaccine (VARIVAX®) was approved in late 1995 by the US Food and Drug Administration after torturous developmental delays.[1] Varicella vaccine coverage among 19- through 35-month-old Oregon children has increased steadily and significantly since then, from 29% in 1997, to 43% in 1998, to 58% in 1999, to 69% by June, 2000.[2] Lingering provider concerns about vaccine safety combined with reluctance to administer a vaccine to prevent a "mild illness" may explain in part why 30–40% of our children are still varicella-unimmunized.[3] In this issue of the *CD Summary* we reconsider varicella infection, and summarize the encouraging results of recently published vaccine safety studies.

VARICELLA RECONSIDERED

Illness caused by the varicella zoster virus (VZV) has always been thought of as mild. Chickenpox, one type of VZV infection, has always been considered "mild," insofar as death and serious complications from the disease are rare. It is also common, extremely uncomfortable and very contagious in young children; though less common, it is more serious and just as contagious in adolescents and adults. Chickenpox victims have a whole-body rash (often with more than 1,000 intensely pruritic vesicular lesions), fever and utter malaise; they can lose as many as nine days of school or work.[4] The risk of complications and death is 10- to 20-fold higher among adults, about 7%–9% of whom are thought to be susceptible.[5] Chickenpox is a well-defined risk factor for severe invasive infection with group A *Streptococcus*.[6]

Zoster, a second type of VZV infection also known as "shingles," occurs in about 15% of recovered chickenpox victims when VZV latent in the dorsal root and sensory nerve ganglia reactivates. Shingles' cutaneous eruptions can be brutally painful, and severe post-herpetic neuralgia can last three months or more. Zoster skin lesions also contain high titers of infectious virus and can transmit varicella to susceptible contacts, sustaining the chain of transmission. And adults are efficient vectors for nosocomial transmission.[4] Mild indeed.

THE VACCINE

To prevent such suffering, the Advisory Committee on Immunization Practices (ACIP) has recommended one subcutaneous dose of vaccine for non-immune children 12 months through 12 years of age and two doses for non-immune persons ⩾13 years old. Parental history is considered a reliable indicator of immunity. The ACIP has made specific recommendations for immunizing special groups of people.[7,8]

Varicella vaccine was 95% effective in pre-licensure clinical trials,[9] and it has since proven itself during post-licensure chickenpox outbreaks.[10,11,12] In clinical trials, a single dose of VARIVAX® given to healthy children ⩽12 resulted in seroconversion rates of 95%. Seroconversion rates among adults were 79%–82% after one dose and 95% after two doses—hence the two-dose recommendation.[9] In the short term, VARIVAX® elicits specific immune responses similar to, but quantitatively less than, those that follow natural infection.[4] Waning immunity would leave people susceptible to VZV in adulthood, but follow-up evaluations of children immunized during the clinical trials found that they were protected for at least 11 years, and studies in Japan indicated protection for at least 20.[13]

ADVERSE EVENTS

Although most common side effects and safety problems associated with a new vaccine emerge during pre-marketing clinical trials, rare events are usually not detected until millions of doses have been administered. The association of intussusception with rotavirus vaccine is a dramatic and unfortunate recent example.[14] Both the FDA and the vaccine manufacturer, Merck & Co. Inc., have passive reporting systems for adverse events following administration of VARIVAX® whereby anyone (physician, parent, you name it) can report the occurrence of a suspected adverse event to the FDA's aptly named Vaccine Adverse Events Reporting System (VAERS) and/or to Merck's Worldwide Adverse Experience System (WAES). Both systems are passive and therefore incomplete; 75% of the reports for VARIVAX® in VAERS are also in WAES.[15,16]

From March 17, 1996 through July 25, 1998, VAERS received 6,574 case reports of adverse events in vaccine recipients, or 68 reports for every 100,000 doses sold. Adverse events most frequently reported to VAERS (which includes everything reported to WAES) were rashes (55%), possible vaccine failures (19%), and injection-site reactions (8%), all of which can be expected after administration of a live-virus vaccine. Four percent of VAERS reports described serious adverse events, including 14 deaths (though none were found to be vaccine-associated after lengthy investigation). There were no cases of congenital varicella syndrome reported after vaccine administration during pregnancy (which is contraindicated).[15]

Although VAERS findings are encouraging with respect to vaccine safety, they may be limited by under-reporting. Findings from another study are, happily, just as encouraging. There were no rare medical events (like encephalopathy) reported from among 89,753 members of the Northern California Kaiser Permanente Medical Care Program who received at least one dose of varicella vaccine; only two died within 60 days of vaccination—from prostate cancer and drowning.[17]

MODIFIED VARICELLA-LIKE SYNDROME

Both a modified varicella-like syndrome (MVLS) and herpes zoster can occur after vaccination; both are usually much less

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severe than naturally occurring chickenpox and shingles. MVLS is distinguished by a maculopapular (vs. vesicular) rash, a tiny number of lesions (<50 vs. >500), shorter duration (<4 days vs. >10), and the absence of fever and systemic symptoms.[4] Both MVLS and shingles can be caused by wild-type or vaccine strains of the virus; both can be transmitted to susceptible contacts.[3] Also called breakthrough infection when it occurs six weeks after vaccination or later,[14] MVLS occurred in 3%–4% of vaccinated children studied both before and after licensure. Breakthrough infection caused by wild-type virus can be acquired from exposure immediately preceding vaccination or as a result of vaccine failure. Risk factors for breakthrough infection include asthma or other reactive airway diseases[11] and household contact with varicella.[18,19] Children and others with MVLS should be treated as if they have chickenpox and excluded from school until their vesicular lesions, if any, are crusted. Susceptible contacts of MVLS or post-vaccination shingles cases should also be offered varicella vaccine.

RECOMMENDATIONS AND SUGGESTIONS

- Store the fastidious varicella vaccine frozen at an average temperature of -15°C (5°F) and reconstitute it not more than 30 minutes before administration—otherwise it won't be effective.
- Administer varicella vaccine to susceptible children ⩾12 months of age according to ACIP recommendations.
- Administer varicella vaccine to susceptible children and adults within three days of exposure to varicella.
- Advise vaccinees who develop MVLS or zoster after vaccination to avoid contact with non-immune immunocompromised people [8,14]
- Report any and all suspected adverse reactions to VAERS at 800/822-7367 (public sector providers report to OHD at 503-731-4020 and we will report to VAERS).
- When adverse events are suspected, obtain appropriate clinical specimens for laboratory identification, and consult directly with CDC's National Varicella Reference Laboratory (404/639-0066) about strain identification.

Shortage of Td

ADULT TETANUS and diphtheria toxoids (Td) will continue to be in short supply for the next 6–12 months.[20] From highest to lowest priority, Td should be administered to:

- travelers to a country where the risk of diphtheria is high;
- persons requiring tetanus vaccination for prophylaxis in wound management;
- persons who have received <3 doses of vaccine containing Td;
- pregnant women and persons at occupational risk for tetanus-prone injuries who have not been vaccinated with Td within 10 years;
- adolescents and adultswho have not been vaccinated with Td within 10 years.

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