An Outbreak of Varicella among Children Attending Preschool and Elementary School in Illinois

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In our investigation of a varicella outbreak among students in preschool, kindergarten, and grades 1–3 in Winnebago County, Illinois, we found an overall varicella vaccine efficacy of 88%, evidence that the circulating virus was a wild-type strain (as determined by polymerase chain reaction analysis), and evidence that vaccination of children ≤15 months of age was associated with an increased risk for breakthrough varicella (relative risk, 3.7; 95% confidence interval, 1.1–13.1; \( P = .04 \)). The efficacy of varicella vaccine might be improved if administration of the initial vaccine dose is delayed until children are ≥15 months of age.

Studies of the use of varicella vaccine in the United States have demonstrated an overall vaccine efficacy of ~85% (range, 70%–100%) \([1–5]\). Data on varicella vaccine efficacy have been derived from clinical trials and from several postlicensure reports \([3, 4, 6]\). However, a recent unpublished report noted a varicella vaccine efficacy of only 42% \([7]\). One of the topics of public health importance that is relevant to the study of varicella vaccine is breakthrough disease (i.e., varicella that occurs despite vaccination). Children who are immunized at 12–15 months of age may have a higher risk for breakthrough varicella \([8]\). Also, given that the vaccine generally is considered to be very efficacious, reasons for incomplete vaccination coverage need to be explored. These issues were examined during an outbreak of varicella among children attending preschool and elementary school in Illinois.

**Patients and methods.** From 1 January 2001 through 31 May 2001, an outbreak of varicella occurred in Winnebago County, Illinois. The Illinois Department of Public Health investigated the outbreak, which involved children at 2 elementary schools. A total of 168 preschool and kindergarten students attended school A, and 340 students in grades 1–3 attended school B. A self-administered questionnaire was distributed to the households of all students to obtain information on demographics, varicella vaccine immunization history (including date of immunization), varicella disease status (recent, previous, or none), and reasons why the varicella vaccine was not received (for children who had not been vaccinated). For students with recent cases of varicella, the questionnaire asked for the date of rash onset, the duration of the rash, the severity of rash-associated illness, underlying illnesses, and health care use (outpatient visits and hospitalization). A "case patient" was defined as a student at school A or school B who had varicella reported to the school nurse during the investigation period. Most cases of varicella were confirmed by the school nurse; however, the number of such confirmed cases was not recorded. Case patients were stratified, according to varicella vaccination status, as either patients with primary varicella (those who were unvaccinated and who had no history of varicella disease) or patients with breakthrough varicella (those who previously had been vaccinated). Calculations of vaccine efficacy were performed as previously reported \([9]\). Data for children who had an unknown vaccination history or a history of varicella disease before this outbreak were excluded from these calculations. RR, CIs, and \( P \) values were generated using EpiInfo statistical software, version 6.04b (Centers for Disease Control and Prevention).

**Results.** The questionnaire was returned for 406 of 508 children at schools A and B (338 households; response rate, 80%). Of the children for whom questionnaires were returned, 218 were reported to have had varicella disease before 1 January 2001. Sixty-nine others were reported to have had either an unknown or an unverifiable history of varicella, and 84 did not develop varicella during the investigation period and were not part of the aforementioned 2 groups. The remaining 35 children who had varicella identified during the period of investigation included 12 children at school A and 23 children at school B. These 35 case patients included 19 males and 16 females (age range, 4–8 years). Eight (23%) of the 35 patients had break-
through varicella. One additional breakthrough case was identified in a case patient’s sibling, who was not of school age. Varicella-zoster virus was recovered from 1 patient with breakthrough varicella. Testing performed at the US Centers for Disease Control and Prevention National Varicella Zoster Virus Laboratory (Atlanta) (PCR LaRussa method [ORF 38/ORF 54] and Loparev method [ORF 62]) [10, 11] demonstrated that the virus was a wild-type strain.

At schools A and B, the varicella attack rates among unvaccinated children were 30% (9 cases among 30 children) and 54% (18 cases among 33 children), respectively; the attack rates among vaccinated children were 3% (3 cases among 88 children) and 9% (5 cases among 58 children), respectively. Overall vaccine efficacy was 88%, as determined by use of the following formula: (attack rate for children who were not vaccinated − attack rate for children who were vaccinated)/attack rate for children who were not vaccinated (i.e., [43% − 5%]/43%). The vaccine efficacy was 89% for children at school A and 84% for children at school B. Of the 8 patients with breakthrough varicella, 5 (62%) had <50 lesions and 3 (38%) had ≥50 lesions.

For 151 children who had not received varicella vaccine and who did not have a history of varicella disease, the following reasons were given for not receiving vaccine: vaccine was not recommended by a pediatrician (27 children [18%]), the vaccine was too new and/or needed more research (20 [13%]), the parent had a lack of either knowledge of or access to the vaccine (17 [11%]), the parent was concerned about the duration of immunity provided by the vaccine versus natural immunity (26 [17%]), the parent was concerned about the number of immunizations (injections) his or her child was receiving (2 [1%]), and no response or no reason (59 [40%]). A total of 227 children (including 9 case patients) had not received the vaccine because they had a history of varicella disease; 132 of these children had developed varicella after August 1995 (the approximate time of commercial availability of the vaccine in the United States), and 95 children had developed varicella before that time.

No case patients were hospitalized. Analysis of 120 children who were vaccinated and for whom information on age at vaccination was available demonstrated that vaccination at ≤15 months of age was associated with an increased risk for breakthrough varicella (RR, 3.7; 95% confidence interval, 1.1–13.1; P = .04, by Fisher’s exact 2-tailed test). This analysis included the one preoutbreak case of varicella identified among the households surveyed.

**Discussion.** We found a high efficacy of the varicella vaccine during the outbreak. The 88% efficacy that we noted was similar to the efficacies found by Vazquez et al. (85%) and Izurieta et al. (86%) [3, 6]. These findings support the observation that the vaccine is highly effective but is not guaranteed to prevent varicella. The data from our study also reveal an important risk factor for breakthrough varicella: immunization with varicella vaccine at ≤15 months of age.

Varicella vaccine is recommended for children ≥12 months of age who are susceptible to varicella infection [12]. The vaccine is typically administered at 12–15 months of age, approximately the time that children receive the measles-mumps-rubella vaccine and the diphtheria-tetanus-pertussis booster. It has been reported that cases of breakthrough varicella occur at a rate of 2%–3% per year [13, 14]. One study of risk factors for breakthrough varicella among healthy children in Singapore who were immunized with a reformulated Oka strain varicella vaccine (SmithKline Beecham Biologicals/Oka) found that vaccination at ≤14 months of age was associated with increased risk. Investigation of the outbreak in Winnebago County revealed 3 important differences between the present study and the Singapore study: (1) the Singapore study included 2 doses of the vaccine, with children randomly assigned to receive either a high or low titer, (2) children as young as 9 months of age could be immunized in the Singapore study, and (3) the vaccine strain used in the Singapore study was different from that licensed for use in the United States (Varivax; Merck).

Additional factors that may produce breakthrough disease include poor handling practices during transport or storage of the vaccine. The vaccine requires a storage temperature of −15°C or less and must be used immediately after reconstitution to avoid loss of potency [12]. Other risk factors for breakthrough disease are a lack of significant host response to the vaccine strain, underlying presence of asthma or other reactive airway disease [6], and the occurrence of an outbreak among a more highly susceptible population, such as children with leukemia or HIV infection.

Two limitations of our investigation were that most cases were not laboratory confirmed and that confirmation by a physician was not routine; therefore, the attack rates may be imprecise. Although incorrect diagnosis of varicella is possible, it is unlikely that this was a major limitation of the investigation, given that these cases occurred during an outbreak of varicella and that the vaccine efficacy observed was very similar to that found by Vazquez et al. [3], who used PCR to confirm the presence of the varicella-zoster virus. Because of the retrospective design of the study and the relatively low number of children whose cases we reviewed, our findings do not prove but, rather, suggest that vaccination of infants at ≤15 months of age increases the likelihood of breakthrough disease.

Factors associated with breakthrough disease, including evaluation of whether a booster dose of vaccine is necessary to maintain immunity or whether, as a possible alternative, administration of the initial dose of vaccine should be delayed until children are ≥15 months of age, merit continued study.
The use of a booster dose may be necessary, because, as the incidence of varicella decreases in the United States, opportunities to naturally boost immunity will decrease [3].

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References