

Impact of 2-Dose Vaccination on Varicella Epidemiology: Connecticut—2005–2008

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In 2006, the Advisory Committee on Immunization Practices recommended that children routinely receive 2 varicella vaccine doses in place of the 1 dose previously recommended. This recommendation's initial impact on varicella epidemiology in Connecticut was assessed. Reported incidence and case-specific data were compared for 2005 and 2008. Varicella incidence decreased from 48.7 cases/100,000 persons in 2005 to 24.5 in 2008. Age-specific incidence decreased significantly ($P < .05$) among children aged 1–14 years. Reported varicella incidence has declined in Connecticut after implementation of routine 2-dose varicella vaccination for children. Continued surveillance is needed to determine the recommendation's full impact.

Before varicella vaccine licensure in 1995, varicella was a universal childhood disease [1], resulting in >10,000 hospitalizations [2] and ~100 deaths annually in the United States [3, 4]. Shortly after the vaccine was licensed, the Advisory Committee on Immunization Practices (ACIP) recommended routine 1-dose vaccination of all children beginning at age 12–18 months, with catch-up vaccination of susceptible older children [5]. Subsequently, a dramatic decrease in varicella incidence and

varicella-related morbidity and mortality were observed as vaccination coverage levels increased [4, 6, 7]. Despite the overall success of varicella vaccine implementation, by 2001, incidence was beginning to plateau, and school outbreaks among well-vaccinated populations were occurring. These trends continued through 2005, indicating that the limits of control had been reached with the 1-dose childhood vaccination program [1, 8].

In 2006, ACIP revised its previous varicella vaccine guidelines to provide improved protection to the ~15% of children who do not respond adequately to the first vaccine dose and to decrease the number of outbreaks [1]. New recommendations include routine 2-dose vaccination for children, with the first dose administered at age 12–15 months and the second dose at age 4–6 years, a catch-up second dose for all persons who had previously received 1 dose, and vaccination of all healthy persons aged ≥ 13 years without evidence of immunity [1]. Limited data have been published on varicella epidemiology after 2005; therefore, the initial impact on varicella epidemiology of ACIP's routine 2-dose recommendation is unknown.

In 2000, Connecticut established requirements for school and 7th grade entry, stipulating proof of varicella vaccination with 1 vaccine dose or history of disease. Shortly thereafter in 2001, chickenpox (varicella) was made a notifiable disease and individual case-based surveillance began. ACIP's initial 1-dose recommendation was well implemented in the state, with 87% of children aged 19–35 months vaccinated with at least 1 dose of varicella vaccine by 2002 (unadjusted for history of varicella); this estimate increased to 93% in 2008. By 2008, ~98% of adolescents without a history of varicella had received at least 1 vaccine dose [9–11]. Although estimates of the proportion of children who have received 2 doses of vaccine in Connecticut are lacking, indirect data indicate that the 2-dose recommendation has been well accepted; in 2008, providers requested and received ~4 times the number of vaccine doses from the Connecticut Immunization Program compared with 2005. Connecticut varicella surveillance data were reviewed for 2001–2008 to (1) provide updated descriptive epidemiology of varicella and (2) assess the initial impact of ACIP's 2006 routine 2-dose varicella vaccination recommendation to affect future public health action related to varicella prevention.

METHODS

Surveillance for varicella in Connecticut is passive. Health care providers, child-care centers, and schools are required to report

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varicella cases by mail ≤ 12 h after recognition or strong suspicion of the disease. Reports are also received from hospitals and laboratories. Any report is accepted; laboratory confirmation is not required. Previously published data for 2001–2004 [8] were reviewed, and reports for 2005–2008 were analyzed for age, vaccination status, history of chickenpox, disease severity, hospitalization, and death. A patient was classified as a breakthrough (ie, vaccinated) case if rash onset occurred ≥ 3 weeks after a vaccine dose administration and as an unvaccinated case if rash onset occurred 0–20 days after vaccination. Classification of disease severity was based on the number of lesions reported (ie, mild, < 50 lesions; moderate, 50–250 lesions; severe, > 250 lesions). To examine changes in incidence by age and changes in clinical and epidemiologic characteristics of varicella, data from 2005 (the last year before the new ACIP recommendation) were compared with data from 2008 (the most recent year for which complete varicella data were available).

School-related outbreaks during 2005–2009 were assessed for number and size. A school year was defined as the period starting on September 1 and ending on June 30. A school-based outbreak was defined as at least 5 persons aged ≤ 12 years or at least 3 persons aged ≥ 13 years at the same school with reported varicella, with each sequential infection linked by an incubation period of ≤ 21 days.

To estimate the proportion of potentially preventable varicella cases by age group in 2008, each patient was assigned to 1 of 4 mutually exclusive immunity categories: unvaccinated, vaccinated with 1 dose, vaccinated with 2 doses, or past history of varicella; if a patient reported a history of varicella and receipt of 1 or 2 vaccine doses, the patient was assigned to the past history of varicella category. Potentially preventable cases were defined as those among patients who were not up to date according to ACIP varicella vaccination guidelines: A history of 1 vaccine dose was required for children aged 1–4 years to be classified as up to date; 2 doses were required for children aged ≥ 5 years and adults to be classified as up to date; and a patient with a past history of varicella was considered unpreventable, regardless of vaccination history. Adults were included in the analysis of potentially preventable varicella cases since, ideally, all adults without evidence of varicella immunity should be vaccinated. Each age group was analyzed separately.

Data were analyzed by using Microsoft Excel (Microsoft) and Epi Info™ 6 (Centers for Disease Control and Prevention) software. Overall reported incidence was calculated by using annual intercensus population estimates from the Connecticut Department of Public Health [12]. Incidence by age was calculated by using estimates from the National Center for Health Statistics [13]. The χ^2 test was used to determine the statistical significance of differences between proportions, including incidence.

This study was designated by the Centers for Disease Control and Prevention's Human Subjects Review (HSR) as public

health surveillance, not research (HSR tracking number 2009–00250).

RESULTS

Reported varicella annual incidence remained relatively stable during 2001–2006 at an average rate of 50.0 cases/100,000 persons (range, 45.5–54.5 cases/100,000 persons). Subsequently, in 2007 the rate declined to 41.0 cases/100,000 persons. In 2008, the incidence further decreased to 24.5 cases/100,000 persons, a $\sim 50\%$ decline compared with 2005 ($P < .001$).

Incidence by age group is presented in Table 1. In 2008 compared with 2005, the varicella rate decreased markedly among children aged 1–14 years, particularly among children aged 5–9 years. The decline among children aged 1–4 years was seen among both those aged 1–3 years and those aged 4 years. Rates among infants, older adolescents, and young adults did not decrease, whereas adults aged ≥ 30 years had a slight but statistically significant increase in incidence.

Clinical and epidemiologic characteristics of varicella are presented in Table 2. Vaccination status was the only statistically significant difference among cases in 2008 and 2005. Although the total percentage of patients having received a vaccination was similar between 2005 and 2008 (78% vs 76%, respectively), the percentage of patients who had received 2 doses of varicella vaccine was higher in 2008 than in 2005 (13% vs $< 1\%$, respectively; $P < .001$).

The number and size of school outbreaks of varicella decreased dramatically during the study period, with 42 outbreaks during the 2005–2006 school year (mean size, 14; range, 5–62) and only 2 outbreaks during the 2008–2009 school year (mean size, 5; range, 3–6).

Analysis of the proportion of potentially preventable varicella cases by age group revealed opportunities for disease prevention among all vaccine-eligible age groups: A total of 23% of children aged 1–4 years were unvaccinated; 73% of those aged 5–9 years had received only 1 dose (68%) or were unvaccinated (5%); 78% of those aged 10–14 years had received only 1 dose (72%) or were unvaccinated (6%); 53% of those aged 15–19 years had received only 1 dose (39%) or were unvaccinated (14%); and 86% of those aged ≥ 20 years had received only 1 dose (8%) or were unvaccinated (78%). Overall, 59% of cases were potentially preventable, and of these, 81% were among persons aged 5–14 years.

DISCUSSION

Reported varicella incidence among children and young adolescents declined rapidly in Connecticut during the 2.5 years after ACIP approved the 2-dose varicella vaccination recommendation. Given that the reduction occurred in the primary age groups for whom the 2-dose regimen is recommended, and

Table 1. Changes in Varicella Incidence by Demographic Group, Connecticut, 2005 and 2008

	2005		2008		Incidence Difference	P value
	No. (%)	Incidence	No. (%)	Incidence		
Overall varicella incidence/100,000 persons	1709	48.7	857	24.5	-24.2	<.001
Incidence by age group, years						
<1	36 (2)	86.9	49 (6)	115.4	28.5	.23
1-4	252 (15)	148.6	178 (21)	105.2	-43.4	<.001
5-9	951 (56)	422.2	324 (38)	148.0	-274.2	<.001
10-14	404 (24)	163.8	209 (24)	89.2	-74.6	<.001
15-19	32 (2)	12.9	35 (4)	14.0	1.1	.84
20-29	11 (<1)	2.7	21 (2)	4.9	2.2	.14
≥30	23 (1)	1.1	41 (5)	1.9	0.8	.03

given the simultaneous reduction in the number and size of school outbreaks, the approximate quadrupling of number of vaccine doses distributed annually in Connecticut during 2005–2008, and continued sharp reductions in disease incidence in 2009 (preliminary data, not shown), the measured decline in varicella incidence is likely the result of the second dose of varicella vaccine.

Additionally, the majority of cases still occurring are among undervaccinated preschool and school-aged children and are potentially preventable. Thus, the 2-dose regimen can be anticipated to have a further impact on reducing varicella incidence.

Table 2. Characteristics of Varicella, Connecticut, 2005 and 2008

Disease factor	2005 No. (%)	2008 No. (%)	P value
Disease severity ^a			.23 ^b
Mild (<50 lesions)	1158 (70)	524 (67)	
Moderate (50–250 lesions)	447 (27)	227 (29)	
Severe (>250 lesions)	43 (3)	28 (4)	
Past history of varicella ^c	118 (8)	65 (9)	.42
Vaccination history ^d			<.001 ^b
1 dose	1313 (78)	508 (63)	<.001 ^e
2 doses	3 (<1)	109 (13)	<.001 ^e
Unvaccinated	362 (22)	193 (24)	.22 ^e
Hospitalization	8 (<1)	9 (1)	.12
Death	0 (0)	0 (0)	N/A

NOTE. N/A, not applicable.

^aIn 2005, a total of 3.6% of data were excluded because of unknown disease severity; in 2008, a total of 9.1% of data were excluded because of unknown disease severity.

^b Overall χ^2 .

^c In 2005, a total of 8.3% of data were excluded because of unknown past history of varicella; in 2008, a total of 10.9% of data were excluded because of unknown past history of varicella.

^d In 2005, a total of 1.8% of data were excluded because of unknown vaccination status; in 2008, total of 5.5% of data were excluded because of unknown vaccination status.

^e χ^2 for each vs the remainder.

Despite the favorable initial trends, disease incidence paradoxically appears not to have decreased and might be increasing among infants, older adolescents, and young adults, and has increased among adults aged ≥30 years. This apparent lack of a broader impact has occurred despite a 50% reduction in varicella cases overall. The reason for this is unclear. Possibly, the 2-dose recommendation has not yet reached enough persons to generate herd immunity beyond that previously conferred by the incidence decrease from the 1-dose recommendation, except in schools and among children aged 1–3 years. In addition, adolescents and young adults who might have immunity from 1 dose of varicella vaccine and who are less likely than historical cohorts to have any kind of exposure to natural boosting might have some degree of waning immunity [14]. Infants too young to be vaccinated might be more likely to be exposed to adults than to siblings, their possibly increasing trend potentially reflecting that of parent-aged adults.

Breakthrough disease appears to be occurring among persons who have been vaccinated with 2 doses of varicella vaccine. Although breakthrough disease among persons with 2 doses can occur [15], breakthrough disease can be difficult to accurately diagnose clinically and might be overreported in the absence of laboratory confirmation. The recognition that varicella does appear to be occurring among 2-dose recipients prompts the question as to whether 2 doses will be sufficient to stop varicella transmission among fully vaccinated age groups and, in particular, in schools.

This study has at least 3 limitations. First, varicella diagnoses were not confirmed by laboratory testing. As varicella infection becomes less common, false-positive clinical diagnoses of varicella might comprise a higher proportion of all reported cases, resulting in an underestimate of a change in incidence. Second, reported incidence rates were compared over time in relation to the 2006 ACIP recommendations; such an ecological approach can suggest causation, but cannot prove it. Third, the estimate of potentially preventable cases among adults might be an overestimate. Adults born before 1980 without a past history of

varicella are often considered to be immune and not candidates for vaccination unless they are in a certain risk group [1]. All cases among adults without a past history of chickenpox or vaccination were assumed to be potentially preventable.

Reported varicella incidence has declined rapidly in Connecticut, coincident with implementation of routine 2-dose varicella vaccination for children. Routine 2-dose vaccination appears to be effective in reducing varicella incidence and school outbreaks, and its full potential likely has not yet been reached. States should consider implementing school-based requirements for 2 varicella vaccine doses, as recommended by ACIP [1]. Continued surveillance is needed to determine the full impact of the 2-dose recommendation.

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