Age-Specific Incidence of Chickenpox

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Synopsis

Because licensure of a chickenpox (varicella) vaccine is likely soon, it is important to ascertain the age-specific incidence of chickenpox. Increasing vaccine coverage and a resulting decrease in transmission may result in an accumulation of susceptible adults, followed by a shift of incidence into those older age groups in future years. Valid baseline age-specific incidence will make it possible to detect this phenomenon.

Two studies were conducted in Kentucky to assess age-specific incidence of chickenpox. The first assessed chickenpox occurrence in two consecutive school-year cohorts of children from a geographically representative sample of Kentucky primary schools. The second gathered information from household members of those persons interviewed in the Behavioral Risk Factor Surveillance System telephone survey.

The age-specific rates are remarkably similar between studies. Rates peak during the preschool and kindergarten years (ages 3–6). Approximately 20 percent of children remain susceptible to chickenpox after age 8 in both studies. The results from these two surveys will be valuable baselines for comparison with findings in incidence studies that will be performed after vaccine licensure.

A VACCINE AGAINST CHICKENPOX has been awaiting licensure in the United States (*1*). Although the vaccine has been shown to be both immunogenic and efficacious (*1–4*), several concerns about its use exist. First, the cost of the vaccine and its addition to an already crowded childhood immunization schedule pose logistical problems. Second, although the risk for developing herpes zoster following vaccination may be less than the risk following natural infection (*5*), any case of zoster following vaccination could pose a liability risk for the vaccine manufacturer. Most importantly, if vaccine coverage is high enough to induce herd immunity to chickenpox but less than universal, or if vaccine-induced immunity wanes in the absence of a boosting effect from circulating wild-type varicella virus, what will be the effect of an accumulation of susceptible adults?

Chickenpox is known to have more severe effects on adults than on children (*6,7*). If enough adult susceptibles accumulate over time, subsequent transmission of chickenpox to adults could result in serious disease in a large number of people. It is important to ascertain accurately the age-specific incidence rates of chickenpox before widespread administration of the vaccine. Valid baseline data would allow early detection of shifts in incidence toward older age groups or specific populations (for example, nonwhite race or low-income groups) who may have lower immunization rates.

National incidence data for chickenpox are unsatisfactory for several reasons. Routine notifiable disease systems in States generally rely on physician, medical facility, or laboratory reporting (*8*); however, persons with chickenpox are often not seen in the medical care system. Not surprisingly, in Kentucky, reported cases total about 5 percent of a birth cohort (true incidence should approximate 100 percent, allowing for year-to-year variation) (*9*).

These data are collected as cumulative counts only, and no age data are available. Some year-to-year variation is seen, but there is no consistent pattern. Other States' reports to the Centers for Disease Control and Prevention (CDC) are similar (*10*).

One study ascertained age-specific chickenpox rates from the National Health Interview Survey for the purpose of calculating a denominator for com-

plication rates (*7*). However, these rates were from the 1970s, and the sample size in person-years was limited because each interviewee was asked about chickenpox history only for the 2 weeks preceding the interview. It was estimated, based on these data, that approximately 18 percent of the population would be susceptible to chickenpox by age 10 (*6*).

The following two studies were designed to assess age-specific rates of chickenpox from representative samples of children in Kentucky. The studies feature different population samples and different methods of data collection. Both ascertain cases independently of whether persons with chickenpox contacted the medical care system.

Methods

School-based study. In the fall of 1990, 58 first-grade classes in Kentucky were selected in such a way as to produce a balanced geographic distribution. The State was divided into three regions, and 20 schools were selected randomly from each region. Each chosen school that elected not to participate was replaced by another school obtained from an additional random list; however, in a few instances, obtaining participation was difficult, and the appropriate school district health coordinator recommended a substitute school.

The principal at each school was asked to select a first-grade class for participation. The teacher of that class was given a half-page form to be completed by a parent or guardian for each student. The forms were given to the students who took them home to have them filled out and then brought back to the teacher.

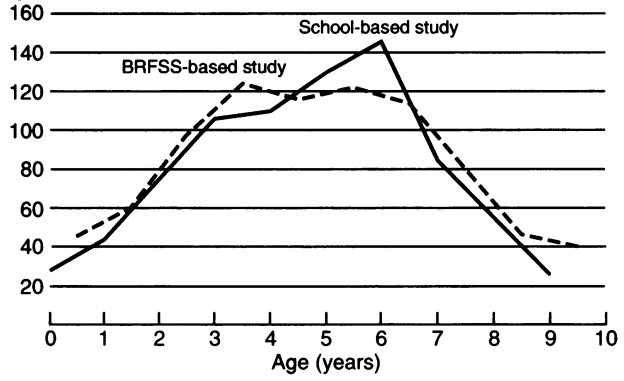
The form requested the following information: (*a*) Has the child ever had chickenpox? (check yes or no), and (*b*) If yes, what year did your child have chickenpox? The teachers tabulated this information and the name and year of birth of the respective student on a line listing. This information was returned to State immunization representatives, who collated the data, followed up with the schools to capture any missing data, and forwarded the completed data sets to the investigators for analysis. The data were gathered from October to December 1990.

In the fall of 1991, a second cohort of 60 first-grade classes (or in some locations, combined first- and second-grade classes) was selected using identical selection procedures. Data were gathered from this cohort from October to December 1991 using the same methods as for the first cohort.

In October through December 1991 and October through December 1992 for the first cohort, and October through December 1992 for the second cohort, students recorded as not having had chickenpox by the time of entry into the study were resurveyed using the same procedures employed at entry. Students who had moved to another school in the same district were located and resurveyed. Students who had left the district were excluded from the portion(s) of the study subsequent to their departure. Chickenpox cases that occurred during the interims between survey points were recorded by calendar year of occurrence.

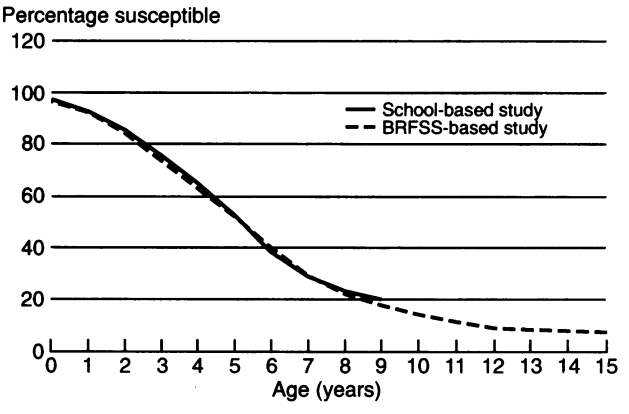
Person-year denominators were calculated by giving each student one-half person-year for his or her year of birth (because, on average, the child's birth occurred halfway through that year) plus 1 person-year for each subsequent calendar year including the calendar year of the survey. Chickenpox cases were

Figure 1. Age-specific incidence per 1,000 population of chickenpox cases among children in two studies,[1] Kentucky, 1990, 1991, and 1992



[1]School-based cohort study, 1990–92, and a Behavioral Risk Factor Surveillance System (BRFSS), 1991 and 1992.

Figure 2. Percentage of children or persons 0—16 years susceptible to chickenpox in two studies,[1] Kentucky, 1990, 1991, and 1992



[1]School-based cohort study, 1990–92, and a Behavioral Risk Factor Surveillance System (BRFSS), 1991 and 1992.

Table 1. Number of schools and children surveyed, school-based study, Kentucky, 1990–92

Group	Number of schools approached	Number of schools surveyed	Percent of schools surveyed	Number of children approached	Number of children surveyed	Percent of children surveyed
Cohort 1	66	58	87.9	1,145	1,125	98.3
Cohort 2	76	60	78.9	1,139	1,099	96.5
Total	142	118	83.1	2,284	2,224	97.4

Table 2. Age-specific incidence per 1,000 population of chickenpox among children, school-based study, Kentucky, 1990–92

Age (years)	Cases of chickenpox[1]	Age-specific[1] person-years	Age-specific rate	95 percent confidence interval[2]	Percentage of children remaining susceptible
0	30.8	1,108.6	27.4	14.8, 40.0	97.3
1	96.3	2,217.3	43.4	27.7, 59.1	92.9
2	162.7	2,217.3	73.3	48.8, 97.9	85.6
3	235.3	2,217.3	106.1	81.4, 130.8	74.9
4	243.6	2,217.3	109.9	75.7, 144.0	63.9
5	290.2	2,217.3	130.1	98.5, 163.3	50.9
6	324.2	2,217.3	146.2	114.7, 177.7	36.4
7	179.5	2,141.1	83.8	62.9, 104.8	27.9
8	81.5	1,444.4	56.4	28.5, 84.3	22.3
9	10.9	418.2	26.3	1.7, 50.8	19.7

[1] Weighted to adjust for multistage cluster sample. [2] Confidence limits.

'. . . two studies were designed to assess age-specific rates of chickenpox from representative samples of children in Kentucky.'

assigned to the calendar year of occurrence. The age label for both numerator and denominator represents the calendar year involved minus the calendar year of birth.

Next, each numerator and denominator were multiplied by a weighting factor consisting of the fraction of total statewide elementary schools that were surveyed divided by the fraction of elementary schools in that geographic region that were surveyed. This adjustment was made because the balanced geographic sample of schools had proportionately underrepresented the more populous Louisville region. The intent was to achieve representation in the study proportional to the total child population. Rates for each year of age and 95 percent confidence limits were calculated using SUDAAN software (*11*).

Behavioral Risk Factor Surveillance System (BRFSS)-based study. The BRFSS is a random-digit-dialed telephone survey supervised and funded by CDC and conducted in most States. Its methods have been described elsewhere (*12*). The primary purpose of the survey is to determine the profile of health behaviors of the interviewee, who must be a household member 18 years or older.

At the beginning of calendar year 1991, with the cooperation of CDC, a module with specific questions about chickenpox was added to the survey conducted in Kentucky. The module differed in approach from the rest of the BRFSS survey in that the questions gathered information about all household members rather than information only about the interviewee. Accordingly, the module began by verifying that the interviewee was knowledgeable about the rest of the household and, if not, whether another household member would be more appropriate and available for the interview. If the latter were applicable, then this other person was interviewed.

The interviewee was then asked to list each person in the household (up to a maximum of eight persons) by age, and to tell whether each person had had chickenpox during the 5 years before the survey. If a household member had had chickenpox, the interviewee was asked the age of the person when the case occurred (the exact wording of the question is available from the authors). The data were recorded in the same manner as for the rest of the BRFSS, then analyzed using SUDAAN. This study covers interviews held in 1991 and 1992.

Person-year denominators were computed by assigning 1 person-year for each of the last 5 age-years lived by each household member named. Totals were then added for each age-year stratum. Chickenpox cases were assigned to the age-year stratum in which they reportedly occurred. Cases occurring at (current age minus 5) were each counted as half a case. (Half of these cases would have been within "5 years ago." The data showed that interviewees reported many cases that were actually found to be 6 years or more before the survey. None of these were counted.)

Each numerator and denominator was weighted using the cluster size adjustment accounting for the multistage cluster design of the BRFSS and for the number of telephone numbers reaching that household. Rates and 95 percent confidence intervals were then computed using SUDAAN software (as was used for the school-based study) for each year of age less than or equal to 15 years.

Comparison. The two sets of rates were compared for ages 9 years or younger. Because an age-year stratum defined as the current calendar year minus the calendar year of birth (as in the school-based study) centers around an exact year of age (1.0, 2.0, and so forth), and an age-year stratum defined by year of age at last birthday (as in the BRFSS-based study) centers around a half-year of age (1.5, 2.5, and so forth), the two curves were graphed one-half year out of phase for more accurate comparison (fig. 1).

Results

School-based study. The numbers of participating schools and children surveyed for each cohort are shown in table 1. This sample represents approximately 4 percent of the State's first-grade students. Eight schools refused to participate in 1990, and 16 in 1991. Two schools were dropped from the 1990 cohort due to administrative error. Of the 2,224 students in the study, 156 (7.0 percent) were censored out at some point because of loss to followup.

Incidence rates were low for children under 3 years; not unexpectedly, rates increased for preschool- and kindergarten-age children, then began to decrease for children in elementary school where there were fewer susceptible children (table 2). In these cohorts, 19.7 percent remained susceptible to chickenpox infection at the end of the 9-year age stratum (numbers were lower in that stratum because not many of the children in the survey had reached 9 years of age).

Figure 2 shows a "survival curve" constructed with the assumption that each child who has had chickenpox is no longer susceptible. The curve will be extended to the right as the children are followed in subsequent years.

Table 3. Composition of households surveyed by the Behavioral Risk Factor Surveillance System, Kentucky, 1991 and 1992

Persons in household	*Total households*	*Total persons*	*Nonwhite persons*[1]
1	927	927	77
2	1,333	2,666	170
3	779	2,337	150
4	661	2,644	204
5	262	1,310	110
6	75	450	66
7	20	140	28
8[2]	10	80	0
Total	4,067	10,554	805
Percent	. . .	. . .	7.6

[1] For the purposes of this analysis, persons in households where the interviewee was nonwhite were counted as nonwhite.
[2] The survey protocol provided for a maximum of 8 persons per household. It is unknown if any of the households reporting an eighth member had additional members.

Table 4. Age distribution of household members surveyed by the Behavioral Risk Factor Surveillance System in 1991 and 1992 compared with Kentucky's population reflected by 1990 U.S. Census

Age (years)	*Persons in sample*		*Population of Kentucky (percent)*[1]
	Number	*Percent*	
Less than 1	132	1.3	1.2
1–4	497	4.7	5.6
5–9	765	7.3	7.2
10–14	919	8.7	7.5
15–19	802	7.6	7.5
20 or more	7,404	70.4	70.8

[1] Data obtained from 1990 U.S. Census (*11*).

BRFSS-based study. A total of 4,115 interviews were conducted. For 48 interviews (1.2 percent), either the interview was terminated before the questions about chickenpox were asked or the interviewee refused to answer those specific questions. The remaining 4,067 households contained a total of 10,554 members (table 3); of these households, 10 initial interviewees (0.2 percent) referred the interviewer to a more knowledgeable household member. Age was unknown or refused for 35 household members (0.3 percent). Thus, the analysis was limited to the remaining 10,519 household members.

The survey method yielded 7.6 percent nonwhites compared with Kentucky's 7.8 percent in the 1990 census (table 3). Therefore, adjustment for race was

Table 5. Age-specific incidence of chickenpox per 1,000 population, Behavioral Risk Factor Surveillance System, Kentucky, 1991–92

Age (years)	Number of cases[1]	Age-specific person-years[1]	Age-specific rate	95 percent confidence interval[2]	Percent of children still theoretically susceptible
0	28.5	628.5	45.3	28.4, 62.3	95.5
1	40.5	674.8	60.0	41.0, 79.0	89.5
2	69.0	704.9	97.8	76.0, 119.8	79.7
3	87.3	702.9	124.1	101.0, 147.3	67.3
4	83.8	722.6	115.8	94.1, 137.7	55.7
5	92.3	755.2	122.1	100.2, 144.1	43.5
6	89.3	779.8	114.4	92.4, 136.5	32.1
7	65.3	811.1	80.4	62.1, 98.8	24.0
8	39.9	850.5	46.9	33.3, 60.5	19.3
9	34.6	873.1	39.6	26.5, 52.7	15.4
10	26.9	874.3	30.8	19.5, 42.2	12.3
11	10.5	853.1	12.3	5.2, 19.4	11.1
12	8.5	820.5	10.4	3.6, 17.2	10.0
13	8.0	796.3	10.0	3.6, 16.5	9.0
14	3.0	778.6	3.9	0.0, 8.2	8.6
15	4.0	752.1	5.3	0.0, 10.2	8.1

[1] Weighted to adjust for multistage cluster sample. [2] Confidence limits.

not considered necessary. Table 4 compares the age distribution of persons in the survey with Kentuckians as reported in the 1990 census. The survey method succeeded in obtaining a representative age distribution.

Likewise, table 5 shows the age-specific incidence rates. The same overall pattern is seen as in the school-based study. Beyond age 15 years (not shown), incidence rates become very unstable because of the few chickenpox cases. In column 5 of this table and in figure 2, a "survival curve" is presented, although it should be understood that this construct, unlike the one for the school-based study, is theoretical (that is, no one cohort of people experienced these rates for all 15 years). If one cohort did experience these rates, which represent an average covering 1986-92, then at age 16 years approximately 8 percent of them (80.6 per 1,000) would be susceptible to infection.

Comparison. In figure 1, the incidence rates from the two studies are compared, with the curves placed one-half year out of phase. The rates are similar with one notable exception. The school-based study showed a peak at age 6 years that was not seen in the BRFSS-based study.

Discussion

The studies have several limitations. First, the epidemiology of chickenpox in Kentucky may differ from that in other States, and existing reporting systems do not identify this difference. It is not possible to ascertain whether differences in our findings from those of Preblud (*7,13*) are due to differences in methodology, period studied, or the geographic area. Both studies depended on parental recall of chickenpox disease, and although recall was limited to 5 years in the BRFSS and 6 years in the school-based study, recall of exact times can be inaccurate. The incidence peak at age 6 years shown in the school-based study could illustrate that recent recall is more accurate than recall of older events. Conversely, although chickenpox is a common disease and is usually easily recognized by parents by the time the infection has run its course, mild cases might be missed. Steele and coworkers found that 73 percent of those without chickenpox histories were immune by serologic testing (*14*). We found no satisfactory data on the accuracy of diagnosis of chickenpox by parents compared with medical providers.

The school-based study may be slightly biased because of the schools that refused participation. Most refusals occurred because school staff did not want to do the work involved. The increase in refusals in 1991 coincided with the implementation of education reform in Kentucky (*15*), which caused an increase in workload for teachers, especially in the elementary grades.

Other possible sources of bias were that different sizes of school populations were not taken into account, and that first-grade classes within each school were not selected randomly. However, it is not clear how the selection criteria could be related to chickenpox occurrence. In the BRFSS-based study, there was no representation from the 10.2 percent of Kentucky households which do not have a telephone

(*16*). This omission could possibly have had an effect on the study results.

As an additional analysis, age-specific rates in the BRFSS study were separated by calendar year of occurrence to see if a cohort effect existed, but the resulting numbers were too small for meaningful analysis. However, no strong trends were seen. The crude rates by calendar year were level enough to show that year-to-year variation in chickenpox incidence had no major effect on the study.

We also briefly examined a series of age-specific rates for those from households with less than $25,000 annual income (approximately half the sample). Surprisingly, in this group, 23.7 percent remained susceptible to chickenpox at age 10 compared with 15.4 percent in the overall sample.

The significance of this finding is unclear. The sample did not include enough households of nonwhite race to perform a similar comparison for nonwhites. The similarity in rates seen in the two studies is encouraging because it may mean that the limitations, most of which were different for the two studies, may not have had much effect. The primary advantage of the school-based study design is the annual opportunity to contact parents to clarify histories. For this reason, public health officials in Kentucky will use the school-based study design as the principal surveillance system for obtaining baseline incidence rates of chickenpox, which can be used as a basis for comparison should a national chickenpox immunization program be undertaken.

Additional cohorts are planned to be added to the study at approximately the time when the first vaccinees reach kindergarten. At that time, rates from the two existing cohorts will be complete through the middle-school grades. The next cohorts may need to be larger in order to have valid data in older age groups when losses to followup are more frequent.

The BRFSS study results validated those from the school-based study; however, the additional module about chickenpox on the BRFSS was expensive to administer (that is, approximately $15,000 per year in Kentucky—25 percent of the BRFSS budget, because it took one-fourth of the interview time). The school-based study, by contrast, was estimated to cost $4,400 per year in salaries, postage, telephone, and travel. In addition, with the rapidly increasing emphasis on health data collection, there is much competition for space on the BRFSS survey. Use of the module has illustrated that the BRFSS can be used successfully to gather health data on entire households.

The ultimate value of these studies will be seen when postmarketing analyses are performed in the United States to examine the effects of widespread use of chickenpox vaccine. The data in these initial, ongoing assessments in Kentucky may provide excellent baselines that will be needed in the future to detect age- and race-specific shifts in incidence of chickenpox. As incidence declines, routine reporting of individual cases will become important to document control of the disease (as has been seen for measles). However, in the interim, other States can and should use the methods described in this paper to assess chickenpox incidence.

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