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BEFORE THE INTRODUCTION of varicella vaccine in 1995, varicella was a universal childhood disease in the United States. During the 5 years preceding implementation of the varicella vaccination program, the approximately 4 million cases that occurred every year resulted in an annual average of 11,000 hospitalizations and 100 deaths. Since varicella is not a nationally reportable disease in the United States, national varicella surveillance data through the National Notifiable Disease Surveillance System were not available to monitor the impact of the varicella vaccination program. Accordingly, in 1995, the Centers for Disease Control and Prevention (CDC), in collaboration with state and local health departments, instituted an active surveillance project in 3 communities. The objectives of this ongoing project were to establish baseline data and to monitor trends in varicella disease following introduction of varicella vaccine. This report summarizes trends in varicella disease and the uptake of varicella vaccine in the surveillance areas from January 1, 1995, through December 31, 2000.

METHODS
Varicella active surveillance was conducted in Antelope Valley, Calif, Travis County, Tex, and West Philadelphia, Pa, through an agreement among the CDC, the Los Angeles County Department of Health Services, the Texas Department of Health, and the Philadelphia Department of Public Health. Antelope Valley is a geographically defined health services district of the Los Angeles County Department of Health Services. Travis County, which includes Austin, is the

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most densely populated county in central Texas. West Philadelphia is an inner-city area in Philadelphia. In 1995, the populations of Antelope Valley, Travis County, and West Philadelphia were 284,000, 666,127, and 291,608, respectively. In Antelope Valley and Travis County, the populations were predominantly white (89% and 85% of the total, respectively) with approximately 20% of the white populations in each area reporting Hispanic ethnicity. The population of West Philadelphia was predominantly (69%) African American. In 1995, the birth cohorts were 5049 in Antelope Valley, 11,278 in Travis County, and 4343 in West Philadelphia.

Case Definition and Reporting Sites
Varicella was a reportable disease in Texas prior to 1995; it was not reportable in California throughout the study period and it became reportable in Philadelphia in 1995. We used the standard varicella case definition recommended by the Council for State and Territorial Epidemiologists, “an illness characterized by acute onset of a diffuse papulovesicular rash without other known cause,” recognizing that the rash in vaccinated persons may be atypical with few or no vesicles.7,8 We excluded cases that did not reside in the surveillance area. Cases were considered verified if they met the case definition when interviewed. Probable cases were those among persons who could not be reached by telephone or home visit or who refused to be interviewed. They comprised 5% to 10% of reported cases and did not vary significantly from year to year. Only verified cases were analyzed for this report.

The following sites reported varicella cases to the 3 surveillance project offices: schools, universities, child care centers and preschools, private health care providers, health maintenance organizations, emergency departments, hospitals, public health clinics, clinics in the Special Supplemental Nutrition Program for Women, Infants, and Children, correctional facilities, homeless shelters, and households. For hospitals, reports were received from infection control practitioners, general and specialty wards, outpatient clinics, and billing records. Households were the source of report for additional cases within families.

In Antelope Valley, there was no sampling of reporting sites; in addition, employers with more than 500 employees also reported. In the other 2 surveillance areas, some sampling of reporting sites occurred. In Travis County, random sampling of public schools and licensed child care centers and preschools resulted in 41% and 34%, respectively, of these sites reporting; private schools were not included. Primary care physicians were requested to report, starting with the largest practices until approximately 50% of physicians were selected. In West Philadelphia, sampling (stratified random selection) of child care centers and preschools resulted in 25% of these centers reporting to the project from 1995 to 1999. From 2000 onward, all child care centers and preschools reported. For physicians, a random sample was initially included as reporters; however, because no reports of varicella cases were received from physicians who were not primary care providers, from October 1998 onward, these physicians were dropped as reporters and all primary care physicians were included. Apart from these increases in the number of reporting sites in West Philadelphia, the number and type of reporting sites were consistent in the surveillance areas throughout the study period.

Reporting and Case Investigation
Sites were requested to report cases every 2 weeks by fax (primarily), mail, or telephone even if they had no cases to report. Surveillance office staff followed up by telephone and fax if sites failed to report on time. At the start of the project and then continuing annually, training was conducted for all reporting sites. Written instructions for reporting and 26 reporting forms (1 for every 2-week reporting period) were provided. Experienced surveillance staff conducted case investigations to collect demographic information and clinical details of illness. Variables collected included age, race, ethnicity, date of rash onset, history of varicella, fever, duration of illness, number of lesions, complications, physician visit, days of work or school missed, preexisting medical conditions, medications taken prior to or during the illness, vaccination status, and source of transmission. Interviews were conducted for all household cases by telephone or by home visit for households without telephones or where telephone contact was not successful. To follow up for secondary and later cases within households, telephone calls were conducted at approximately 3-week intervals until no new cases in the household occurred.

Data Management and Analysis
Each project office checked for duplicate case reports using date of birth, last name, and address. Surveillance project offices transmitted case data every quarter to the CDC. We used Excel version 5.0 (Microsoft Excel, Redmond, Wash) and SAS version 6.12 (SAS Institute, Cary, NC) for data analysis.

We calculated annual rates of reported varicella per 1000 population in all sites and annual rates of varicella hospitalizations per 100,000 population for all sites combined for all years using 1995 through 2000 population estimates from the US Census Bureau. We used linear regression models to test for trend and set significance at P≤.05. In Antelope Valley, because there was no sampling in any age groups, we calculated annual age-specific rates of reported disease to compare reported rates of disease by age group. Because of sampling in Travis County and West Philadelphia (except for 2000), the rates of reported disease calculated underestimate the true rate of disease in these communities.

Vaccine Use and Coverage
We examined all available sources of data to describe vaccine use. Since there was redistribution of vaccine outside the surveillance areas, we did not report vaccine doses distributed. Coverage data among children aged 19 to 35 months were available from the Na-
tional Immunization Survey (NIS) from January 1997 to December 2000 for Los Angeles County, Texas, and Philadelphia County (comprising the city of Philadelphia). Methods for the NIS have been previously described.9

RESULTS

In 1995, there were 2934 verified varicella cases reported in Antelope Valley, 3130 in Travis County, and 1197 in West Philadelphia. In all sites, the number of cases declined in 1996 and remained fairly stable until 1998; a marked decline in the number of reported cases occurred in 1999. In 2000, there were 837, 491, and 250 reported cases in Antelope Valley, Travis County, and West Philadelphia, respectively. From 1995 to 2000, varicella cases showed springtime seasonality with the highest number of cases reported between March and May (FIGURE).

In Antelope Valley in 1995, the overall rate of reported varicella cases was 10.3 per 1000 population with the highest age-specific rate (54.9/1000) among children aged 5 to 9 years, followed closely by children aged 1 to 4 years (48.8/1000). Ninety-three percent of cases occurred among children younger than 15 years. Adults had the lowest rate of reported cases (0.8/1000 population) accounting for 5% of all cases. By 2000, the overall rate of reported cases was 2.5 per 1000 population and rates of disease had declined in all age groups at a statistically significant level (TABLE 1). In Travis County and West Philadelphia, the overall rate of reported varicella cases declined from 4.7 and 4.1 per 1000 population, respectively, in 1995, to 0.6 and 0.9 per 1000 population, respectively, in 2000; these declines were statistically significant (Table 1 and Figure). Between 1995 and 2000, in the 3 surveillance areas, the total number of cases declined 71% to 84%. The most marked reduction in cases occurred among children aged 1 to 4 years; however, reported cases declined in all age groups (TABLE 2).

Considering all surveillance areas together, from 1995 through 1998, varicella hospitalizations ranged from 34 to 53 per year (average 40 per year). In 1999 and 2000, 8 and 20 varicella hospitalizations were reported, respectively: 50% to 80% lower than the average number of hospitalizations from 1995 through 1998. Rates of hospitalization ranged from 2.7 to 4.2 per 100000 population from 1995 to 1998, declining to 0.6 and 1.5 per 100000 population in 1999 and 2000, respectively; however, this decline was not statistically significant ($P = .15$). Children and adolescents (<20 years) accounted for the majority of hospitalizations every year (range, 60%–90%).

Among children aged 19 to 35 months, vaccine coverage in Los Angeles County, Texas, and Philadelphia County was 40.0%, 23.0%, and 43.0% in 1997, increasing to 82.1%, 73.6%, and 83.8%, respectively, in 2000 (TABLE 3).
COMMENT

Four years after implementation of the varicella vaccination program in the United States, data from active surveillance areas showed dramatic evidence of vaccine impact with a marked decline in reported cases in all age groups. The decline in disease was greatest among preschool children; however, declines occurred in every age group including infants and adults, indicating reduced transmission of varicella zoster virus in these communities.

Consistent with prelicensure vaccine efficacy data, postlicensure studies in outbreak, community, and clinical settings have provided vaccine effectiveness estimates ranging from 71% to 86%. However, to demonstrate disease decline in a community, a vaccine must not only be effective, it must also be used at high enough levels to lead to a decline in disease. The decrease in disease we demonstrated in all age groups supports and extends data from a postlicensure study in which declines in varicella incidence and reduced disease transmission were reported among children attending 11 day care centers and preschools in North Carolina where vaccine coverage was about 60%. As varicella cases decline, an increasing proportion of cases will occur among vaccinated persons. In fact, this is the case in our surveillance areas where cases among vaccinated persons accounted for less than 1% of all reported varicella cases in 1995 and 26% of all reported cases in 2000. This is a function of both vaccine effectiveness and increasing coverage.

We interpreted the decline in cases in 1996 as year-to-year variation in disease rather than evidence of vaccine effect. First, the vaccine was not widely available in the public sector until the federal contract for purchase of varicella vaccine was finalized in May 1996 and distribution through this mechanism did not occur until the end of 1996. Although during 1996 some vaccine was distributed through the private sector, by the fourth quarter of 1996, national coverage among 19- to 35-month-old children was only 18%. Second, in the prevaccine era, periodicity of varicella disease with peak years of reported disease every 3 to 4 years and year-to-year variations of reported incidence from 36% to more than 100% has been described from surveillance data in the United States as well as from France and

<table>
<thead>
<tr>
<th>Year, %</th>
<th>1997</th>
<th>1998</th>
<th>1999</th>
<th>2000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Los Angeles County</td>
<td>40.0</td>
<td>48.4</td>
<td>69.0</td>
<td>82.1</td>
</tr>
<tr>
<td>Texas</td>
<td>23.0</td>
<td>40.1</td>
<td>53.0</td>
<td>73.6</td>
</tr>
<tr>
<td>Philadelphia County</td>
<td>43.0</td>
<td>60.7</td>
<td>65.3</td>
<td>83.8</td>
</tr>
<tr>
<td>National</td>
<td>25.8</td>
<td>43.2</td>
<td>57.5</td>
<td>67.8</td>
</tr>
</tbody>
</table>

*Annual national estimates for varicella vaccine coverage commenced in 1997. For 1996, national coverage estimates were available for the third (14%) and fourth (18%) quarters. Data available at http://www.cdc.gov/nip/coverage.

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VARICELLA DISEASE AFTER VACCINE INTRODUCTION

<p>| Table 1. Numbers of Varicella Cases and Rates per 1000 Population, 1995-2000* |</p>
<table>
<thead>
<tr>
<th>---------------------------------</th>
<th>--------------</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solo Valley, Calif</td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>134 (19.7)</td>
</tr>
<tr>
<td>1-4</td>
<td>1127 (48.8)</td>
</tr>
<tr>
<td>5-9</td>
<td>1228 (54.9)</td>
</tr>
<tr>
<td>10-14</td>
<td>235 (10.8)</td>
</tr>
<tr>
<td>15-19</td>
<td>65 (3.1)</td>
</tr>
<tr>
<td>≥20</td>
<td>145 (0.8)</td>
</tr>
<tr>
<td>Total</td>
<td>2934 (10.3)</td>
</tr>
</tbody>
</table>

Travis County, Tex

| Total | 3130 (4.7) | 1550 (2.3) | 1770 (2.6) | 1511 (2.1) | 534 (0.7) | 491 (0.6) | .009 |

West Philadelphia, Pa

| Total | 1197 (4.1) | 579 (2.0) | 605 (2.1) | 410 (1.5) | 271 (1.0) | 250 (0.9) | .02 |

*Numbers and rates should not be compared among the sites due to variation in sampling of reporting sites. Age-specific rates of verified disease were calculated only for Antelope Valley because sampling of reporting sites in the other 2 surveillance areas affected age groups disproportionately; comparisons of rates across age groups are invalid. †Test from linear regression.

| Table 2. Reduction of Reported Varicella Cases in 2000 Compared With 1995 |
|---------------------------------|--------------|
| Age, y | Antelope Valley, Calif | Travis County, Tex | West Philadelphia, Pa |
|---------------------------------|--------------|
| <1 | 69 | 81 | 68 |
| 1-4 | 83 | 90 | 83 |
| 5-9 | 63 | 77 | 77 |
| 10-14 | 65 | 75 | 80 |
| 15-19 | 85 | 83 | 81 |
| ≥20 | 66 | 64 | 68 |
| Total | 71 | 84 | 79 |

| Table 3. Varicella Vaccine Coverage for 19- to 35-Month-Old Children From National Immunization Survey, 1997-2000* |
|---------------------------------|--------------|
| Year, % | 1997 | 1998 | 1999 | 2000 |
|---------------------------------|--------------|
| Los Angeles County | 40.0 | 48.4 | 69.0 | 82.1 |
| Texas | 23.0 | 40.1 | 53.0 | 73.6 |
| Philadelphia County | 43.0 | 60.7 | 65.3 | 83.8 |
| National | 25.8 | 43.2 | 57.5 | 67.8 |

*Annual national estimates for varicella vaccine coverage commenced in 1997. For 1996, national coverage estimates were available for the third (14%) and fourth (18%) quarters. Data available at http://www.cdc.gov/nip/coverage.
the United Kingdom.\textsuperscript{16-20} We expect that some fluctuation in cases and hospitalizations from year to year will continue, as demonstrated by the increase in cases in Antelope Valley and hospitalizations overall in 2000, until high levels of vaccine coverage are achieved and sustained. Since disease remained relatively stable in 2 of the 3 surveillance areas from 1996 until 1998, it was not until 1999 when cases further declined in all 3 sites that evidence of vaccine impact was unequivocal. This decline in disease was not due to declines in levels of reporting since reporting improved over the study as evaluated by a variety of methods. In Antelope Valley, considering 2 sites (child care centers/schools and physicians) for reporting cases among children aged 2 to 18 years, estimated completeness was approximately 45%\textsuperscript{21} and when all sites of reporting were considered, completeness increased from approximately 65% to 75% during the study period. In contrast, in the early years of the measles vaccination program, approximately 5% to 10% of measles cases were passively reported via the National Notifiable Disease Surveillance System. Reassuringly, the change in reporting in West Philadelphia in 2000 with all child care centers and preschools reporting led to an increase in varicella cases reported in the 1- to 4-year-old age group, although overall, and in all other age groups, cases declined.

In the early years of implementation of the varicella vaccination program, concerns were raised regarding the rate of uptake for varicella vaccine.\textsuperscript{22,23} Identified barriers to use have mirrored those described for the introduction of other childhood vaccines including safety, availability, cost, reimbursement, storage and handling, effectiveness, duration of immunity, the effect of vaccination on the epidemiology of disease, absence of child care and school requirements, and the perception that the disease is not serious enough to warrant routine childhood vaccination.\textsuperscript{24-28} Our data indicate that uptake of varicella vaccine increased rapidly following its widespread availability in the public sector, suggesting that barriers to its use are being overcome. At the national level, coverage among children aged 19 to 35 months increased from 25.8% in 1997 to 67.8% in 2000.\textsuperscript{29} Among physicians, improved knowledge of the potential health burden due to varicella, including deaths, hospitalizations, and severe complications that may occur, postmarketing vaccine safety and effectiveness data, and recommendations for states to consider implementing child care and school requirements may have contributed to more rapid acceptance of the vaccine.\textsuperscript{4,5,22,31-37} By September 2001, 26 states had implemented child care requirements and 19 states had implemented school requirements for varicella vaccine. In the surveillance areas, vaccine coverage was higher than the national level perhaps due to heightened awareness of varicella and its consequences in these communities.

Varicella is a more severe disease among adults.\textsuperscript{3,3} With implementation of an effective childhood vaccination program, cases are expected to decline among both children and adults. However, cases will decline more among young children, the age group targeted for vaccination. This will lead to an increase in the proportion of cases occurring in older age groups, which should not be a cause for concern provided that disease rates in adults are declining. Our data highlight these expected changes and provide reassurance that implementation of the vaccination program has reduced the varicella disease burden among both children and adults. In the surveillance areas, there has been a decline in rates of disease in all age groups including infants, who are not eligible for vaccination, and susceptible adults, who probably have a much lower vaccine coverage than young children. There has also been a substantial reduction in severe consequences of varicella, as evidenced by the decline in hospitalizations. Since varicella hospitalizations are a relatively rare event, our data did not provide enough power to detect a statistically significant decline; however, because the magnitude of the decline in numbers and rates of hospitalizations is similar to that in cases, we consider this decline to be of public health importance.

With evidence of reduced disease transmission, our surveillance data underscore the importance of not only continuing efforts to achieve more than 90% vaccine coverage among young children but also of implementing existing policy recommendations for catch-up vaccination of susceptible older children and adolescents to prevent increasing susceptibility in these groups.\textsuperscript{1-2,22,24,37} Health care providers should document history of varicella disease in the medical record and offer vaccine to all susceptible persons.\textsuperscript{22} This will allow more accurate monitoring of vaccine coverage in all age groups and assist with targeting vaccination programs.

The following strengths and limitations should be considered. This active surveillance project was population-based and covered all age groups. Experienced staff tracked and maintained high levels of disease reporting using a variety of methods including feedback of data via newsletters to all reporters, lectures to health care providers and school nurses, and annual training and reorientation of reporting site staff. A small number of project staff (3-5 per site) conducted all case investigations throughout the 6-year study period. Regarding vaccine coverage, there were no estimates available for Travis County from the NIS; coverage estimates for Texas may not accurately reflect coverage in Travis County. However, a coverage survey conducted in 1998 among children attending the child care centers that reported to the Travis County surveillance project estimated that 75% of susceptible preschool-aged children were vaccinated. This indicates that coverage in Travis County was higher than in Texas as a whole. In all the surveillance areas, we were unable to calculate and report vaccine coverage for older children, adolescents, and adults since we had no accurate count of vaccine doses administered nor any measure of disease susceptibility in these age groups, especially as the vaccination program progressed. In Travis County from 1995...
to 2000 and in West Philadelphia from 1995 to 2000, rates of disease were un-
derestimated because of the high proportion of cases reported in vaccinated
persons. The proportion of cases reported in vaccinated persons may represent vaccine-related rash; how-
ever, throughout the study years, only 5% to 15% of cases reported in vac-
cinees had rash onset 7 to 14 days fol-
lowing vaccination when a varicella-like rash could be due to either wild or
canine varicella zoster virus.

Our data demonstrate the importance of establishing and maintaining surveillance systems for monitoring the implementation and impact of new vaccination programs and as a basis for addressing concerns and for establishing and evaluating vaccine policy. In contrast to measles, rubella, and mumps, which were reportable diseases when their vaccination programs were im-
plemented in the United States, varicella was not a nationally reportable disease in
1995 so there were no national surveillance data to monitor the impact of the national vaccination program. Continuing active surveillance for varicella in these surveillance areas and establishing and enhancing passive varicella surveillance systems at the state level with attention focused on monitoring vaccine coverage among adolescents as well as young children will be important to ensure that coverage continues to in-
crease to the high levels that will be re-
quired for sustained reduction of vari-
cella US morbidity.

Author Contributions: Study concept and design: Seward, Watson, Peterson, Mascola, Brodovicz, Wharton.
Acquisition of data: Watson, Peterson, Pelosi, Zhang, Maupin, Goldman, Brodovicz, Jumaan, Wharton.
Analysis and interpretation of data: Seward, Watson, Peterson, Pelosi, Zhang, Maupin, Goldman, Brodovicz, Jumaan, Wharton.
Drafting of the manuscript: Seward.
Critical revision of the manuscript for important in-
tellectual content: Seward, Watson, Peterson, Mascola, Pelosi, Zhang, Maupin, Goldman, Brodovicz, Jumaan, Wharton.
Statistical expertise: Zhang, Jumaan.
Obtained funding: Watson, Peterson, Mascola, Pelosi.

Administrative, technical, or material support: Seward, Watson, Peterman, Honein, Maupin, Gold-
man, Brodovicz, Jumaan, Wharton.
Study supervision: Seward, Watson, Peterson, Mascola, Jumaan, Wharton.

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for surveillance purposes. The compari-
son of reduction in disease from 1995 to 2000 in West Philadelphia is conserva-
tive since reporting sites increased in 1998 and 2000. Finally, a small propor-
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