Comparing Active and Passive Varicella Surveillance in Philadelphia, 2005–2010: Recommendations for the Transition to Nationwide Passive Varicella Disease Surveillance

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ABSTRACT

Objective. The Philadelphia Department of Public Health (PDPH) conducts active surveillance for varicella in West Philadelphia. For its approximately 300 active surveillance sites, PDPH mandates biweekly reports of varicella (including zero cases) and performs intensive case investigations. Elsewhere in Philadelphia, surveillance sites passively report varicella cases, and abbreviated investigations are conducted. We used active varicella surveillance program data to inform the transition to nationwide passive varicella surveillance.

Methods. We compared classification of reported cases, varicella disease incidence, and reporting completeness for active and passive surveillance areas for 2005–2010. We assessed reporting completeness using capture-recapture analysis of 2- to 18-year-old cases reported by schools/daycare centers and health-care providers.

Results. From 2005 to 2010, PDPH received 3,280 passive and 969 active surveillance varicella case reports. Most passive surveillance reports were classified as probable cases (18% confirmed, 56% probable, and 26% excluded), whereas nearly all of the active surveillance reports were either confirmed or excluded (36% confirmed, 11% probable, and 53% excluded). Overall incidence rates calculated using confirmed/probable cases were similar in the active and passive surveillance areas. Detection of laboratory-confirmed, breakthrough, and moderate-to-severe cases was equivalent for both surveillance areas.

Conclusions. Although active surveillance for varicella results in better classified cases, passive surveillance provides comparable data for monitoring disease trends in breakthrough and moderate-to-severe varicella. To further improve passive surveillance in the two-dose-varicella vaccine era, jurisdictions should consider conducting periodic enhanced surveillance, encouraging laboratory testing, and collecting additional varicella-specific variables for passive surveillance.

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To monitor the impact of the varicella vaccination program, the Centers for Disease Control and Prevention, in collaboration with the Philadelphia Department of Public Health (PDPH) and Los Angeles County Department of Health Services, conducted varicella surveillance through the Varicella Active Surveillance Project (VASP) from 1996–2011.¹ This new program was essential, because when varicella vaccine was recommended for use in the United States in 1996, varicella was not nationally notifiable; varicella had been removed from the list of notifiable conditions in 1981 because reporting the then-common disease was not feasible in many states.² VASP has supplied vital information for programmatic decision-making, including the 2007 recommendation for a second dose of varicella vaccine.³

With the success of the varicella vaccination program in reducing the incidence of disease, relatively small active surveillance areas cannot accurately monitor further declines in varicella incidence, changes in age distribution, and disease severity. Therefore, more widespread passive surveillance is required. In 2003, varicella was again added to the national notifiable diseases list, and the Council of State and Territorial Epidemiologists (CSTE) recommended that all states implement case-based surveillance by 2005.^{4–6} To mitigate the burden of varicella surveillance, CSTE recommended that states begin by focusing on the collection of three varicella-specific variables: age at disease onset, number of lesions (as a proxy for disease severity), and vaccination status, adding variables, including rash characteristics, varicella-related complications, and diagnostic laboratory data, when feasible.² As of 2010, 38 states were conducting case-based passive surveillance, but the completeness of information collected is unknown.⁷

In this article, we briefly summarize the characteristics of active and passive surveillance in Philadelphia, Pennsylvania, and compare active and passive varicella surveillance data for 2005–2010 as the basis for recommendations to optimize the quality of national passive surveillance. Specifically, we compared (1) the proportions of confirmed, probable, and excluded cases among overall reports; (2) the proportions of cases reported by type of reporting site; (3) the overall reported incidence of varicella; (4) the completeness of reporting assessed by capture-recapture methodology; and (5) the extent of laboratory testing and findings from testing. Our results suggest that optimizing passive surveillance in the U.S. will require efforts to improve the identification and exclusion of non-varicella cases through periodic enhanced surveillance, laboratory testing, or more thorough investigation of rash characteristics.

METHODS

Reporting sources

This comparative study is based on active and passive surveillance data for varicella cases reported to PDPH from January 2005 to December 2010. Suspected varicella case reports were received by PDPH from health-care providers (including hospitals, internal medicine practices, pediatricians, student health centers, public health clinics, infectious disease specialists, dermatologists, and family planning clinics) and school/daycare sites using routine active and passive surveillance methods. Additional case reports were identified from monthly electronic billing reports sent by health-care providers and, in the active surveillance area, electronic syndromic reports from hospital emergency rooms, which were evaluated for individuals with chief complaints that were suggestive of potential varicella infection. Health-care provider sites were routinely encouraged to collect varicella rash specimens for confirmatory varicella-zoster virus (VZV) testing.

According to 2010 U.S. Census estimates, about 20% of the residents in both the active and passive surveillance areas were children <18 years of age.⁸ Most children in Philadelphia have received at least one dose of the varicella vaccine.^{4,9}

Active surveillance. Active surveillance was conducted in West Philadelphia (WP), which houses approximately 20% of Philadelphia's 1.4 million residents. Cases of varicella were reported to PDPH by more than 300 participating surveillance sites in WP. PDPH mandated that all sites report the presence or absence of varicella in their facility twice a month. PDPH staff contacted sites that missed a reporting period (usually about 25% of all sites) to verify the absence of any varicella cases. All identified cases were interviewed using a detailed case investigation form that collected information on age, race, ethnicity, date of rash onset, history of varicella, fever, duration of illness, number of lesions, complications, physician visits, days of work or school missed, preexisting medical conditions, medications taken prior to or during the illness, vaccination status, and source of transmission.^{4,10} Information about potential epidemiologic links, additional suspected cases, and susceptible contacts in the household were also collected.

Passive surveillance. Passive surveillance was conducted in the remainder of Philadelphia, representing approximately 80% of the entire population. Sites in this region passively reported varicella cases as they occurred. Abbreviated case investigation forms were completed by the reporting source or, if necessary, by PDPH staff

interviewing the case. In contrast to the detailed case investigation used for active surveillance, the passive surveillance short form only collected information on age, race, ethnicity, date of rash onset, number of lesions, and vaccination status.

Case classification

A case of varicella is one that meets the clinical case definition of an illness with acute onset of diffuse (generalized) maculopapulovesicular rash without other apparent cause. All passive and active case reports were given a final classification by PDPH of confirmed, probable, or excluded based on the CSTE case definitions.¹¹ Confirmed cases met the clinical case definition and were either laboratory confirmed or epidemiologically linked to another probable or confirmed case.¹² Probable cases met the clinical case definition but were not laboratory confirmed or epidemiologically linked to another probable or confirmed case. Breakthrough varicella cases (i.e., varicella disease in individuals who received varicella vaccine >42 days previously) with a laboratory-positive test or epidemiologic link were also confirmed even though these cases often presented with atypical rash consisting of <50 skin lesions and few or no vesicles. Cases were excluded if they failed to meet either the probable or confirmed case definitions, including those that met the clinical case definition but tested negative for VZV deoxyribonucleic acid in an adequate specimen.

Varicella disease incidence

Annual varicella disease incidence rates in the passive and active surveillance areas were calculated using varicella cases (confirmed and probable combined) and population estimates from the 2010 U.S. Census for active and passive surveillance areas.¹³

Completeness of reporting

We estimated the actual number of confirmed and probable varicella cases among people aged 2–18 years in both surveillance areas using a capture-recapture method (Unpublished data. Perella D, Watson B, Spain CV, Bialek S, Daskalaki I, Heath K, et al. Laboratory testing and clinical case definitions to confirm breakthrough varicella in children aged 1–14 years. 2013). The estimate is based on an assessment of the overlap in confirmed and probable cases reported from health-care providers and from daycares/schools. For each surveillance area, we present the percentage of this estimated total that was actually reported.

Reporting of varicella case characteristics

Varicella case reports received from 2005 to 2010 from passive and active surveillance areas were compared for the following characteristics: the proportion of laboratory-positive cases by polymerase chain reaction (PCR), direct fluorescent antibody (DFA) test, or VZV culture; the proportion of breakthrough cases; and the proportion of moderate or severe cases. Disease severity was based on lesion number, the only rash detail available on the passive surveillance short form, and categorized as mild (<50 lesions), moderate (50–249 lesions), moderate-to-severe (250–499 lesions), and severe (≥ 500 lesions). Hospitalized cases were also categorized as severe regardless of lesion number.

Statistical analysis

Active vs. passive surveillance comparisons were tested for differences using the Chi-square test. Analyses were conducted using SAS[®] version 9.1.3.¹⁴

RESULTS

Case classification

PDPH received a total of 4,249 varicella case reports from 2005 to 2010. Of these cases, 969 were reported through active surveillance, and 3,280 were reported through passive surveillance. While more than half (51%) of the active surveillance reports were excluded, only 26% of the passive surveillance reports were excluded (Figure 1). The primary reasons for excluding reports from both active and passive surveillance were

Figure 1. Percentage of confirmed, probable, and excluded varicella cases among children aged 2–18 years obtained through active and passive surveillance: Philadelphia, Pennsylvania, 2005–2010

health-care provider diagnosis of a non-VZV-related rash (45% and 34% for active and passive surveillance, respectively) and negative laboratory results (26% and 39% for active and passive surveillance, respectively) (Table 1). Among reports that met the varicella case definition (i.e., confirmed or probable), 91% from the active surveillance area and 31% from the passive surveillance area were classified as confirmed, respectively ($p<0.01$) (Figure 1). Most cases from both areas were confirmed based solely on an epidemiologic link to another case (82% and 68% for active and passive surveillance, respectively) (Table 1). The proportion of cases classified as confirmed from the passive surveillance area declined during the study period from 41% in 2005 to 13% in 2010 (data not shown).

The main reporting source for varicella case reports received from both the active and passive surveillance areas was a health-care provider (75% and 56% for active and passive surveillance, respectively) (Table 1). Approximately half of these reports were received electronically (53% and 51% by active and passive surveillance sites, respectively). In both the active and passive surveillance areas, cases reported by schools were more likely to be confirmed (48% and 27% by active and passive surveillance sites, respectively) than those reported by providers (33% and 11% by active and passive surveillance sites, respectively) (data not shown).

Varicella disease incidence

Annual varicella incidence rates were similar for active and passive surveillance (Figure 2). However, while the proportion of confirmed reports remained fairly stable over time in the active surveillance area (98%–100%), only 15% were classified as confirmed in the passive surveillance area from 2008–2010 as compared with 43% in 2005–2007 ($p<0.01$) (data not shown).

Completeness of reporting

Average completeness of confirmed and probable case reporting from 2005–2010 was higher in active than in passive surveillance sites. While approximately 66% of cases among people aged 2–18 years from the active surveillance area were reported by daycares/schools and health-care providers, only 40% of cases from the passive surveillance area were reported by both surveillance site types (data not shown).

Reporting of varicella case characteristics

Among all probable and confirmed cases reported from 2005 to 2010, 62 (14%) cases from the active surveillance area and 277 (11%) cases from the passive surveillance area had varicella laboratory testing results.

Of the cases that underwent laboratory testing, 73% of those from the active surveillance area and 62% from the passive surveillance area were positive for VZV. Among all varicella cases, the majority of those reported by either surveillance area were breakthrough cases in people who had received only one varicella vaccine dose (55% and 58% of active and passive surveillance reports, respectively). Both surveillance areas reported a similar proportion of two-dose cases (10% and 8% of active and passive surveillance reports, respectively) (Table 2).

Among varicella cases reported to PDPH during the study period, a similar proportion of cases in the active and passive surveillance areas had information reported on the number of lesions (90% and 83% for active and passive surveillance, respectively) (data not shown). Varicella cases with moderate or severe disease (≥ 250 lesions) accounted for 6% and 8% of reports from the active and passive surveillance areas, respectively ($p=0.1$). The proportion of cases hospitalized was 2% in both surveillance areas (Table 2). The majority of hospitalized cases had <250 lesions (71% and 61% for active and passive surveillance, respectively) and were not immunocompromised (80% and 77% for active and passive surveillance, respectively) (data not shown).

DISCUSSION

We compared active and passive varicella surveillance data from Philadelphia from 2005–2010, finding that case classification is one of the main challenges for passive surveillance. Fewer than half of the passive surveillance reports in Philadelphia were assigned a definitive status (i.e., confirmed or excluded), compared with 89% of active surveillance reports. Given that some cases classified as probable are likely to be non-varicella cases, a high proportion of probable cases can result in unreliable estimates of disease incidence. Management of non-cases as true cases of varicella can also result in an unnecessary strain on time and resources, both for the misdiagnosed individual and for health departments, schools, and daycares that initiate outbreak control measures to prevent disease transmission.

In addition to misclassifying non-varicella cases as cases, passive reporting may also result in underascertainment of true cases. This underascertainment is especially problematic in the two-dose varicella vaccination program era, now that a growing number of reported cases occur in vaccinated people and are milder. These disease presentations can be easily mistaken for other skin diseases, including herpes simplex,

Table 1. Final classification of varicella cases among children aged 2–18 years, by surveillance type and reporting source: Philadelphia, Pennsylvania, 2005–2010

	Final case classification							
	Active surveillance				Passive surveillance			
	Confirmed (n=352) (36%) N (percent)	Probable (n=105) (11%) N (percent)	Excluded (n=512) (53%) N (percent)	All (n=969) (100%) N (percent)	Confirmed (n=595) (18%) N (percent)	Probable (n=1,839) (56%) N (percent)	Excluded (n=786) (26%) N (percent)	All (n=3,280) (26%) N (percent)
Reason status assigned								
Laboratory positive	18 (5)	NA	NA	NA	125 (21)	NA	NA	NA
Epidemiologically linked	287 (82)	NA	NA	NA	402 (68)	NA	NA	NA
Laborative positive and epidemiologically linked	47 (13)	NA	NA	NA	68 (11)	NA	NA	NA
Other diagnosis	NA	NA	230 (45)	NA	NA	NA	285 (34)	NA
Incorrectly reported	NA	NA	119 (23)	NA	NA	NA	150 (18)	NA
Laboratory negative	NA	NA	133 (26)	NA	NA	NA	333 (39)	NA
Titer for varicella immunity	NA	NA	30 (6)	NA	NA	NA	78 (9)	NA
Reporting source								
Health-care provider	237 (67)	82 (78)	409 (80)	728 (75)	212 (36)	979 (53)	658 (78)	1,849 (56)
School or daycare	115 (33)	23 (22)	103 (20)	241 (25)	383 (64)	856 (47)	185 (22)	1,424 (43)
Self/parent/guardian	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (<1)	3 (<1)	7 (<1)

NA = not applicable

Figure 2. Annual varicella incidence among children aged 2–18 years in active and passive surveillance areas: Philadelphia, Pennsylvania, 2005–2010

impetigo, allergies, and insect bites. Indeed, the discrepancy in reporting completeness between school and provider reporters (66% for active surveillance vs. 40% for passive surveillance) suggests that some cases of varicella went undetected by school nurses or misdiagnosed by health-care providers at passive surveillance sites. Although breakthrough varicella may be mild, it is contagious.¹⁵ Varicella cases that go unrecognized and unreported increase the risk of outbreaks and lead to inaccurate estimates of disease incidence.

Due to limited public health resources, most jurisdictions will only have the capacity to conduct passive surveillance for varicella. Based on our findings, passive varicella surveillance could be strengthened in a number of ways. As a start, it may be useful to expand the number of variables that are routinely collected as part of passive varicella surveillance to better clas-

sify varicella cases. From 2005 to 2010, the majority of cases in Philadelphia were confirmed as a result of an identified epidemiologic link to another confirmed or probable case. However, as the number of varicella cases diminishes, epidemiologic links are becoming more difficult to establish. To address this issue in Philadelphia, we have recently added more in-depth person-to-person exposure questions to the passive surveillance short form regarding congregate living situations, close contact with chickenpox or shingles cases, household contacts with a similar rash illness, and attendance or employment in high-risk settings. It may also be worthwhile to expand the current case definition to include specific rash characteristics. Several states, including Oregon, Rhode Island, Utah, Massachusetts, Minnesota, and New Jersey, collect some of these variables as well as other variables on antiviral

Table 2. Detection of laboratory-positive, breakthrough, and moderate-to-severe disease among confirmed and probable cases of varicella in children aged 2–18 years, by reporting source: Philadelphia, Pennsylvania, 2005–2010

Cases	Active surveillance (n=457) N (percent)	Passive surveillance (n=2,434) N (percent)	P-value
Laboratory-tested cases	62 (14)	277 (11)	0.2
Laboratory-positive cases	45 (73)	172 (62)	0.1
Breakthrough disease	295 (65)	1,613 (66)	0.4
One-dose varicella vaccine	250 (55)	1,410 (58)	
Two-dose varicella vaccine	45 (10)	203 (8)	
Cases with ≥250 lesions	22 (6)	150 (8)	0.1
Hospitalized	10 (2)	43 (2)	0.9

use and prior history of varicella, suggesting that the collection of additional information to facilitate case confirmation is now feasible in larger surveillance areas.

Reliability of the new epidemiologically linked and rash variables as predictors of laboratory-confirmed varicella has recently been demonstrated. As such, it may be prudent to focus laboratory testing on individuals with characteristics most highly predictive of seropositivity: 10–14 years of age; parental report of a generalized, itchy rash; and household disease transmission (Unpublished data. Perella D, Watson B, Spain CV, Bialek S, Daskalaki I, Heath K, et al. Laboratory testing and clinical case definitions to confirm breakthrough varicella in children aged 1–14 years. 2013). While laboratory confirmation may not be critical to the medical management of mild cases, it is increasingly needed for implementing appropriate exclusion policies and preventing the spread of varicella to people who remain susceptible and for whom varicella vaccine is contraindicated. If possible, it would also be worthwhile to conduct periodic enhanced surveillance to confirm the epidemiologic profile of varicella in particular U.S. jurisdictions. A random sample of cases could be selected biennially for enhanced data collection/routine laboratory testing, or periodic active surveillance could be set up for a limited period. Together, these recommendations should improve case classification and guide changes in the clinical case definitions used for varicella surveillance.

Limitations

This study was subject to several limitations. For one, the setting in which we conducted this study is somewhat unique, and there may be limitations to the generalizability of our findings on the completeness of passive varicella surveillance. PDPH, in conjunction with hundreds of community partners in WP, has conducted active surveillance for varicella for more than 15 years and has played a key role nationally in describing changes in varicella epidemiology after the introduction of varicella vaccine. Given the proximity of the active and passive surveillance areas in Philadelphia and the awareness of providers throughout Philadelphia of the active surveillance project, passive surveillance in this area may not be representative of passive surveillance in other regions of the U.S. It is likely, for example, that health-care providers in Philadelphia are more apt than providers in other areas to consider breakthrough varicella as a potential cause of rashes. In addition, PDPH staff, because they are trained to conduct both active and passive surveillance, may be more experienced in collecting varicella-specific variables, such as lesion number, and identifying epi-

demologic links that are needed to confirm a case. It is unknown whether these differences resulted in under- or overascertainment of varicella by Philadelphia vs. other passive surveillance sites.

CONCLUSIONS

Varicella surveillance data collected by the WP VASP were critical to our understanding of how varicella epidemiology changed during the one- and two-dose varicella vaccine eras. These data have also aided in understanding the current state of passive surveillance and identifying aspects of passive surveillance that can be strengthened as the transition is made to national varicella surveillance. Nationwide passive case-based surveillance has become feasible, as varicella incidence has declined 90% since the introduction of the varicella vaccine. Full participation in case-based varicella surveillance by all states, increased use of laboratory testing by health-care providers, and possibly collecting additional information on rash characteristics will be needed to assure high-quality national surveillance that can be used in the future to monitor the impact of the varicella vaccination program in the absence of active surveillance for varicella.

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