Knowledge, Attitudes, and Practices for Diagnosing Breakthrough Varicella in the Outpatient Setting

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ABSTRACT

Objectives. We assessed provider knowledge, attitudes, and practices for the management of breakthrough varicella and identified barriers to implementation of laboratory testing and reporting.

Methods. We surveyed 145 health-care providers (HCPs) from 30 pediatric practices in Philadelphia who did not have a history of laboratory testing for breakthrough varicella. The self-administered survey instrument collected information on clinicians' practices for management of children presenting with rash, infection-control strategies, reporting to public health agencies, and laboratory testing.

Results. Among the 144 HCPs who completed the survey, 73 (51%) had practiced for more than 10 years. While 115 HCPs (80%) would elect to evaluate a child with rash in the office, only 19 (13%) would submit diagnostics. When patients had a known recent exposure to varicella, 84 HCPs (58%) would use laboratory tests: 40% would use direct fluorescent antibody staining on a specimen from a cutaneous lesion, 24% would use polymerase chain reaction on a lesion specimen, 21% would use acute and convalescent serology, and 10% would use other tests. While waiting for test results, 82 HCPs (57%) would advise that the child be kept at home, 39 (27%) would notify the local health department, and 33 (23%) would inform the school nurse.

Conclusion. As varicella becomes increasingly uncommon, laboratory confirmation becomes more critical for appropriate diagnosis, similar to poliomyelitis and measles. Our findings suggest that HCPs need further education regarding laboratory confirmation, containment, and reporting of breakthrough varicella.

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In the post-varicella vaccine era, a dramatic reduction in the overall number of varicella cases has been documented, with the proportion of previously vaccinated cases increasing as the number of vaccinees has increased.¹⁻⁴

While, historically, varicella diagnosis was made clinically, given the distinctive appearance of classic varicella in unvaccinated individuals (i.e., a generalized vesicular rash with lesions in different stages preceded by fever and malaise), breakthrough varicella is usually mild, with fewer lesions, fewer or no vesicles, and no fever, and usually lacks the characteristic evolution of the rash in “crops or waves.”³⁻⁹ As a result, its rash can be confused with other conditions (e.g., herpes simplex infection, scabies, poison ivy, and even insect bites), and is more challenging to diagnose clinically.^{6,9,10} Remarkably, school outbreaks have occurred because of delayed recognition of breakthrough varicella cases and postponed implementation of control measures.^{3,5,11-15}

Varicella (but not herpes zoster) was added to the list of nationally notifiable diseases in 2003, and most states, including Pennsylvania, are mandating the report of varicella cases to a public health agency. To monitor the changing epidemiology of varicella disease after vaccine licensure, the Philadelphia Department of Public Health (PDPH) has conducted active surveillance for varicella and herpes zoster in the area of West Philadelphia since 1995. In the remaining areas of Philadelphia, passive surveillance has been conducted for varicella and herpes zoster because both conditions are reportable by local regulation. To support clinical management and disease surveillance of varicella and herpes zoster, PDPH has encouraged collection of specimens for testing by the National Varicella-Zoster Virus (VZV) Laboratory at the Centers for Disease Control and Prevention by advertising these laboratory services (which are free of charge) through newsletters and on-site in-service sessions, especially in the West Philadelphia active surveillance area. Although more than 50 practices throughout the city routinely utilize these services, only 30% of the suspected breakthrough varicella cases from the West Philadelphia area in 2007 had laboratory testing performed.

The purpose of this study was to assess knowledge, attitudes, and practices regarding the diagnosis, clinical management, and especially the role of laboratory testing for varicella by health-care providers (HCPs) in Philadelphia.

METHODS

In 2009, an in-person self-administered survey was given to HCPs in 30 practices in Philadelphia, outside

the West Philadelphia active surveillance area. All staff within each practice, including physicians, physician assistants, nurse practitioners, and nurses, were encouraged to attend the educational session. The survey was offered only to staff who were present the day of the educational session and was selectively scheduled on a day when most physicians would be present at the practice. Information on physicians or nurse practitioners not present on the day of the session was not collected. We selected practices based on a criterion of 600 or more pediatric (<19 years of age) patients registered. The survey was followed by an educational session. We targeted practices that had not submitted specimens since 2007 or did not have a history of testing breakthrough varicella cases reported to PDPH, as we thought these practices could benefit from the educational session following the survey.

The survey instrument comprised 11 closed-ended multiple-choice questions. The first questions were based on a clinical scenario of a 2-year-old child who was previously vaccinated with one dose of varicella vaccine and who presented with maculopapular rash after being exposed to an uncle diagnosed with herpes zoster. A picture of the rash was projected while the survey respondents were answering questions about the case history. Following the questions based on the clinical scenario, the survey collected information on clinician recommendations for parents of children with rash, containment strategies, collection of laboratory specimens, varicella diagnostics, and reporting responsibility for varicella and herpes zoster to the local health department.

After HCPs completed the survey, PDPH staff provided an educational session on site, focusing on varicella disease in the post-vaccine era. To prevent the introduction of bias, PDPH staff did not reveal the specific survey and educational session objectives to the participating HCP offices when scheduling the sessions and, after the survey was completed, responses were collected before beginning the formal educational presentation. Study analyses were conducted to identify gaps in knowledge and barriers to implementation of VZV laboratory testing. Our main analyses were limited to physicians and nurse practitioners. The survey responses were entered into a Microsoft® Access database, and analyses were conducted using SAS® version 9.1.3.¹⁶

The study introduced no significant risks to the participants, and the Institutional Review Board of the Philadelphia Department of Public Health determined it to be exempt from full review and granted a waiver of informed consent for participation.

RESULTS

All 30 practices that were approached for the survey and educational session participated. Of the 145 HCPs who were offered the survey, 144 completed it; the survey respondents' characteristics are shown in the Table. The median number of children younger than 19 years of age served by the participating practices was 1,700 (mean: 1,965; range: 600–4,500). Information on socioeconomic and insurance status of the children served by the practices was not collected.

Of the 144 HCPs who participated in the survey, 115 (80%) would advise the parent of a preschool attendee with maculopapular rash (described in the clinical scenario of the survey) to bring the child to the office for evaluation, but only 19 (13%) would order laboratory tests to confirm or rule out diagnoses from their differential diagnosis list. Once the HCPs were informed of a clear exposure to VZV in the following survey question, 84 HCPs (58%) indicated they would order laboratory tests to confirm the diagnosis (Table).

While the majority (57%) of respondents would advise that a child be kept at home while a test result for VZV was pending, 40 HCPs (28%) did not select any answer addressing advice for school attendance. Only 39 HCPs (27%) would report a possible varicella case to the local health department, and 33 HCPs (23%) would inform the child's school nurse. Even when the case of the clinical scenario was confirmed as breakthrough varicella, only 42 of 144 HCPs (29%) said they would report it to the local health department, despite the fact that the majority of HCPs ($n=110$, 76%) recognized varicella as a reportable disease in Philadelphia.

Table. Characteristics of Philadelphia health-care providers who completed a survey on knowledge, attitudes, and practices in handling breakthrough varicella in the outpatient setting, 2009 ($n=144$)

Characteristic	N (percent)
Health-care provider type	
Physician	128 (89)
Nurse practitioner	16 (11)
Gender ^a	
Female	86 (60)
Male	57 (40)
Years practicing ^b	
<1	15 (11)
1–5	42 (30)
6–10	11 (8)
>10	73 (51)

^aMissing one response

^bMissing three responses

Also, 97 HCPs (67%) were aware that varicella should be reported to the state public health system, and 85 (59%) were aware that it should be reported to the national public health system. Fewer HCPs ($n=69$, 48%) identified herpes zoster as a reportable disease in Philadelphia, whereas 57 (40%) erroneously thought that herpes zoster was reportable in Pennsylvania, and 50 (35%) mistakenly thought it was reportable nationally (data not shown).

The tests HCPs said they would conduct for laboratory confirmation of breakthrough varicella are shown in the Figure. Stratification by HCP years of practice showed that 15 (18%) of the 84 HCPs with >5 years of practice said they would conduct laboratory testing for a maculopapular rash vs. three (5%) of the 57 HCPs with ≤5 years of practice ($p=0.03$). After exposure to varicella was provided in the history, 67% of HCPs practicing for >5 years said they would test lesions for VZV, compared with 33% of those practicing for ≤5 years ($p=0.02$). Selection of test for confirming breakthrough varicella did not differ by HCP years of practice. Reporting to PDPH differed by years of practice as well; 64% of those practicing for >5 years said they would report a possible or confirmed varicella case to PDPH, compared with 46% of those practicing for ≤5 years ($p=0.03$). Ninety-three percent of HCPs practicing for >5 years recognized varicella as reportable in Philadelphia vs. 75% of HCPs practicing ≤5 years ($p=0.004$) (data not shown).

DISCUSSION

While the epidemiology and clinical presentation of varicella disease have changed dramatically post-vaccine implementation,¹ our results suggest that management of varicella cases in the outpatient setting is still mostly based on clinical judgment, at least in our area. After implementation of the second dose of the varicella vaccine, further declines in varicella incidence were reported.¹⁷ However, elimination is not expected, and outbreaks have occurred in populations with high two-dose coverage.¹⁴ Pockets of susceptible individuals in the population remain for various reasons, including limitations on administration of live-virus vaccines to some immunocompromised individuals, erroneous perception of varicella being a relatively benign disease, religious or philosophical objections to vaccination, and residence in institutional facilities from a young age.¹⁸

We advocate for increased awareness regarding the use of available laboratory tests for varicella. An effort to educate physicians on the importance of laboratory confirmation of potential breakthrough varicella cases

Figure. HCP test of choice for laboratory confirmation of breakthrough varicella: survey of Philadelphia HCPs on knowledge, attitudes, and practices in handling breakthrough varicella in the outpatient setting, 2009 (n=144)

^an=31 when excluding providers of a hospital-based ambulatory clinic where DFA is readily available and recommended by the hospital infectious diseases group

HCP = health-care provider

DFA = direct fluorescent antibody

PCR = polymerase chain reaction

is crucial as, frequently, its nonspecific appearance can be confused with other rashes of noncommunicable diseases.^{6,9,10} As with other exanthematous vaccine-preventable diseases (e.g., measles and rubella) that are now rare in the United States and with clinical presentation modified by immunization, we believe that clinical identification alone for breakthrough varicella is not reliable. We suspect that the diagnostic challenge is even greater for younger physicians who train in the post-vaccine era and rely mostly on textbook descriptions of vaccine-preventable viral exanthems. Our study shows that physicians practicing for ≤ 5 years are not as likely to test for breakthrough varicella as physicians with > 5 years of practice, even when an exposure to varicella is provided in the history. Although one could expect that younger physicians would have less trust in their clinical judgment in making the diagnosis and be more prone to test, we speculate that many might have a low index of suspicion for breakthrough varicella.

Survey participants were not alerted to a diagnosis of VZV by the description of the rash as maculopapular even though a lack of vesicles and predominance of maculopapular lesions have been described with breakthrough varicella in both clinical trials and post-varicella vaccine licensure studies.^{3,4,6,8,9} While a clear exposure history to VZV prompted most HCPs to consider breakthrough varicella, it is doubtful that exposure information would be available in daily practice, as

most source cases would also have a modified clinical appearance and may not be recognized as varicella. The contagiousness of breakthrough varicella is lower than varicella in unvaccinated individuals, depending also on the number and type of lesions, but can still be spread to close contacts.¹⁹ In addition, exposure to herpes zoster may go under recognized because there is only moderate awareness that herpes zoster is contagious via airborne droplets and not only from direct contact with skin lesions.^{18,20-22} There is no doubt that various causes of maculopapular rashes exist and some of them are noninfectious. While it is not feasible to test every patient with a maculopapular rash for a variety of reasons, we believe that once varicella is suspected, one should test to confirm the diagnosis, because of the related public health implications.

The survey results indicate that there is uncertainty about which test should be selected for laboratory confirmation of breakthrough varicella. Three different tests were equally popular among clinicians for this purpose (Figure): direct fluorescent antibody (DFA), polymerase chain reaction (PCR), and serology (comparison of acute and convalescent immunoglobulin G [IgG] titers). DFA has been used to diagnose varicella and differentiate it from herpes simplex-related rashes, but its performance relies on adequate specimen collection, and it is also less sensitive than PCR.²³ PCR is both highly sensitive and specific and has recently

been recognized as the test of choice for diagnosing breakthrough varicella.^{23,24} Measurement of serum IgG antibody against varicella is only useful to provide proof of immunity to natural infection and does not have adequate sensitivity to detect change in IgG antibody titer of vaccinated individuals after breakthrough varicella.²⁵

The limited availability of the PCR test for varicella may explain in part the fact that many HCPs did not select PCR as their first-choice test. We believe that PCR for varicella should be made readily available so that HCPs are encouraged and empowered to laboratory confirm suspected cases, as it is taught with other vaccine-preventable diseases and diseases with public health consequences. As a component of their bioterrorism preparedness programs, state public health laboratories were given the capability to test for varicella along with the necessary training, as varicella is the first diagnosis in the differential for smallpox.²⁶ Although a specific funding mechanism will be needed to support the continued use of VZV laboratory services, having these public health laboratories process specimens collected to rule out breakthrough varicella may provide a solution and facilitate diagnosis and management. Use of these laboratory services on a regular basis could also help the technicians in these laboratories maintain skills related to testing for orthopoxviruses. While PCR is a relatively costly test, control of outbreaks resulting from missed diagnoses is also very labor- and resource-intensive. A cost-benefit analysis was outside the scope of this study but should shed some light on the use of PCR as a confirmatory test in the future.

Notably, 28% of the clinicians would not advise a patient's family on school attendance when a child has an exanthematous illness. The reluctance of the survey participants to weigh in on school attendance is corroborated by the fact that most would not report a possible case of varicella to a public health agency and would not notify the school. Physicians' underreporting of communicable diseases to public health agencies has been documented previously.²⁷ We believe there is significant lack of recognition on the important role primary HCPs can play in protecting and promoting public health. By notifying public health agencies, outbreaks can be prevented and contained, and individuals at greater risk for morbidity and mortality can be protected. We advocate that suspicion of breakthrough varicella should prompt physicians to report their suspicion to public health, conduct a confirmatory test, and offer counseling on containment strategies until the test rules in/out the diagnosis, as is the case for other vaccine-preventable diseases (e.g., measles and pertussis).

Limitations

Our study had certain limitations. We surveyed a small subset of HCPs in Philadelphia, and results may not be generalizable to other areas. Because West Philadelphia has been an active surveillance site for varicella and zoster for several years, we would have expected greater awareness and knowledge about optimal management of breakthrough varicella cases than would be found in other locations. While the responses provided by HCPs in the survey might not reflect their actual actions in daily practice, the testing history and the survey responses of these practices seem consistent. We performed analysis on HCP responses without controlling for the effect of providers working in the same practice. A cost analysis to determine cost-effectiveness of the use of PCR as the confirmatory test for suspected varicella cases was beyond the scope of this study.

CONCLUSION

While further reduction of varicella cases has been seen after widespread implementation of the second varicella vaccine dose,¹⁷ continuous efforts to educate physicians on reporting to public health agencies, responsibility for containing potentially communicable patients, and laboratory confirmation of breakthrough varicella will allow more accurate measurements of the impact of vaccination and improve our understanding of the evolving epidemiology of varicella.

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