Transmission of Varicella Zoster Virus From Individuals With Herpes Zoster or Varicella in School and Day Care Settings

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(See the editorial commentary by Bloch and Johnson, on pages 1331–3.)

Background. Because the varicella incidence has declined following varicella vaccine licensure, herpes zoster (HZ) cases may play a larger role in varicella zoster virus (VZV) transmission. We investigated how HZ and varicella cases contribute to the varicella incidence in schools and day care centers.

Methods. Surveillance data collected in Philadelphia during September 2003–June 2010 were analyzed. A varicella case was considered to be sporadic if it was reported from a school or day care facility >6 weeks after or ≥10 days before other reports of VZV transmission. A varicella case was considered to be secondary if it occurred 10–21 days after report of a case of HZ or sporadic varicella. Analysis compared VZV transmission from individuals with HZ or sporadic varicella, stratified by varicella vaccination status and disease severity.

Results. Of 290 HZ cases reported, 27 (9%) resulted in 84 secondary varicella cases. Of 1358 sporadic varicella cases reported, 205 (15%) resulted in 564 secondary varicella cases. Approximately half of the HZ and sporadic varicella cases resulted in single secondary cases. The proportion of individuals who had secondary cases with mild disease was similar for those exposed to HZ and those exposed to varicella (70% and 72%, respectively). VZV transmission was highest from unvaccinated individuals with sporadic varicella ($P < .01$).

Conclusions. VZV transmission from individuals with HZ contributes to varicella morbidity. More research is needed to understand risk factors and guide recommendations for preventing VZV transmission from individuals with HZ.

Primary infection with varicella zoster virus (VZV) causes varicella (chickenpox). After primary infection, VZV establishes latency within sensory ganglia and can reactivate as herpes zoster (HZ), a disease characterized by a painful skin rash affecting ≥1 dermatomes [1]. VZV can be transmitted from individuals with varicella or HZ through direct contact with skin lesions, as well as through inhalation of aerosolized virus from the rash [2–5]. VZV has been detected in the physical environment surrounding individuals with varicella and HZ, including on air filters and surfaces such as lockers, beds, and chairs [4–6]. While current infection control guidelines allow for individuals with HZ to remain in group settings as long as the HZ rash is covered, recent findings suggest that this may not be adequate to prevent all VZV transmission from individuals with HZ [4, 7].

In the first 10 years following the 1996 recommendation of a routine 1-dose varicella vaccination program, there has been a dramatic reduction in varicella-associated morbidity and mortality in the United States [8–10]. With the implementation of a routine second dose of varicella vaccine, further declines in the incidence of varicella are expected. As the epidemiology of varicella changes, it is likely that exposure to HZ
cases will play a more prominent role in VZV transmission and account for an increasing proportion of varicella cases. We investigated how HZ contributed to varicella incidence in schools and day care facilities in Philadelphia by determining the proportions of secondary varicella cases that were associated with exposure to cases of HZ or varicella reported between September 2003 and June 2010. We assessed the influence of varicella vaccination status and disease severity on VZV transmission from individuals with HZ or varicella, and we used multivariate analysis to explore potential characteristics of HZ cases that might make transmission of VZV more likely.

**MATERIALS AND METHODS**

This retrospective analysis is based on HZ and varicella surveillance data for cases reported from schools and day care facilities in Philadelphia during 7 consecutive academic years, defined as the interval from September through June. The study period started with the 2003–2004 academic year, when the Philadelphia Department of Public Health (PDPH) began documenting enforcement of requirements for varicella vaccination among children entering the school system for the first time (ie, 1 dose before entering kindergarten through fourth grade or sixth through ninth grade, with additional grades added in subsequent years).

**Case Ascertainment**

Since 1995, both varicella and HZ have been reportable in Philadelphia. PDPH has conducted active surveillance for these conditions in West Philadelphia, where approximately one-fifth of the city’s 1.4 million residents reside, and passive surveillance for both in the remainder of the city. Active surveillance is conducted in >300 sites, including 211 schools and day care facilities, where cases or the absence of cases are reported twice a month. In the passive surveillance areas, cases are reported when they occur.

For cases reported from active surveillance sites, investigators use a detailed case investigation report, which has been described previously, to collect clinical and demographic information for all suspected cases of varicella and for suspected cases of HZ in individuals aged <20 years or ≥49 years [10, 11]. For cases reported from sites in the passive surveillance area, investigators use a modified active surveillance form as part of nationwide case-based varicella surveillance efforts recommended by the Council for State and Territorial Epidemiologists [12]. Mild varicella is defined as the presence of <50 lesions, while moderate disease is defined as the presence of ≥50 lesions. Information on varicella vaccination status for all investigations from both active and passive surveillance is confirmed using the PDPH immunization registry, a mandated system for reporting vaccines administered to children aged <19 years. Postvaccination (ie, breakthrough) varicella was defined as varicella occurring >42 days after receipt of an age-appropriate dose of varicella vaccine. To estimate the 2-dose varicella vaccine coverage for the purposes of this study, data from the immunization registry were extracted for 4–6-year-old children living in Philadelphia who had records of receiving ≥1 vaccination (of any type). The proportion of these children who received 2 varicella vaccine doses was assessed. The majority of cases in our study occurred in otherwise healthy individuals, of whom <1% were immunosuppressed.

**Defining Transmission Links in Schools and Day Care Facilities**

We categorized varicella cases in schools and day care facilities as either “sporadic” or “secondary.” A varicella case was considered to be sporadic if it was reported from a school or day care facility >6 weeks after and ≥10 days before (minimum incubation period) other reports of varicella or HZ from the same facility. A varicella case was considered to be secondary if it occurred between 10 days and 3 weeks after a report of a case of HZ or sporadic varicella from the same institution. For 2 large outbreaks (one associated with an HZ case and the other with a sporadic varicella case), tertiary cases occurring ≤1 incubation period after the last secondary case were also included. An outbreak was defined as the occurrence of ≥5 secondary varicella cases at the same facility within 3 weeks of the HZ or sporadic varicella case that could have been associated with transmission.

**Environmental Testing**

To further assess the dynamics of VZV transmission, environmental sampling in a limited number of schools and day care facilities that reported HZ cases was conducted during the 2008–2009 and 2009–2010 academic years. Samples were collected ≤3 days after disease onset. Sterile wet swabs were used to collect dust samples from surfaces (ie, tables, desks, lockers, and computer keyboards) in the room in which the individual with HZ worked or attended classes. Samples were sent to the Centers for Disease Control and Prevention for VZV detection and genotyping [13].

**Data Analysis**

We determined the total number of HZ and varicella cases reported from a school or day care facility by reviewing active and passive surveillance reports from September 2003 through June 2010. We also determined the proportion of single cases and outbreaks of varicella associated with HZ versus those associated with sporadic varicella. We examined the relationship between varicella vaccination status among individuals with HZ or sporadic varicella and their association with secondary varicella cases in a school or day care facility. Specifically, we calculated the relative risk (RR) for a secondary case of varicella resulting from transmission from a vaccinated individual with sporadic varicella, from a vaccinated individual with...
HZ, from an unvaccinated individual with sporadic varicella, and from an unvaccinated individual with HZ. Vaccinated individuals with sporadic varicella served as our reference group for this analysis. We also analyzed the relationship between HZ and sporadic varicella exposure and the severity of disease in secondary cases.

Univariate models were used to assess the impact of clinical and epidemiologic factors of individuals with HZ on VZV transmission. These included age, vaccination status, HZ rash location, HZ rash size, and whether the school or day care facility implemented outbreak-control precautions. Multivariable analysis was conducted to test for potential confounding and effect modification.

All analyses were limited to persons who had complete information for that analysis from case investigations, and all analyses were conducted in SAS 9.1.3 (SAS Institute; Cary, NC).

RESULTS

During September 2003–June 2010, PDPH was notified of 2296 cases of HZ and varicella from a school or day care setting in Philadelphia. Of this total, 1648 cases were HZ or sporadic varicella, including 290 HZ cases (18%) and 1358 sporadic varicella cases (82%) (Figure 1). The remaining 648 cases were secondary varicella, of which 499 (77%) had complete information available from detailed or modified case investigations; none reported exposure to VZV outside of the school or day care setting. A total of 24% of HZ cases and 17% of sporadic varicella cases in school and day care facilities throughout Philadelphia were reported through active surveillance conducted in West Philadelphia. Although these proportions corresponded to the proportion of the population residing in this area of active surveillance (20%), the proportion of secondary varicella cases (8%) reported by active surveillance was lower (data not shown). A marked decrease in the number of HZ cases and sporadic varicella cases, as well as the total number of secondary varicella cases, was observed beginning in 2007 (Figure 2), coincident with an increase in 2-dose varicella vaccine coverage among 4–6-year-olds in Philadelphia.

Of the 648 secondary varicella cases, 84 (13%) resulted from exposure to 27 HZ cases (9% of the 290 HZ cases) in a facility and 564 (87%) resulted from exposure to 205 sporadic varicella cases (15% of the 1358 sporadic varicella cases) in a facility. Exposure to HZ or sporadic varicella cases resulted in similar proportions of single secondary cases (55% and
56%, respectively) and outbreak-associated cases (14% for both). The remaining secondary cases were in clusters of 2–4 cases.

The median numbers of secondary cases among outbreaks associated with exposure to HZ and sporadic varicella cases were 8 and 10, respectively ($P = .2$). However, 1 sporadic varicella case was linked to a 7-month outbreak with 35 secondary cases, and 1 HZ case was linked to a 3-month outbreak with 30 secondary cases.

The proportion of individuals with secondary varicella who had mild disease was similar for those exposed to HZ and varicella (70% and 72%, respectively) (Figure 1). Most individuals with secondary varicella associated with exposure to HZ or sporadic varicella cases had been vaccinated with 2 doses of varicella vaccine (92% and 90%, respectively).

We limited the analysis of the impact of vaccination status on transmission to individuals aged <20 years whose vaccination status was known. Overall, 92% of individuals with HZ and 99% with sporadic varicella were in this age group, and vaccination status was known for 27% and 75%, respectively.

Of the 1097 individuals aged <20 years whose vaccination status was known, 1018 (85%) with sporadic varicella and 79 (47%) with HZ reported having received ≥1 dose of varicella vaccine (Table 1). A greater proportion of unvaccinated individuals with sporadic varicella were associated with VZV transmission (29%), compared with the proportion of vaccinated individuals with HZ (8%) or sporadic varicella (18%) ($P < .01$). The proportion of unvaccinated individuals with HZ who were associated with transmission (23%) was not statistically significantly different from the proportions of vaccinated and unvaccinated individuals with sporadic varicella associated with transmission.

Univariate (crude) analysis of the impact of particular clinical and epidemiologic factors (age, vaccination status, HZ rash location, HZ rash size, and whether the school or day care facility implemented outbreak-control precautions) on VZV transmission from individuals with HZ was assessed (Table 2). No significant associations were observed between any of these factors and VZV transmission. Multivariable analysis was also conducted, using the 79 HZ cases with complete information available from case investigations; their mean age was similar to the mean age of individuals with HZ cases not included in the model ($P > .05$). Again, no significant associations were observed. Individuals with rashes on the trunk, an area usually covered by clothing, had the same probability of being associated with transmission as those with rashes on the hands and arms (RR, 1.0; 95% confidence interval [CI], .8–1.3) or legs (RR, 1.1; 95% CI, .8–1.3). Individuals with HZ cases had a higher risk of being associated with transmission if they attended schools or day care facilities that mailed exposure letters and/or excluded contacts, relative to those attending facilities that did not employ these outbreak precautions (RR, 2.4; 95% CI, .7–8.5); however, this difference was not statistically significant.

Environmental samples were obtained from 9 elementary schools from which HZ cases were reported; none were associated with secondary varicella cases. Seven of the 9 cases involved individuals aged ≥20 years who had a history of varicella and were unvaccinated. The remaining 2 involved students aged 6 and 11 years who had received 2 doses of

Figure 2. Association between 2-dose varicella (Var) vaccine coverage of 4–6-year-olds and number of herpes zoster (HZ), sporadic (Spora) varicella, and secondary varicella cases.
varicella vaccine. Environmental samples were negative for VZV in investigations of 6 cases and positive for VZV in investigations of 3 (ie, 2 cases involving students and 1 involving a 57-year-old staff member). Wild-type VZV DNA was identified in specimens collected from a doorknob, a computer keyboard, and desks that were used by the individuals with HZ in these 3 institutions.

**DISCUSSION**

This study is the first to compare the dynamics of VZV transmission from individuals with HZ and varicella in school and day care settings since implementation of routine varicella vaccination. Now that circulation of VZV has been reduced, control efforts are focused on preventing disease among susceptible individuals at risk of more-severe varicella and for whom varicella vaccination is contraindicated. Our results indicate that, in these group settings, VZV transmission from individuals with HZ contributes to varicella morbidity. Indeed, 10% of the total cases reported during the study period were epidemiologically linked to HZ. It is important to note that while VZV transmission from individuals with HZ likely contributed to the total varicella caseload even before vaccination was widespread, it would have been difficult to recognize its role at a time when varicella incidence was high.

None of the additional risk factors that we examined, including age, vaccination status, rash location, and rash size, were associated with VZV transmission from an individual with HZ. It was especially surprising that rash size and location were not associated with identification of secondary cases, given that primary HZ cases involving larger rashes and rashes in dermatomes more likely to be exposed would be expected to more readily transmit VZV. Our finding that HZ cases involving rashes on the trunk were just as likely to spread disease as those involving exposed rashes on the arms and legs supports evidence that transmission can occur even when an HZ rash is covered [4]. Viral particles in other locations of VZV replication, such as the throat, may also contribute to VZV spread [14]. Interestingly, stratification by vaccination status suggested that vaccinated individuals with HZ were as likely as vaccinated individuals with varicella to be associated with secondary varicella cases.

Environmental sampling for VZV DNA has been used in a limited number of outbreak investigations in group settings. VZV DNA can be widely spread and has been documented to persist in the environment for \(3\) months, although it is not known how long it remains infectious [6]. Detection of VZV DNA in the environment may provide information on the extent to which populations in group settings with a case of HZ or varicella may have had an opportunity for exposure to VZV. We successfully collected VZV DNA from the school environment of 3 HZ case-patients. Environmental samples collected from the 2 schools frequented by vaccinated individuals with HZ due to wild-type VZV does occur frequently in vaccinated children. This is presumably due to VZV infection prior to varicella vaccination or to breakthrough varicella resulting from wild-type VZV infection after vaccination.

### Table 1. Impact of Varicella Vaccination Status Among Individuals With Sporadic Varicella or Herpes Zoster on Transmission of Varicella Zoster Virus (VZV)

<table>
<thead>
<tr>
<th>Received Vaccine, Disease Type</th>
<th>No, No. (%) of Cases</th>
<th>Yes, No. (%) of Cases</th>
<th>Risk Ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>112 (71)</td>
<td>45 (29)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>34 (81)</td>
<td>8 (19)</td>
<td>0.6 (.3–1.2)</td>
<td>.3</td>
</tr>
</tbody>
</table>

**Table 2. Univariate Analysis of the Impact of Clinical and Epidemiologic Factors on Varicella Zoster Virus (VZV) Transmission From Individuals with Herpes Zoster (HZ)**

<table>
<thead>
<tr>
<th>Variables</th>
<th>No, No. (%)</th>
<th>Yes, No. (%)</th>
<th>Risk Ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccination status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaccinated</td>
<td>34 (92)</td>
<td>3 (8)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Unvaccinated</td>
<td>34 (81)</td>
<td>8 (19)</td>
<td>2.7 (.6–10.9)</td>
<td>.2</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20 years</td>
<td>81 (87)</td>
<td>12 (13)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>&gt;20 years</td>
<td>11 (79)</td>
<td>3 (21)</td>
<td>1.8 (.4–7.6)</td>
<td>.4</td>
</tr>
<tr>
<td>HZ rash location</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trunk</td>
<td>35 (85)</td>
<td>6 (15)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Head, arm, or hand</td>
<td>24 (89)</td>
<td>3 (11)</td>
<td>0.8 (.2–2.8)</td>
<td>.7</td>
</tr>
<tr>
<td>Leg or foot</td>
<td>9 (82)</td>
<td>2 (18)</td>
<td>1.2 (.3–5.3)</td>
<td>.8</td>
</tr>
<tr>
<td>HZ rash size</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 cm²</td>
<td>53 (83)</td>
<td>11 (17)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>10 cm²</td>
<td>23 (92)</td>
<td>2 (8)</td>
<td>0.5 (.1–2.0)</td>
<td>.3</td>
</tr>
<tr>
<td>Outbreak precautions at facility</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>32 (78)</td>
<td>9 (22)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>34 (89)</td>
<td>4 (11)</td>
<td>0.5 (.2–1.4)</td>
<td>.3</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.
This study has several limitations. There may have been differences in completeness of ascertainment and reporting of HZ cases, compared with varicella cases. Since many HZ rashes are hidden from view, some reporting facilities may have been unaware that an affected student had HZ. This could have led to an underestimation of the number of HZ cases. There is also a possibility that varicella cases we categorized as secondary cases contracted disease from an unrecognized or unreported case of HZ or varicella in school or day care facility or from exposure to a case outside the school or day care facility. Further, we were unable to assess secondary attack rates, since we did not obtain detailed information on exposed individuals attending facilities where there were HZ or sporadic varicella cases. Thus, we cannot rule out the possibility that differences in the number of secondary varicella cases that arose from HZ versus varicella were influenced by differences in the number of people exposed or in varicella vaccine coverage among exposed individuals. Finally, our assessment of VZV transmission from individuals with HZ was limited to a small proportion of HZ cases, which reduces the power of this analysis.

As varicella cases continue to decline as a result of increased 2-dose varicella vaccine coverage, HZ cases are likely to play a proportionately greater role in disease circulation. Thus, further studies are required to better assess the role of exposure time and risk factors for VZV transmission from individuals with HZ and the effectiveness of existing control measures. At present, it remains challenging in many group settings to fully implement existing control measures in a timely fashion, especially since localized HZ rashes may go unnoticed by school and day care staff. Vigilance by medical professionals, school nurses, teachers, and day care staff are critical for implementation of these measures to prevent spread of varicella, especially to individuals who have no evidence of immunity to VZV infection and are unable to receive varicella vaccine. It is an encouraging sign that active surveillance sites with well-established outbreak control measures reported a lower proportion of secondary varicella cases than passive surveillance sites. In addition, further declines in the number of index and secondary varicella cases coincident with the implementation of the routine 2-dose varicella vaccination program in 2006 suggest that vaccination will result in further reductions in the circulation of VZV in these settings.

Notes

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References