Varicella Zoster Virus Transmission in the Vaccine Era: Unmasking the Role of Herpes Zoster

Karen C. Bloch and James G. Johnson
Division of Infectious Diseases, Department of Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee

(See the article by Viner et al, on pages 1336–41.)

Varicella (chickenpox) is a highly contagious disease caused by varicella zoster virus (VZV). After infection, the virus remains dormant in sensory dorsal root ganglia. Reactivation of latent VZV is associated with cutaneous disease occurring in ≥1 dermatomes, termed herpes zoster (HZ). Historically, HZ has been considered significantly less infectious than varicella and has not been thought to play an important role in person-to-person transmission. Since the licensure of the varicella vaccine in 1995 and the more recent recommendation that a second dose of vaccine be given to children aged 4–6 years [1], the epidemiology of pediatric varicella infection has shifted dramatically [2].

Efforts to quantify the burden of varicella in the community since vaccine licensure have been hindered by the absence of mandatory case-based reporting in most jurisdictions [3]. The article by Viner et al in this issue of the journal [4] provides important new insights into the epidemiology and transmissibility of VZV in a highly immunized, healthy pediatric population. The authors analyzed data obtained through a combination of active and passive surveillance for both varicella and HZ in Philadelphia schools and day care centers during 7 academic years. Cases were linked to the Philadelphia Department of Public Health immunization registry for ascertainment of vaccine status. Through this comprehensive surveillance system, 2296 cases of VZV-associated infection were identified, with 28% categorized as secondary varicella.

Much of what is known about VZV transmission dynamics in the community comes from outbreak investigations at elementary schools or day care centers. In these settings, varicella attack rates among children who had previously received a single dose of varicella vaccine ranged from 12%–42% [5–7]. A recent report found that prior receipt of a second dose of vaccine did not appreciably decrease the attack rate during a school outbreak [8]. In contrast, in an elementary school outbreak during which the second dose of vaccine was given as an intervention for outbreak control, the attack rate was reduced from 43% among children who had received only a single vaccination to 5% among 2-dose recipients [9]. Large-scale, school-based varicella outbreaks such as these serve as important sentinel events but may not be representative of the true burden and infectivity of VZV in the community.

In the study by Viner et al, >80% of epidemiologically linked transmissions involved <4 secondary cases and, in the absence of a dedicated varicella surveillance system, would be unrecognized and unreported.

Despite the continued documentation of outbreaks among immunized school children, the varicella vaccine epitomizes a public health success story. In the prevaccine era, varicella was an almost universal disease of childhood. After the widespread implementation of pediatric vaccination in the United States, incidences of VZV-related infection, hospitalization, and death have all markedly declined [10, 11]. In the present study, >90% of children who developed secondary varicella had received ≥1 doses of vaccine before the onset of infection, representing vaccine failures. However, even in these breakthrough cases, the benefits of vaccination are evident. As has been reported elsewhere [12, 13], >70% of breakthrough varicella cases had mild disease characterized by <50 skin lesions. Vaccinated varicella cases were associated with a significantly lower proportion of secondary cases compared with unvaccinated cases, presumably related to lower virus burden and shorter duration of viral shedding. Finally, there was a significant decline in the incidence of all VZV-related infections in Philadelphia schools beginning in 2007.
correlating with the recommendation for a second dose of vaccine for school-aged children. These ecological data are supported by a case control study reporting that the odds of developing varicella were decreased 95% among children after receipt of a second dose of varicella vaccine [14]. Based on these results, it is anticipated that with increasing 2-dose coverage, the rates of varicella among children will continue to decline.

Paradoxically, although the number of varicella cases has decreased since the introduction of the varicella vaccine, the incidence of HZ has been increasing [15, 16]. One hypothesis to explain this phenomenon is that reexposure to VZV among individuals with latent wild-type infection causes humoral boosting and improved virologic control [17]. As the number of children with varicella declines, waning immunity among previously infected adults may allow viral reactivation clinically manifested as HZ. Additionally, HZ may occur in immunocompetent children after immunization [18, 19].

How does this shifting balance between varicella and HZ affect the transmissibility of VZV infection? Historically, localized HZ has been considered a lower infectious risk than disseminated HZ or primary varicella [20]. However, in the study by Viner et al, there was substantial linkage between secondary varicella cases and antecedent exposure to an individual with HZ. Almost 10% of HZ cases were associated with secondary varicella, compared with 15% of sporadic varicella cases. Herpes zoster cases were as likely as varicella cases to be associated with clusters of >2 secondary cases, and the severity of secondary varicella did not differ after exposure to HZ or varicella.

Transmission of VZV occurs primarily via inhalation of airborne droplet nuclei, aerosolized either from the respiratory tract or from vesicular skin lesions [21]. Virus aerosolization has been documented with both HZ and primary varicella [22, 23], and reports of secondary varicella after exposure to a source patient with localized HZ have been described elsewhere [24, 25]. Varicella zoster virus DNA may persist in saliva and blood after HZ, and exposure to these fluids may constitute additional potential routes of transmission [26, 27]. Varicella infection is most common after close contact with a source patient, with environmental reservoirs unlikely to play a significant role in transmission [28].

Prevention of varicella transmission in both the community and the healthcare setting depends on universal VZV vaccination, as well as appropriate identification and isolation of infected individuals [21]. Current guidelines recommend standard precautions for hospitalized patients with localized HZ, whereas both airborne and contact isolation are recommended for disseminated HZ (including localized HZ in an immunocompromised patient) or primary varicella [29]. In the community, patients with HZ are generally allowed to return to group settings such as work or school if the skin lesions can be covered [21]. The study by Viner et al calls the approach to localized HZ into question. Not only was the risk of secondary infection with HZ comparable to that of primary varicella, the risk was similar regardless of the anatomic location of HZ. This finding contradicts the assumption that coverage of active skin lesions with dressings or clothing reduces VZV aerosolization and, if substantiated through further investigation, may warrant a change in current recommendations for VZV prevention.

The study by Viner et al offers compelling epidemiologic data regarding the increasing importance of HZ in ongoing transmission of VZV in school settings. However, several features limit the interpretation of these findings. Misclassification of unrelated skin eruptions as HZ or varicella may have occurred, based on the lack of virologic confirmation of VZV infection. Alternatively, mild VZV infections may have been overlooked or underreported. Because contact tracing was limited to the school environment, acquisition of VZV infection through family or social networks may have been unrecognized, potentially leading to exposure misclassification. Future studies would be strengthened by molecular epidemiology to better characterize infections as vaccine-type or wild-type strains of VZV [30].

The landmark study by Viner et al highlights the critical importance of public health surveillance programs to document the natural history of VZV infections after implementation of vaccination programs. Despite almost universal varicella vaccination, secondary cases of varicella were reported in children exposed to HZ at a frequency comparable to that reported in children exposed to sporadic varicella cases. As the absolute number of varicella infections continues to decline with universal implementation of a 2-dose varicella vaccine schedule, it is anticipated that HZ will play an increasingly significant role in secondary transmission. Recognition of the importance of HZ in perpetuating VZV infections has significant implications for public health practices in pediatric group settings. Further studies focused on HZ infectivity in both the community and hospital are needed to accurately quantify risk and guide prevention strategies.

Notes

Financial support. This work was supported by an Emerging Infections Program cooperative agreement (GR1032692) with the Centers for Disease Control and Prevention to K. C. B. J. G. J. has received funding for research through the National Institutes of Health Vanderbilt Institute for Clinical and Translational Research. J. G. J. received fellowship funding through the Sanofi-Pasteur Fellowship in Healthcare Epidemiology.

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References


EDITORIAL COMMENTARY • JID 2012:205 (1 May) • 1333