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Nosocomial Varicella: Worth Preventing, but How?

Exposure to and infection with the highly communicable varicella-zoster (VZ) virus is virtually unavoidable during one's lifetime.[1] The virus is the agent responsible for both varicella (the manifestation of primary infection in a susceptible individual) and zoster (the result of reactivation of latent virus). It is estimated that there are approximately 3.5 million cases of varicella and 300,000 cases of zoster in the United States annually; patients with either disease may transmit the virus to susceptibles.[1–3]

Since infection with the VZ virus is nearly universal, there are multiple opportunities for exposure in a wide variety of settings. The hospital is no exception, as documented by the detailed experience described in the paper by Weber and colleagues in this issue of the Journal and the large number of other references on the subject accompanying the paper.[4] What makes the introduction of VZ virus into the hospital environment so special is the increased probability of exposing and infecting persons at high risk for serious varicella-associated complications, including death. These individuals include immunocompromised persons, neonates exposed in utero shortly before delivery, and adults—particularly pregnant women.[2,5,6]

A number of steps have have been taken to minimize introduction and subsequent transmission of the VZ virus among patients and staff. The Centers for Disease Control (CDC) has developed and published isolation precautions for hospitalized patients who either have active disease or have been exposed to varicella or zoster.[7] As noted in the appendix of Weber's article, attempts have also been made to ask patients and visitors about recent exposure to the virus to prevent entry of persons who may be incubating varicella and unknowingly shedding virus.[4,8–10]

The CDC has also issued recommendations to minimize virus transmission to and from hospital personnel.[11] These include a recommendation to consider serological screening of personnel with an unknown or negative history of previous varicella infection in order to identify susceptibles accurately (persons with a positive history can be considered to be immune).[12] Ideally, this would involve a one-time mass VZ antibody screening program with subsequent routine pre-employment screening of all new personnel. This approach avoids the confusion that may be associated with post-exposure testing. VZ antibody screening appears to be quite practical given the increased availability of reliable commercial tests. Current estimates are that approximately 30 per cent of personnel will not report a history of past infection and would need to be tested.[4,13–15] While the $50 per test figure reported by Weber *et al*, might dissuade institution-wide testing in a large facility with 4,000 to 5,000 personnnel with an annual turnover rate of 20 per cent,* I suspect that testing can be accomplished at a lower cost.[4,15,16] Skin testing, if eventually commercially available, also would probably be relatively inexpensive.[14]

Prioritized screening would reduce the cost, but it may be difficult to decide what areas of the hospital should be excluded since nosocomial VZ virus transmission has been documented in various sites within the hospital, on both pediatric and adult wards and in both inpatient and outpatient settings.[4,15] While it is clear that personnel working in the pediatric environment are at increased risk of exposure and may transmit infection to high-risk children, the importance of adult patients as sources of infection should not be underestimated. Both Weber and Krasinski reported that the majority (60–80 per cent) of patient-related exposures involved adults.[4,15]

*Weber D: Personal communication, September 1987.

Institutions have modified the CDC management guidelines when applicable; this is encouraged.[7,17] These modifications are usually conservative. For example, Weber, *et al,* are not alone in isolating exposed patients or furloughing exposed personnel who are susceptible 8–21 days after exposure rather than the CDC-recommended interval of 10–21 days.[4,5,7,8,18,19] As is frequently practiced in other institutions, Weber, *et al,* also elect to place normal patients with localized zoster in strict isolation (as is recommended for all patients with varicella or disseminated zoster and immunocompromised patients with localized zoster) rather than instituting only drainage and secretion precautions as recommended by CDC.[4,7]

In spite of these guidelines and practices, nosocomial varicella still occurs, and it is costly, both in terms of time and money.[4,15,16,20,21] At least three factors contribute to the difficulties associated with effective control of VZ virus in the hospital setting. First, due to the nature of varicella infection itself, patients excrete virus a few days before rash onset.[9,10] Thus, many exposures will have taken place before the correct diagnosis is made and the appropriate infection control measures are implemented. Second, appropriate control procedures may not be implemented because of misdiagnosis, ignorance, or non-compliance. Non-compliance may be on the part of staff (e.g., failure to implement appropriate isolation orders or to report exposure or illness immediately to employee health) or of patients (e.g., failure to remain in room isolation).[4,15] Overall, this is a major problem. Krasinski reported that improper infection control techniques were instituted for 73 per cent of 62 patients with varicella or zoster.[15] For 60 per cent of the patients, no precautions at all were instituted! Third, there is no clear definition of an adequate exposure. This problem is complicated by the fact that air-borne transmission can, under certain circumstances, lead to infection of persons not usually considered to be at risk of exposure.[13,22]

Given these facts, it would be ideal if a varicella vaccine could be offered to hospital personnel, as is the case for rubella and measles, to provide permanent, solid protection and to minimize the expense and disruption of hospital activities which are largely due to furloughing and reassigning of personnel.[4,15,16,23–26] However, varicella vaccine is not yet licensed in this country and it is not yet certain if varicella vaccine-induced immunity will be complete or lifelong.

While thousands of susceptible healthy and leukemic children worldwide have received the Japanese-developed live attenuated Oka strain of varicella vaccine, relatively few adults have been vaccinated under study conditions.[27–30] One of the largest data bases on varicella vaccination of adults is provided by the experience of Gershon and colleagues from the Varicella Vaccine Collaborative Study Group, sponsored by the National Institute of Allergy and Infectious Diseases.[30]** Based on preliminary data from 187 healthy adults susceptible to the VZ virus, only 80 per cent (136/169) of vaccinees seroconverted after receiving a single dose of vaccine. However, 94 per cent (114/121) made antibodies after two doses. This experience is similar to that for leukemic children but is in contrast to that for healthy children, 95 per cent of whom seroconvert after a single dose of vaccine.[29] While vaccinated adults, like leukemics, are protected from serious infection following exposure, mild breakthrough infections are not uncommon. For example, six of 10 adults vaccinated at a mean of three years earlier contracted varicella after a household exposure, but the mean number of vesicles was only 16 with a range of 1–40. Overall, there was a total of 10 mild infections in adult vaccines with two occurring in physicians; nosocomial spread did not occur. Although seropositive vaccinees rarely became infected, vaccine-induced antibodies were detectable in only 66 per cent of 67 vaccinees at one year, in 68 per cent of 28 vaccinees at two to three years, and in 77 per cent of 13 vaccinees at four to six years following vaccination. While mild breakthrough infections also occasionally occur in normal children, the protective efficacy and persistence of vaccine-induced antibody appear to be much greater in normal children than in normal adults.[28]

As is the case with healthy children and leukemics, adults tolerate the vaccine well. Local reactions at the injection site occurred in 10 per cent, rash in 7 per cent, and fever in 2 per cent of adults after one dose of vaccine. The incidence of these reactions was lower after the second dose. Of note is the observation that vaccine virus was cultured from the rash of one vaccinee. Vaccine virus has also been isolated from vesicular fluid of a healthy child with a vaccine-associated rash.[31] However, transmission to susceptible contacts has, to date, been limited to leukemic vaccinees.[29]

While studies in adult vaccinees are continuing, the available data suggest that varicella vaccination would help control spread of virus to and from hopsital personnel but would not eliminate nosocomial transmission involving personnel. The data also indicate that vaccination programs would not be as simple as might have been envisioned based on the data for healthy children. One would probably have to plan on administering two doses of vaccine with one or more booster doses being likely at as yet unspecified intervals. Costs of vaccine and serologic testing would help determine practices regarding pre-vaccination screening of new vaccinees, testing after the first dose, and periodic testing of all vaccinees to identify those requiring booster immunizations. Routine pre-vaccination screening would provide accurate information on immunity status and would limit the number of vaccinees that would need follow-up serologic testing. Based on a pool of 4,000–5,000 employees, a negative or unknown history of previous infection in 30 per cent, and an overall susceptibility rate of approximately 10 per cent, one would expect to have to monitor vaccine-induced immunity in a total of 400–500 susceptibles out of 1200–1500 persons who denied ever having had varicella. The discrepancy between the number of persons reported to be susceptible and the number actually susceptible would be twice as great if the overall susceptibility rate was only approximately 5 per cent.[4,15,16]

Since vaccine virus can be cultured from vesicular fluid, recently vaccinated employees might need to have their activities and patient-care responsibilities altered temporarily. Further studies on transmission of vaccine virus will be necessary to address this concern. Because of the risk of breakthrough infection, albeit mild, vaccinated personnel would also have to be very diligent about reporting any type of rash illness suspected of being varicella, particularly after a recognized exposure. These precautions would also apply to those vaccinated after exposure, if such a practice were recommended. In one post-exposure vaccination study of children with household exposures, the protective effect (i.e., no clinical illness) was 67 per cent if vaccine was administered within five days of rash onset in the index case; the efficacy increased to 90 per cent if vaccine was given within

**Gershon A: Personal communication, September 1987.

three days.[32] All illnesses in the vaccinees were mild. However, there are no such data for adults to date. Finally, it is not certain if a history of vaccination will be a reliable indicator of immunity without "recent" serologic testing to detect VZ virus antibodies.

There still are unanswered questions about varicella vaccine use in adults. If the vaccine should ultimately prove to be safe and effective in this population, vaccination of hospital personnel seems more than justified. Management of varicella in hospitals is expensive and disruptive.[4,15,16,20,21] If the vaccine is licensed for universal use, the risk of nosocomial varicella will be reduced further as the risk of introduction of the virus from the community decreases. In the absence of an effective, safe vaccine, it is even more important to take all possible measures to maximize the effectiveness of the existing recommendations for control of VZ virus infections.

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