Changing Epidemiology of Influenza B Virus

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(See the Major Article by Heikkinen, Ikonen, and Ziegler on pages 1519–24.)

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Influenza B virus is an important cause of acute respiratory illness that tends to be overlooked because of the prominence of influenza A. On average, influenza B is responsible for about 25% of laboratory-documented influenza. Morbidity is highest in schoolchildren, but all age groups are at risk [1]. Comparisons of the clinical presentation and complications for influenza A and B infections have shown little difference; infected children tend to be slightly older during influenza B epidemics and may be more likely to have myalgia or myositis [2]. The epidemiology of influenza B has changed over the past 30 years. From 1974 to 1985, 4 epidemics caused by influenza B viruses were observed in Houston, Texas [3]. These epidemics were relatively discreet and varied considerably in intensity. Younger schoolchildren aged 5–14 years had the highest attack rates, resulting in high rates of school absenteeism [4]. Observations through the influenza B/Hong Kong epidemic of 1976–1977 showed that 73% of the infections detected during the first one-third of the epidemic occurred in students 5–19 years of age. As the epidemic proceeded, the proportion of infections in schoolchildren dropped and proportions for preschool children and adults increased; this observation along with others supported the hypothesis that schoolchildren are the main spreaders of influenza in the community. The epidemiology changed with the emergence of 2 antigenically distinct lineages of influenza B virus in the mid-1980s [4]. The lineages are represented by B/Victoria/2/87-like and B/Yamagata/16/88-like viruses. B/Yamagata viruses continued to circulate, but B/Victoria-like viruses were virtually absent in Texas after 1988 until the autumn of 2002 [5]. B/Victoria viruses reappeared in November and produced a series of intense community epidemics that swept from northeast to central Texas, resulting in school closings averaging about 4 days in 91 school districts of 62 counties. The high attack rates at that time due to B/Victoria in schoolchildren demonstrated vividly the lack of cross-protection afforded by B/Yamagata. Children aged <12 years had had no exposure to B/Victoria prior to 2002.

Both influenza B lineages have continued to circulate annually with varying intensity since 2002. A comprehensive review of published studies of influenza B-infected patients in outpatient and hospital settings defines the worldwide burden since 1995 [4]. From these publications it was estimated that 25% of influenza-related illnesses were caused by influenza B viruses. If the estimate is limited to children, the B-related burden is greater; 37.6% of laboratory-confirmed pediatric deaths between 2004 and 2012—excluding the A(H1N1) pandemic year, 2009–2010—were due to influenza B [6]. It should be noted that a substantial number of deaths were attributed to influenza B in each of the seasonal epidemic years and that those reported represent a fraction of the total that may have been caused by influenza B but were not confirmed or reported.

The contribution of influenza B viruses to the total burden of disease caused by influenza is confirmed by observations of influenza surveillance in Finland by Heikkinen et al., published in this issue of Clinical Infectious Diseases [7]. Between 1999 and 2012, they found that 26.0% of 34,788 laboratory-confirmed cases of influenza were caused by influenza B viruses. Heikkinen and colleagues compared the predominant influenza B lineage prevalent each year with the lineage used to produce the influenza B component of the trivalent influenza vaccine for that year. They found that a lineage mismatch occurred for 3750 of 8993 (41.7%) B infections detected during that period. The vaccine antigen for the B lineage did not match the predominant circulating virus for 10.8% of total...
influence of influenza; the proportion of persons at risk was greater at 16.8% for students 10–14 years of age and lower for elderly persons. The extensive surveillance in Finland provides the best measure of the impact of vaccine–epidemic mismatch to allow for calculation of the cost benefit for a quadrivalent vaccine containing both influenza B lineages.

Belshe reported that mismatch between the influenza B lineage used to prepare the trivalent influenza vaccine and predominant circulating influenza B virus occurred in 5 of 10 seasons in the United States between 2000 and 2010 [8]. Cross-protection between influenza B lineages is not dependable and would be infrequent for children with limited experience with influenza infection and vaccination. The quadrivalent live attenuated influenza vaccine (LAIV) administered by nasal spray is now recommended in the United States for healthy children 2–8 years of age because of superior efficacy. It should be preferred for students up to 11 years of age, particularly for use in school-located vaccine clinics, because of the ease of administration and acceptance by students. In addition, LAIV gives almost immediate protection, probably due to nonspecific innate immunity generated by the localized infection in the upper respiratory tract. A single dose of LAIV provides significant protection for naive children who are not protected by a single dose of inactivated vaccine. LAIV gives better cross-protection against new variants of influenza viruses that may appear after the components of yearly vaccine are set. The cost of LAIV compared with inactivated vaccine is not an issue. LAIV is supplied in a single-dose applicator, and a quadrivalent inactivated vaccine in a single-dose syringe has a similar cost.

Multidose vials of inactivated product are less expensive, but the added cost of syringes, alcohol sponges, and personnel time (eg, for filling syringes) more than makes up the difference.

The burden of disease caused by influenza B virus infection is established and this burden is heaviest for children and adolescents. Universal immunization with influenza vaccine for all persons >6 months of age is recommended. The problem to be solved is development of infrastructure to deliver the vaccine each year to the millions of persons who need it. Pannaraj et al provide an example of use of school-located vaccine delivery before an influenza epidemic that was predominantly due to influenza B [9]. Children in 4 elementary schools were offered influenza vaccine, and vaccine coverage ranged from 26.9% to 46.6% in the four schools. This vaccine coverage reduced the risk for all students in the intervention schools by 30%. Indirect benefit for unvaccinated students was most apparent in the school with 46.6% coverage. School attendance was significantly higher in the intervention schools compared than in 4 control schools. In an accompanying commentary, Gaglani summarized similar studies that demonstrated benefit not only for students in the schools but also for the community [10]. Both influenza A and B infection rates are highest for school-aged children, and protection of these children will reduce the risk of exposure for persons in the community—especially for the elderly and immunocompromised persons who may not respond adequately to active immunization. School-located vaccine programs require coordinated efforts of schools, local public health entities, the medical community, and parents of students. School-located vaccine clinics combined with delivery of vaccine to employees in the workplace will provide reduction of illness and an important barrier to spread of influenza viruses—both A and B.

Note

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References