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Learning Objectives

After studying the literature presented in this issue, participants should be able to:

- Assess the feasibility of mass vaccination of schoolchildren with intranasally administered, live attenuated influenza vaccine in a public school system
- Outline the relationship between early thimerosal exposure and neuropsychological outcomes in children

Target Audience

This educational activity is designed for pediatricians, primary care physicians, pediatric and family nurse practitioners, neonatologists, infectious disease specialists, allergists, pulmonologists, immunologists, and other healthcare professionals involved in the care and management of pediatric respiratory patients.

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Feasibility of Free, Mass Vaccination With Intranasally Administered Influenza Vaccine in a Public School System

The rates of school-aged children infected with influenza are higher than that of all other age groups, and can reach as high as 25% to 30%. Influenza vaccination of school-aged children has been considered an important strategy for controlling influenza in the community. Vaccination of schoolchildren reduced overall influenza morbidity in a small Michigan community during the 1968-1969 Hong Kong influenza pandemic, and routine vaccination of schoolchildren in Japan reduced influenza-related death rates among the elderly. Recent studies further demonstrated that the occurrence of acute respiratory illness decreased both in families and the community after vaccination of school-aged children with intranasally administered, live attenuated influenza vaccine (LAIV).

LAIV is a temperature-sensitive vaccine that allows for vaccine virus replication in the upper respiratory tract. Until recently, it was licensed for use only among children and adults 5 to 49 years of age although now it is approved for children as young as 2 years of age. LAIV is generally well tolerated by children and is administered as a nasal spray into each nostril. It has been reported to provide durable immunity, including protection against antigenically drifted strains not included in the vaccine. These characteristics make LAIV an attractive choice for use in school-based mass vaccination programs. In this study, Carpenter and colleagues assessed feasibility of a mass vaccination campaign of schoolchildren with LAIV in a large, metropolitan, public school system in Knox County, Tennessee. The objective of this campaign was to provide LAIV on-site administration, free of charge, to all

eligible students ≥5 years of age in kindergarten through 12th grade as well as to school staff members.

Of 53,420 students from the Knox County public school system who participated in the campaign, 24,198 (45%) students were vaccinated with at least 1 dose of LAIV at school. The proportions of students vaccinated were 56% among elementary school students, 45% among middle school students, and 30% among high school students. Schools with higher levels of enrollment of black or low-income families had lower vaccine coverage levels. Of 5,841 school staff members, 3,626 (62%) were vaccinated; 1,464 (40%) received LAIV, and 2,162 (60%) were given trivalent inactivated influenza vaccine (for individuals not eligible for LAIV).

No severe adverse reactions to LAIV nor marked changes in absenteeism among students were noted during the 2 weeks after vaccination. The health department and school system, however, expended 6,900 person-hours during the campaign. Furthermore, various health department clinics were closed for a total of 84 half-days during the 5-week vaccination campaign.

Questionnaires were mailed to primary-care physicians as well as homes of students in the community. Most physicians (80%) were supportive of the vaccination campaign, and frequently advised participation for eligible patients. Physicians (80%–90%) considered influenza vaccination of schoolchildren important to the students' health, as well as to their families and the community. However, some physicians had misunderstandings about LAIV contraindications. Concern regarding vaccine virus transmission was

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Disclosures:

* Dr Piedra is professor of pediatrics and molecular virology and microbiology at Baylor College of Medicine. He has indicated relevant financial relationships as noted: he receives grant/research support from MedImmune, Inc. and sanofi pasteur; he is a member of the speakers bureau for MedImmune, Inc.; he is an expert witness for sanofi pasteur; he is an ad hoc consultant for MedImmune, Inc., sanofi pasteur, GlaxoSmithKline, Novartis, and Roche; and he is part of a collaborative research agreement with NIH and Baylor.

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Feasibility of Free, Mass Vaccination With Intranasally Administered Influenza Vaccine

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a notable barrier to campaign participation. Parental concerns included vaccine adverse effects (29%), having asthma (23%), negative physician advice (11%), and nonparticipation in any vaccination program (10%) and were reasons for students not participating.

Carpenter and associates concluded that mass influenza vaccination in a large public school system achieved relatively high overall vaccine coverage levels among school-aged children. However, this campaign also required a substantial resource commitment from

the local health department. The authors suggested that plans for future campaigns include provisions to reduce the public health resource burden, as well as to improve targeted education for groups with low vaccination coverage and communications with community physicians.

Carpenter LR, Lott J, Lawson BM, et al. Mass distribution of free, intranasally administered influenza vaccine in a public school system. *Pediatrics*. 2007;120(1):e172-e178.

COMMENTARY

JAY M. LIEBERMAN, MD, Professor of Clinical Pediatrics, University of California, Irvine

Over the past several years, the recommendations for routine annual influenza vaccination have expanded to include infants and young children aged 6 to 59 months. The primary reason for these recommendations was the recognition that influenza results in significant morbidity in children—the highest rates of hospitalization are in young infants. In addition, vaccinating young children can lead to secondary benefits because they often serve as the focal point for community-wide influenza outbreaks. School-aged children have the highest rates of infection, and there is some evidence that routine immunization of schoolchildren can reduce the burden of disease in the community and even reduce mortality among the elderly. School-based influenza immunization programs are a logical way to reach this population, and this study shows that school-based programs can be effective. However, it took an extraordinary amount of public health resources to accomplish this, and misperceptions and misconceptions serve as barriers to the use of live attenuated influenza vaccine (LAIV). For example, at least four obstetricians advised pregnant women to avoid school on the day of vaccination to avoid possible exposure to vaccine virus! Clearly, continuing education is required regarding the safety and effectiveness of LAIV, and investments in health infrastructure are necessary before school-based influenza immunization programs become reality.

Association of Early Thimerosal Exposure With Neuropsychological Outcomes in Children

Thimerosal containing 49.6% ethyl mercury by weight has been used as a preservative in vaccines and immune globulin preparations since the 1930s. In 1999, the United States Food and Drug Administration (FDA) raised concerns that the amounts of mercury that some infants received from immunizations exceeded the limits for exposure to methyl mercury set by the Environmental Protection Agency. Although there was no evidence that the low levels of mercury in vaccines had caused any harm to children, it was recommended that thimerosal be removed from vaccines as a precautionary measure. Subsequent evidence obtained from multiple epidemiologic and ecologic studies has shown no relationship between thimerosal exposure in childhood and neurodevelopmental outcomes including autism. Nonetheless, the perception persists among some parents that thimerosal is to blame for increases in reported cases of autism and other neurodevelopmental problems. In the present study, Thompson and colleagues sought to assess the relationship between early ethyl mercury exposure and neuropsychological deficits in children 7 to 10 years of age.

A total of 1,047 children between 7 and 10 years of age were enrolled from four health maintenance organizations (HMOs) participating in the Vaccine Safety Datalink sponsored by the Centers for Disease Control and Prevention. Eligible children were administered 3-hour standardized tests assessing 42 comprehensive neuropsychological outcomes (autism-spectrum disorders were not included). Exposure to ethyl mercury from thimerosal was determined from computerized immunization records, medical records, personal immunization records, and parental interviews. Information on potential confounding factors was obtained from the interviews and medical charts. Associations between neuropsychological performance and exposure to ethyl mercury from thimerosal during the prenatal period, the neonatal period (birth to 28 days), and the first 7 months of life were assessed.

The median cumulative exposure to ethyl mercury from thimerosal from birth to 7 months was estimated at 112.5 μg (range, 0 to 187.5 μg). Among the 42 neuropsychological outcomes analyzed, only a few significant associations

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Association of Early Thimerosal Exposure With Neuropsychological Outcomes in Children

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were observed with increased exposure to ethyl mercury from thimerosal-containing vaccines and immune globulin preparations. The detected associations were small and almost equally divided between positive and negative effects.

For example, increasing prenatal exposure to ethyl mercury was associated with better performance on one measure of speech and language, the Developmental Neuropsychological Assessment speeded naming test, but with poorer performance on one measure of attention and executive function, the digit-span test of backward recall on the Wechsler Intelligence Scale for Children, third edition (WISC-III), which was observed in the overall population as well as in the boy-specific group. Conversely, higher ethyl mercury exposure from birth to 7 months was associated with better performance on one measure of fine motor coordination, the Grooved Pegboard Test of the nondominant hand, and on one measure of attention and executive function, the WISC-III digit-span test.

Moreover, increasing ethyl mercury exposure during the neonatal period (from birth to

28 days) was also associated with better performance on one measure of fine motor coordination, the Finger Tapping Dominant Hand test, in overall population and boy-specific group, but with significantly poorer performance on one measure of speech articulation, the Goldman-Fristoe Test of Articulation.

Thompson and associates concluded that the weight of the evidence presented in this study does not support a causal association between early exposure to ethyl mercury from thimerosal-containing vaccines and immune globulin preparations administered prenatally or during the first 7 months of life and deficits in neuropsychological performance in children at 7 to 10 years of age. In addition, the significant associations observed may have been chance findings from the large number of statistical tests performed.

Thompson WW, Price C, Goodson B, et al. Vaccine Safety Datalink Team. Early thimerosal exposure and neuropsychological outcomes at 7 to 10 years. *N Engl J Med.* 2007;357(13):1281-1292.

Clinical Insights® in Pediatric Respiratory Care Post-Test (November 2007)

1. Among the students from kindergarten through 12th grade who participated in the mass vaccination campaign with intranasally administered LAIV, which group of students in the Knox County public school system had the highest vaccination coverage levels?
 - a. Middle school
 - b. High school
 - c. Elementary school
 - d. Kindergarten
 - e. None of the above
2. Regarding the relationship between early thimerosal exposure and neuropsychological outcomes in children, which of the following statements is **false**?
 - a. Increasing levels of mercury exposure from thimerosal are associated with deficits from all 42 neuropsychological outcomes tested.
 - b. The data presented in this study do not support a causal association between early thimerosal exposure and neuropsychological outcomes in children.
 - c. There are few significant associations between exposure to mercury from thimerosal and performance of neuropsychological functioning.
 - d. Increasing levels of mercury exposure from thimerosal-containing vaccines are associated with both positive and negative effects on neuropsychological outcomes.

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1. c. Elementary school. The proportions of students vaccinated were 56% among elementary schools, 45% among middle schools, and 30% among high schools.
2. a. Among the 42 neuropsychological outcomes analyzed, only a few significant associations with exposure to mercury from thimerosal were observed and the detected associations were almost equally divided between positive and negative effects.

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