Influenza Vaccine for Children

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(See the article by Ruben on pages 678–88)

If history repeats itself, and the unexpected always happens, how incapable must Man be of learning from experience.

George Bernard Shaw

The consequences of this year’s highly publicized influenza epidemic should not be surprising. Although the timing and severity vary from year to year, influenza epidemics occur annually. These epidemics close schools, postpone important events, and generally disrupt life within our communities. All segments of the population are susceptible to influenza virus, which inflicts a self-limited respiratory disease in the majority of infected persons and is deadly in others. Influenza is the leading cause of vaccine-preventable death in the United States [1]. However, despite these well-known facts, millions of doses of influenza vaccine were unused at the end of the past season. This year, demand is high, and supplies are running short. What will happen next year? Will health care providers and the public remember the consequences of this year’s influenza season? Will we learn from this experience?

In October 2003, the Centers for Disease Control and Prevention’s Advisory Committee on Immunization Practices recommended that influenza vaccine be administered to all children aged 6–23 months beginning in 2004. Influenza vaccination continues to be strongly recommended for all children aged ≥6 months with underlying high-risk conditions. But do healthy children really need influenza vaccine? Is the pediatric morbidity and mortality that has occurred the past 2 influenza seasons an anomaly, or is pediatric morbidity simply underappreciated [2]? In the great pandemics of the past century, the highest influenza attack rates were reported in children, and high influenza-associated mortality rates occurred at the extremes of age (i.e., in young children and elderly individuals) [3, 4]. Since that time, population-based data from interpandemic periods indicate that children of all ages with underlying chronic medical conditions have high hospitalization rates during influenza season. Among healthy children, those aged <2 years have hospitalization rates similar to the rates among older adults for whom annual influenza vaccine is routinely recommended [5–7]. Although hospitalizations are rare for older children, illnesses that result in health care visits, antibiotic use, and missed school (and missed work for the caregivers) are common. In addition, influenza may lead to a myriad of serious complications in children, including lower respiratory tract disease, bacterial superinfection, encephalopathy, and death. The individual risk for any of these latter events is quite low, but the cumulative national toll of these preventable catastrophes is daunting. Thus, history and current data indicate that children are commonly afflicted with influenza and that its consequences may be serious.

In this issue of Clinical Infectious Diseases, Ruben [8] comprehensively reviews studies of influenza vaccines used for children. The subject is a difficult one for several reasons: (1) the method of production and antigen content of influenza vaccines have changed over the years, (2) the age and immune status of a child influences his or her response to influenza vaccine, (3) the inherent variability of the influenza virus itself leads to year-to-year variability in attack rates and vaccine-antigen “match,” and (4) the influenza vaccine is actually 3 vaccines (influenza A/H1N1, A/H3N2, and B) in one, and the immune
response to the antigen components may differ significantly. Thus, the ideal influenza vaccine trial involving children would span multiple influenza seasons to allow assessment of efficacy of all 3 antigen components, include sufficient numbers of children to assess efficacy by age group, and include laboratory and clinical outcome measures. Unfortunately, these qualifications do not exist in any single trial. However, Ruben [8] presents much information by examining the cumulative evidence obtained from many smaller studies in children. The consistent messages from these studies are that inactivated influenza vaccine is safe and well-tolerated in children of all ages and that it can be immunogenic, even in very young children (i.e., those aged 6–12 months).

In terms of vaccine efficacy, reductions in laboratory-confirmed influenza rates have been demonstrated for all 3 types of influenza across multiple age groups. However, the estimates of vaccine efficacy/effectiveness vary considerably by year, by antigen, and by age group. In the largest trial to date to have used the current influenza vaccine, Edwards et al. [9] demonstrated that efficacy against laboratory-confirmed influenza A/H1N1 and A/H3N2 increased with increasing age among children aged 1–15 years who were studied over 4 influenza seasons. In all age groups combined, vaccine was 91% and 77% efficacious against A/H1N1 and A/H3N2 culture-positive disease, respectively [10]. In this and other studies that have included children aged <5 years who received the split-virus, trivalent vaccine, the rate of efficacy against laboratory-confirmed illness ranged from 0% to 83%, with a median efficacy of 47% [10]. In many of these studies, children received only 1 dose of influenza vaccine, not the 2-dose schedule routinely recommended for vaccine-naive children aged <8 years. No studies have been large enough to assess the effectiveness of the vaccine for prevention of serious outcomes, such as hospitalizations. However, it is a reasonable assumption that, if influenza vaccination can prevent culture-proven influenza illness in children, it can also prevent the associated serious complications. The efficacy estimates for young children are similar to those from the single published randomized, controlled trial of the current influenza vaccine in elderly adults. In that trial, receipt of influenza vaccine was associated with a 50% reduction in laboratory-proven influenza and a 53% reduction in clinical influenza in vaccinated persons [11]. Population-based observational studies show significant reductions in hospitalizations and deaths among elderly persons who receive the influenza vaccine. Similar population-based observational studies involving young children are on-going and will help determine the impact of more widespread use of influenza vaccine on a population level.

Expanding annual influenza vaccination to a larger pediatric population will be challenging. There is no other childhood vaccine that must be readministered yearly. There is an unpredictable time period each year between when vaccine becomes available and when influenza virus circulation begins. Strategies that improve the efficiency of influenza vaccine delivery can help solve some of these logistical issues, but uncertainty regarding the influenza vaccine supply will remain. Collaborations between government and industry are needed to ensure that there is an adequate vaccine supply that is available in a timely manner each year. Influenza is a non-specific disease, and other respiratory viruses that circulate during fall and winter may cause similar disease in children. Thus, influenza vaccination can only be expected to prevent a portion of the respiratory disease seen each winter. Education of parents and health care providers should be an integral component of any pediatric influenza vaccination program.

The accumulated evidence, as presented by Ruben [8], indicates that, in most years, influenza vaccination will help children. We need to learn from this accumulated experience and from the current influenza season and to prepare accordingly. On a population basis, certain age groups and risk groups are more likely to have serious complications associated with influenza, and health care providers and parents should ensure that these children are vaccinated early in the influenza season. However, every child is susceptible to influenza virus infection, and the message to the public needs to be clear: influenza vaccination is safe and effective and should be offered to anyone aged ≥6 months who wishes to reduce his or her chances of becoming ill from influenza. For healthy children aged ≥5 years, either inactivated or live-attenuated intranasal vaccine may be given. Increasing the number of children who receive influenza vaccine may have benefits beyond protection of the individual child. Children are important in the transmission of influenza virus within households and communities, and increasing influenza vaccine coverage among children may interrupt transmission and attenuate community epidemics. These strategies will be particularly important when history repeats itself and the next severe influenza season rolls around.

References


