Influenza vaccination of children: can it be accomplished?

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(See the article by Neuzil et al., on pages 1032–9.)

Influenza virus circulates each year, infecting between 15% and 30% of school-aged children and resulting in numerous outpatient visits, increased antibiotic use, and excessive school absenteeism [1, 2, 3, 4]. In addition to the individual disease burden, there is convincing evidence that school-aged children serve as vectors for intrafamilial influenza transmission [4]. For this reason, some advocate universal vaccination of school-aged children to reduce influenza disease in the entire population [5]. In Japan, a universal vaccination program of school-aged children appeared to be effective in decreasing influenza-related morbidity and mortality in the entire population [6]. Ecologic analyses of the Japanese experience showed a marked blunting of the annual seasonal mortality during the period of time when vaccination of school-aged children was mandatory and resumption of the large seasonal peaks in mortality when this practice was abandoned.

Because the evidence for indirect benefit of influenza vaccination of school-aged children is only suggestive, recommendations for their routine use will likely depend on confirmation of the direct benefit to them rather than on herd effects. Because influenza rarely causes death or permanent disability in school-aged children, a large share of the costs associated with influenza illness in children stems from outpatient medical care and indirect costs associated with lost work of caregivers. For influenza vaccination of children to be cost effective, inexpensive and convenient ways to deliver relatively inexpensive vaccines to schoolchildren must be developed.

To provide practical information about the implementation of widespread vaccination of schoolchildren, Neuzil and colleagues, in this issue of the Journal of Infectious Diseases, compared the safety and immunogenicity of 1 versus 2 doses of trivalent inactivated vaccine (TIV) in children 5–8 years of age [7]. They identified a previously unimmunized cohort of >200 children enrolled in their health plan since birth and administered 2 doses of TIV to this group. Both doses were well tolerated, with only slightly more pain after the second dose in the older subjects. Serologic studies after 2 TIV doses indicated that protective antibody responses were seen in >90% of children for both A/H1H1 and A/H3N2 strains but in only 64% for the B component. Children who were seronegative for a specific vaccine antigen before the first dose required 2 doses to achieve hemagglutinin inhibition titers ≥1:40, the level associated with protection. In contrast, children who were seropositive for an antigen at baseline required only 1 dose. Unfortunately, neither clinical nor demographic characteristics of the children predicted their serostatus; even a substantial number of the oldest children were seronegative. Thus, the authors concluded that all previously unvaccinated children required 2 doses of TIV, because baseline serostatus could not be predicted and serologic testing for pre-existing immunity before vaccination was impractical.

In addition to confirming the need for 2 doses of vaccine in this age group, the authors also raised a number of implementation issues. When they reviewed health plan records for the combined 2001–2002 and 2002–2003 influenza seasons, they found that only 495 of the 5–8-year-old children were vaccinated, and, of these, only 12% received 2 doses of vaccine. If universal vaccination of school-aged children were recommended, could 2 doses of TIV be administered within the short time window of vaccine availability? Would universal recommendations increase overall vaccination rates?

TIV vaccination rates in younger children provide important data on implementation after universal recommendation. Beginning in 2002, the Advisory Committee on Immunization Practices (ACIP) encouraged the vaccination of
children 6–23 months of age to reduce influenza hospitalizations, and, in 2004, it recommended universal vaccination in this age group. By use of data from the National Immunization Survey (a random-digit-dialed telephone survey of households followed by a mail survey to vaccine providers to obtain vaccination data), influenza vaccination coverage rates before the universal recommendation have been calculated as 7.4% and 17.5% for 1 dose and 4.4% and 8.4% for 2 doses in the 2002–2003 and the 2003–2004 influenza seasons, respectively [8, 9]. During the 2004–2005 influenza season, the first season when influenza vaccine was universally recommended for children 6–23 months of age, the Immunization Information System Sentinel Site Project, an expanded vaccination registry in 6 sentinel sites, demonstrated that TIV coverage rates ranged from 8.2% to 47.6% for 1 dose and from 2.1% to 18.5% for 2 doses [10]. These results suggested that universal vaccination recommendations resulted in an increase in immunization rates but that immunization was by no means “universal” and the rates varied among study sites. In addition, the frequency of complete immunization with 2 doses of TIV remained quite low. Similarly, when universal influenza immunization of all age groups was implemented in the province of Ontario, Canada, in 2000, overall vaccination rates, and from 18% to 35% [11].

In addition to clear recommendations from the Centers for Disease Control and Prevention or other authoritative groups, other strategies have been found to further increase influenza immunization rates. Kempe et al. demonstrated that private practices were able to immunize >50% of 6–23-month-old children by establishing special influenza vaccination clinics and by using reminder recall systems to inform patients about the need for influenza vaccination [12]. Others have shown the impact of utilizing media coverage to highlight expanded vaccine recommendations [13]. Szilagyi et al. proposed practice-level strategies to improve TIV immunization rates by using all visits and not only well visits for vaccination; providing vaccine for the maximum duration possible, by starting as soon as the vaccine is available and continuing until late in the season; and implementing short vacation-only visits [14]. It is also important to note that as universal vaccination is implemented in the younger age groups, fewer older children will require 2 doses. Finally, innovative vaccine schedules have also been tested. In one such approach, Englund et al. administered 1 dose of the previous season’s influenza vaccine in the spring to prime for an enhanced immune response to the second dose of TIV in the fall [15]. This strategy was highly effective when the antigens did not change but was less effective when antigenic shift in the vaccine strains occurred. The administration of live attenuated influenza vaccine in school-based clinics or community centers has also been shown to effectively decrease rates of medically attended illnesses in both the vaccinated and household contacts [16, 17]. The ease of administration of the live attenuated nasal spray vaccine may make nontraditional but more-convenient vaccination sites, such as pharmacies and schools, more attractive. Combined vaccination schedules using both TIV and cold-adapted vaccines are under study in some populations and may provide another effective approach to immunizing schoolchildren.

With the expanded ACIP influenza recommendations to immunize all children ≤5 years of age in the upcoming season, it will be important to extend the successful innovative approaches used to increase immunization in 6–23-month-old children to 2–4-year-old children. Monitoring vaccination rates and documenting impediments and solutions will also be critical. Finally, direct and indirect effectiveness of expanded vaccination should be assessed. Pilot studies or demonstration projects that could measure the effect that immunizing schoolchildren in selected communities has on their own medical care utilization, as well as on more-serious morbidity and mortality in adults in their community, would contribute substantially to our knowledge about the potential to actually control influenza epidemics. Armed with these data, we could then make more-informed decisions about the benefit of universal immunization of all children.

References


