An Update on Childhood and Adolescent Vaccines

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On completion of this article, you should be able to (1) put into practice the new influenza vaccination recommendations, (2) adopt the new infant rotavirus vaccine schedule and incorporate that schedule into practice, and (3) summarize the safety information regarding human papillomavirus vaccine.

In 2008, the recommendations for vaccines in children and adolescents changed substantially. The Advisory Committee on Immunization Practices expanded the routine use of influenza vaccines. New recommendations also addressed the newly licensed rotavirus vaccine. Furthermore, the Advisory Committee on Immunization Practices addressed the use of the meningococcal conjugate vaccine in children aged 2 to 10 years who are at high risk of that disease. Finally, the Food and Drug Administration and the Centers for Disease Control and Prevention reviewed the safety data collected about the human papillomavirus vaccine since its licensure and reaffirmed their recommendations for its use. This article discusses some of the important changes that should be of concern to the practitioner.

***Mayo Clin Proc.* 2009;84(5):457-460**

ACIP = Advisory Committee on Immunization Practices; CDC = Centers for Disease Control and Prevention; FDA = Food and Drug Administration; HPV = human papillomavirus; LAIV = live attenuated influenza vaccine; MCV = meningococcal conjugate vaccine; MPSV = meningococcal polysaccharide vaccine; TIV = trivalent inactivated influenza vaccine

Routine vaccination against infectious diseases remains one of public health's greatest accomplishments. Continued advances in science and technology have facilitated a cornucopia of advances in routine vaccination in the past 3 decades, resulting in frequent additions and revisions to the routine vaccination schedule. In 2008, the availability of vaccines as well as the licensure and recommendations for the use of vaccines in children and adolescents changed substantially. This article describes some of the more important changes that should concern the practitioner.

INFLUENZA VACCINATION

The Advisory Committee on Immunization Practices (ACIP) has made new recommendations regarding the influenza vaccine, advising that all children should now routinely receive the influenza vaccine and expanding the upper age limit of routine childhood vaccination to 18 years.[1] The ACIP also recommends the continued focus on vaccinating children aged 6 to 59 months as well as those who are at higher risk and their contacts. Furthermore, the ACIP recommends that the live attenuated influenza vaccine (LAIV) or FluMist (MedImmune Vaccines, Gaithersburg, MD) be given routinely to healthy, nonpregnant persons aged 2 to 49 years as an alternative to the trivalent inactivated influenza vaccines (TIVs). Previously, the recommendation for the use of LAIV was limited to healthy, nonpregnant persons aged 5 to 49 years.

The antigens selected for the 2008-2009 influenza vaccine series include the influenza A/Brisbane/59/2007(H1N1)–like antigens, the A/Brisbane/10/2007(H3N2)–like antigens, and the influenza B/Florida/4/2006–like antigens.[1] These were selected because they represent the antigen determinants of viruses forecasted to be circulating in the United States during the current season and because they grow well in eggs. They were used in both the LAIV and TIV formulations.

The 2007-2008 influenza season peaked in mid-February.[1] The season was particularly deadly; the rate of mortality and hospitalizations of children younger than 5 years was higher than that for the previous 3 seasons. The antigens selected for the 2007-2008 season were a poor match for the viruses circulating, specifically for the influenza A/H3N2 and influenza B strains.[2] Poor matches occur on average about every other year. Still, data available for TIV indicate that vaccination was 44% effective overall (58% effective against the influenza A/H3N2 strain and 0% effective against the influenza B strain).

In 2008, with the lowering of the age for the LAIV, the ACIP reminded physicians to screen potential recipients for possible asthma, particularly those aged 2 to 4 years with a history of recurrent wheezing or recent wheezing, and to use instead the TIV for those screening positive, given the data indicating an association with transient wheezing after LAIV in this age group among those with such a history.[1]

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TABLE. **New Rotavirus Vaccine Schedule**

	Rotarix	RotaTeq
No. of doses	2	3
Age at administration (mo)	2 and 4	2, 4, and 6
Minimum age at 1st dose (wk)	6	6
Maximum age at 1st dose (wk, d)	14, 6	14, 6 (previously, 12)
Minimum interval (wk)	4	4
Maximum age for final dose (mo, d)	8, 0	8, 0 (previously, 32)

The ACIP has consolidated the recommendations for the LAIV and the TIV formulations with regard to the timing of a second dose in children younger than 9 years receiving their influenza vaccinations for the first time.[1] Specifically, children aged 6 months through 8 years should receive 2 doses of the influenza vaccine in the current season if they have never previously received the vaccine. With both LAIV and TIV formulations, the new recommendation holds that the second dose should be given 4 weeks after the first. In the past, the timing for the LAIV was 6 weeks between doses. Furthermore, the ACIP in 2008 clarified its recommendations regarding the need for 2 doses in children younger than 9 years who were receiving their first influenza vaccination, regardless of formulation (LAIV or TIV). If the child received 2 doses in the previous season, then the child needs only 1 dose in the current season and in seasons to come. If the child received only 1 previous dose and that dose was given in the preceding season, then the child should receive 2 doses in the current season. If the child received just 1 dose but it was more than a season ago, then the child needs only 1 dose in the current season.

ROTAVIRUS VACCINATION

Two rotavirus vaccines have been approved by the Food and Drug Administration (FDA): the RotaTeq vaccine (Merck, Whitehouse Station, NJ) in February 2005 and the Rotarix vaccine (GlaxoSmithKline Biologicals, Rixensart, Belgium) in 2008. The ACIP recommends using either vaccine, with RotaTeq administered as a 3-dose series and Rotarix as a 2-dose series.[3] The ACIP harmonized the dosing schedule and age eligibility (Table).

The ACIP recommends completing the rotavirus vaccine schedule with the same species (that is, 2 doses of Rotarix or 3 doses of RotaTeq).[3] However, practitioners are not to delay completing the vaccination. Although practitioners should plan to be able to complete the series with the same species in their office, patients presenting to the office who have begun receiving the other series should complete the series. If the child has received any dose of RotaTeq or if any of the doses are of an unknown species, that child will need 3 doses. If the previous dose was Rotarix, the series can be completed with 1 more dose of Rotarix.

We have already seen substantial success from the rotavirus vaccine practice. Comparing the 2007-2008 rotavirus season (RotaTeq was approved in February of 2005 at the end of the 2004-2005 series) with the previous 15 seasons provides dramatic evidence of the efficacy of the RotaTeq vaccine.[3] The typical season in the 15 years peaked about week 9. The 2007-2008 season, however, began later and peaked at week 18. Furthermore, during that season, the number of tests with positive findings appeared to be approximately half that seen in the lightest of the preceding 15 years. This was accomplished despite the novelty of the vaccine and light uptake. The estimated coverage for 1 dose was only 49% in 2007 and 56% in 2008. Estimates for coverage with 3 doses were 3% in 2007 and 34% in 2008. Given the incomplete coverage, the halving of the number of cases and the delay in the peak both support the likelihood of substantial herd immunity.

MENINGOCOCCAL VACCINATION

On October 17, 2007, the FDA expanded the age indications for the use of the meningococcal conjugate vaccine (MCV) Menactra (Sanofi Pasteur, Swiftwater, PA).[4] The new indications include children aged 2 to 10 years. Previously, the vaccine was licensed only for those aged 11 to 55 years. Studies showed that, in children aged 2 to 10 years, the MCV compared favorably with the meningococcal polysaccharide vaccine (MPSV) or Menomune (Sanofi Pasteur). The MCV was shown to be noninferior to the MPSV for immunogenicity across the 4 serotypes (A, C, Y, and W135) and for reactivity and safety, while also having the promise of greater durability and boostability.

On the basis of the change in licensure, the ACIP reviewed the supportive data and now recommends using the MCV in preference to the MPSV for children aged 2 to 10 years, but only for those who are at increased risk of meningococcal disease.[4] Children at increased risk would include those who are travelers or residents in regions where the disease is hyperendemic or epidemic, those who have terminal complement deficiencies, and those who have an anatomic or functional asplenia. The vaccine may also be used electively in children infected with the human immunodeficiency virus. Furthermore, state and local health departments should prefer the MCV to the MPSV for the control of local outbreaks. Children who have received the MPSV more than 3 years previously who are still at high risk should receive the MCV to boost their immune status.

New recommendations are expected from the ACIP.[4] Children at high risk are likely to need subsequent doses of MCV even though the vaccine probably has extensive

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durability compared with that of MPSV. For children at high risk, a booster vaccination could be needed every 10 years. The ACIP is monitoring the available data. Also, the phase 3 studies of MCVs in infants are promising. Such vaccines are quite likely to greatly reduce the disease burden, particularly if they contain the serotype B.

Practitioners may question why, given the FDA licensure of vaccination for children aged 2 to 10 years, we continue to routinely vaccinate children aged 11 to 12 years. The answer can be found in epidemiology. Just as the cost-effectiveness data do not support vaccinating food handlers against hepatitis A, data do not support vaccinating children aged 2 years with MCVs.[4] If a child aged 2 years is given 1 dose of the MCV, the resulting immunity will likely not last until that child reaches his or her late teens or enters college. Furthermore, data are lacking on the effectiveness and durability of boosting the MCV. Alternatively, replacing the current vaccination recommendation in children aged 11 years with routine vaccination of children aged 2 years would not be cost-effective. The cost of saving 1 life with the strategy of vaccinating when children are aged 11 years is $90,000 vs $160,000 for 1 life saved with the strategy of routinely vaccinating children aged 2 years. Also, we are unlikely to vaccinate in time. In children aged 2 to 10 years, 44% of meningococcal disease occurs between the second and fourth birthday. In fact, 75% of the disease in children aged 2 years occurs in the first 5 months of that second year. We are unable to deliver the vaccine at the nominal age of 2 years and would end by vaccinating only a portion of the eligible children. We learned this with hepatitis A. In the states with the highest rates of hepatitis A, the ACIP recommended special routine vaccination at age 2 years. Nevertheless, even after 5 years, only 54% of children aged 35 months had received a single dose of hepatitis A vaccine (a 2-dose series) in those states.

HUMAN PAPILLOMAVIRUS VACCINATION

The FDA licensed the human papillomavirus (HPV) vaccine or Gardasil (Merck) on June 8, 2006, for females aged 9 to 26 years.[5] The ACIP approved its routine use in girls aged 11 to 12 years with catch-up vaccinations for those aged 13 to 26 years. The media have recently focused on HPV safety, and the FDA and the Centers for Disease Control and Prevention (CDC) have conducted a review of the data available.[6]

To date, 16 million doses of HPV have been distributed. As of August 31, 2008, the Vaccine Adverse Event Reporting System had received 10,236 reports associated with HPV,[6] 94% of which were not serious. These included events such as syncope or fainting, pain at the injection site, headache, nausea, and fever. Serious adverse events, constituting 6% of total events, occurred in approximately 600 patients, 27 of whom died of a wide variety of causes. The FDA and CDC reviewed the autopsies, death certificates, and medical records of these patients and found no pattern to suggest that the HPV vaccine was associated with the cause of death. The FDA and CDC also examined reports of Guillain-Barré syndrome that some feared were associated with the vaccine and found the rate no higher than expected for that age group. Among the cases of thromboembolic events, risk factors existed that would better explain the events. The FDA and CDC concluded that the HPV vaccine was safe and effective. The FDA will continue to review the manufacture of the vaccine and, along with the CDC, will monitor its safety. Merck, the manufacturer, is also conducting a postmarketing study of the vaccine's safety.

CONCLUSION

The newest recommendations from the ACIP call for physicians to expand the group of children they are vaccinating against influenza to include all children aged 18 years or younger. Physicians should also routinely provide 1 of the 2 licensed rotavirus vaccines using the new infant rotavirus vaccine schedule. Furthermore, they should stop using the MPSV in children aged 2 to 10 years at high risk of meningococcal disease and instead use the MCV. Finally, physicians should continue to reassure families regarding the HPV vaccine and proceed with both its routine use in children aged 11 to 12 years and with "catch-up" vaccinations for adolescent females and women aged up to 26 years.

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CME Questions About Childhood and Adolescent Vaccines

1. The Advisory Committee on Immunization Practices (ACIP), which formerly recommended routine annual influenza vaccination of healthy children aged up to 5 years, recently expanded the upper age limit. Which *one* of the following is the *new* upper age limit recommended by the ACIP?

   a. 9 years
   b. 11 years
   c. 13 years
   d. 17 years
   e. 18 years

2. If a toddler aged 18 months received only 1 dose of influenza vaccine previously and that dose was given during the previous fall, which *one* of the following represents what should be given to the toddler *this fall*?

   a. One dose of vaccine
   b. No doses of vaccine
   c. Two doses of vaccine, 4 weeks apart
   d. Two doses of vaccine, 6 weeks apart
   e. Not enough information given

3. Which *one* of the following is the *oldest* age at which an infant can start the rotavirus vaccine schedule?

   a. 8 weeks
   b. 12 weeks
   c. 14 weeks and 6 days
   d. 32 weeks
   e. 8 months and 0 days

4. The new ACIP recommendations include the use of meningococcal conjugate vaccine (MCV) in children aged 2 to 10 years. Which *one* of the following statements is *true* about the MCV?

   a. The vaccine is available for those families who wish protection against meningococcal disease
   b. The vaccine is available to be used for the routine vaccination of children against meningococcal disease
   c. The vaccine should be used instead of the meningococcal polysaccharide vaccine (MPSV) in children at high risk of meningococcal disease
   d. The vaccine offers protection against type B disease, the most common cause of meningococcal disease in children aged 2 to 10 years
   e. The vaccine should not be used in children with terminal complement deficiencies

5. Which *one* of the following statements *best* summarizes our current understanding of the safety of the human papillomavirus (HPV) vaccine?

   a. Fewer than a million doses have been distributed and little is known about its safety
   b. Fewer than a hundred safety reports have been received regarding the HPV vaccine by the Vaccine Adverse Events Reporting System
   c. Almost 10,000 deaths have been reported in association with the HPV vaccine, but fewer than 20 have been directly a result of the vaccine
   d. The vaccine is associated with a small but increased rate of Guillain-Barré syndrome
   e. The occurrence of thromboembolic events after administration of HPV is no more frequent than otherwise expected

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