Immunization updates and challenges

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Purpose of review

Childhood vaccination recommendations in the United States have increased throughout the years. Many providers, patients, and families are overwhelmed and have concerns regarding the safety and efficacy of vaccines. Various barriers and challenges exist for healthcare providers to successfully implement the vaccination recommendations. This review will discuss the 2009 and newly released 2010 immunization recommendations, as well as challenges and strategies to improve vaccination in children and adolescents.

Recent findings

Seasonal influenza immunization continues to be promoted for all children, and recommendations for vaccination against novel influenza A have emerged as well. Concerns surrounding vaccine safety and necessity may cause increasing rates of vaccine refusal among some parents, but clear messages from providers and unbiased information about benefits and risks of immunization may counteract these doubts. Barriers to immunizing adolescents continue as access to healthcare in this age group changes.

Summary

Pediatric providers currently face numerous challenges in improving rates of immunization among children and adolescents. Promoting coverage through the influenza vaccines, counseling parents with clear information about the risks and benefits of vaccines, and taking advantage of nonpreventive visits for immunization are some strategies suggested to address these challenges.

Keywords

children, immunization, vaccine, vaccine refusal, vaccine safety

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Introduction

Childhood immunization recommendations in the United States have undergone major changes in the last few decades, including at least eight new vaccines and the emergence of several combination vaccines [1]. Table 1 summarizes the revisions included in the 2009 and 2010 recommended immunization schedules. In 2009, changes to the schedule were relatively minor but notably addressed the continued expansion of the influenza vaccine age range to 18 years [2••,3]. Significant revisions in the 2010 schedule include recommendations for the use of combination vaccines, revaccination with meningococcal conjugate vaccine (MCV4) for children at increased risk of meningococcal disease, and a recommendation for the use of the quadrivalent human papillomavirus (HPV) vaccine in high-risk boys aged 9 through 18 years [4••]. In addition, because of the pandemic outbreak of novel influenza A (H1N1), recommendations for the vaccine made in late 2009 remain in place for children 6 months and above [5•,6].

Although the prevalence of several infectious diseases has been greatly impacted through the implementation of the vaccination program in the United States [7], continuous additions and revisions to the immunization schedule may affect compliance by both providers and families. This article will briefly review some of the more notable updates to the immunization schedule for 2009 and 2010, as well as discussing the most recent challenges and strategies to improve vaccination rates in children and adolescents.

Influenza vaccination recommendations

Vaccine discussions in 2009 primarily revolved around influenza, both seasonal and H1N1. The American Academy of Pediatrics (AAP) Committee on Infectious Diseases recently issued a policy statement for the prevention and treatment of influenza in children for 2009–2010 [8••]. Use of inactivated vaccine and live-attenuated influenza vaccine (LAIV) against both seasonal influenza and H1N1 in children is discussed, and the use of antiviral chemoprophylaxis is also addressed. In

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Table 1 Summary of revisions in the 2009 and 2010 recommended immunization schedules

2009 revisions [2••,3]	
Rotavirus	Vaccine maximum starting age was changed from 12 weeks to 14 weeks 6 days, and maximum age for final dose was changed from 32 weeks to 8 months to synchronize with the newly approved two-dose rotavirus.
Hib	Indication for the vaccine was expanded to allow immunization of persons aged 5 years and older at risk for invasive Hib disease.
HPV	Vaccination catch-up interval is to be the same as routine dosing interval.
Tdap	Interval between tetanus–diphtheria and Tdap immunizations of less than 5 years is acceptable for those who require pertussis immunity.
Seasonal influenza	Vaccine recommended for annual administration to children 6 months through 18 years of age. Two doses 1 month apart of the vaccine are required for those under 9 years of age receiving the vaccine for the first time or for those who were vaccinated for the first time last season but only received one dose.
Other	Most of the footnotes for the individual vaccines have been revised to provide additional information and to clarify recommendations provided in the schedules.
2010 revisions [4••]	
IPV	The fourth dose of the vaccine is now recommended on or after the fourth birthday. If four doses were administered before the age of 4 years, a fifth dose is recommended between 4 and 6 years of age.
HepA	Vaccine may now be given to children older than 23 months if immunity is desired.
MCV4	Revaccination is recommended for children at high risk of meningococcal disease, after 3 years if first dose was given through 6 years of age or after 5 years if the first dose was at 7 years or older.
HPV	Recommendations include use of the bivalent vaccine for girls, and the quadrivalent vaccine is now recommended for boys aged 9 through 18 years at high risk for acquiring genital warts.
H1N1 [5•,6]	Vaccine recommended for annual administration to children 6 months through 24 years of age. Two doses 1 month apart are required for those under 10 years of age.
Other	The use of combination vaccines is now addressed in the introductory paragraph. Combination vaccines are generally preferred over separate injections of their component vaccines as long as patient choice, provider assessment, and risk of adverse events have been considered.

H1N1, novel influenza A; HepA, hepatitis A; Hib, *Haemophilus influenzae* type b conjugate; HPV, human papillomavirus; IPV, inactivated poliovirus; MCV4, meningococcal conjugate; Tdap, tetanus and diphtheria toxoids and acellular pertussis.

addition, a brief review of the Centers for Disease Control and Prevention (CDC) estimates for the first several months of the H1N1 outbreak in the United States is presented.

Seasonal influenza

Recommendations continue to emphasize the importance of annual seasonal influenza immunization for children 6 months through 18 years of age [8••]. Children at high risk for complications from the flu should be especially targeted, including the immunosuppressed or those with chronic illnesses. Particular attention is also encouraged among the school-aged population, as they currently bear the greatest influenza disease burden [8••,9]. Household members and caregivers of high-risk children and all children under the age of 5 years are also strongly encouraged to receive the vaccine [8••].

The LAIV is administered intranasally and is licensed for use in individuals who are 2 years old and above, but only for healthy individuals and those living among healthy households [8••]. Early studies [8••,10•] have shown increased levels of immunity for the LAIV in children, although more solid research is necessary. Children aged 9 years and older may continue to receive one dose of the trivalent inactivated vaccine, whereas children under 9 years of age should receive two doses in their first year receiving the vaccine and then one annual dose afterward [8••]. If these children did not receive two doses in their first year of receiving it, they should have two doses in their second year and then continue with the annual single dose. Contraindications to all flu vaccines include age under 6 months, severe allergy to egg, moderate-to-severe febrile illness, and history of serious adverse events with previous vaccines. In addition to the above, contraindications to the LAIV include age under 2 years, pregnancy, nasal congestion, and any chronic illness or disorder that may compromise respiratory or immune function. Thus, children with wheezing or asthma should not receive the LAIV. Living in a household with persons with the conditions mentioned above is also a contraindication to receiving LAIV.

Although influenza vaccination recommendations were expanded in the beginning of the 2008–2009 season to include all children, coverage remained low in the United States [11•]. According to data analyzed by the CDC from the Behavioral Risk Factor Surveillance System, total influenza vaccination coverage for children 6 months through 17 years was estimated at only 24%. Especially concerning was the low rate of vaccination among school-aged children of 5–17 years (20.8%). Greater efforts must be made to ensure that the new recommendations for this age group are promoted effectively, as this group may bear the greatest influenza disease burden [8••,9]. The AAP Policy Statement [8••] contains a simple algorithm helpful for providers to capture those who need to be vaccinated.

Novel influenza A

In response to the H1N1 outbreak in 2009, recommendations soon appeared for its vaccine for children similar to those for seasonal influenza, with the exception of the upper age limit extended from 18 to 24 years [5•,6].

Current studies do not show cross-reactive antibody to H1N1 in children who have received the seasonal influenza vaccine, and, therefore, receipt of both vaccines is recommended. It is permissible to immunize with both inactivated vaccines simultaneously, provided that different injection sites are used. Simultaneous administration of LAIV for both flu vaccines, however, is not recommended. A second dose of the H1N1 vaccine is recommended for children under 10 years [6]. This is in contrast to the seasonal influenza vaccine, wherein children under 9 years need two doses for the first time [8••].

Antiviral chemoprophylaxis recommendations have been issued by the CDC as adjunct therapy to influenza vaccination [8••,12•]. Unvaccinated children undergoing influenza treatment or chemoprophylaxis are also eligible and recommended to be immunized with the inactivated vaccines [12•]. Up-to-date influenza decision-making and treatment algorithms for healthcare providers can be found on the CDC website (see Table 2).

In December 2009, the CDC released estimates of the prevalence of H1N1 influenza cases, hospitalizations, and deaths in the United States through 14 November 2009 [13]. According to this report, between April and mid-November, prevalence was estimated at between 34 and 67 million infected individuals. Approximately one-third of these were pediatric patients, with estimates between 12 and 23 million infected children 0 through 17 years of age. During this time period, there were an estimated 51 000–101 000 pediatric hospitalizations and 790–1550 pediatric deaths related to H1N1 in children 0 through 17 years of age. These numbers represented a dramatic 2.5 times increase from estimates reported in mid-October

Table 2 Online resources for pediatric providers about immunizations and related information

Website address	Organization	Description
www.cdc.gov/vaccines	CDC	General information about vaccines Access to current ACIP recommendations and immunization schedules Vaccine Information Statements and patient education materials Information regarding use of an IIS and local IIS contact information
www.immunize.org	IAC	Vaccine policy, licensing, and safety Free print education materials in 40 languages Summary grid of current recommendations, intervals, and contraindications IAC Express: weekly free e-mail notification with up-to-date information about vaccine approvals, new vaccine recommendations, new immunization resources and current events, and journal articles
www.aap.org/immunization	AAP: Childhood Support Immunization Program	Information for patients, parents, providers, and media on vaccines and vaccine-preventable diseases State level (AAP Chapter) immunization-related activities and initiatives
www.vaccineinformation.org	IAC	Information designed for patients, parents, providers, and media on vaccines and vaccine-preventable diseases (also available in Spanish)
http://kidshealth.org/teen/your_body/health_basics/immunizations.html	Nemour Foundation: Kids Health	Health and vaccine information directed towards adolescents
www.nnii.org	National Network for Immunization Information	Up-to-date information on immunization science and research including synopses of articles from peer-reviewed literature related to vaccines and immunization
www.vaccinesafety.edu	Johns Hopkins Institute for Vaccine Safety	Information on vaccines and safety to help guide and educate physicians, the public and the media about issues surrounding the safety of vaccines
www.who.int/immunization	WHO	Global policy, guidelines, and information about vaccines and related diseases
www.hhs.gov/nvpo	US Department of Health and Human Services National Vaccine Program Office	Publications and reports on vaccine-preventable diseases, vaccine safety, vaccine coverage, immunization laws, and immunization registries
www.cdc.gov/flu	CDC	Current information on seasonal flu activity and surveillance Vaccine and prevention information for providers and patients Algorithm for antiviral treatment and prevention of influenza
www.flu.gov	US Department of Health and Human Services	Comprehensive government-wide information on seasonal, H1N1 (swine), H5N1 (bird), and pandemic influenza for the public and professionals
www.preventchildhoodinfluenza.org	Childhood Influenza Immunization Coalition: National Foundation for Infectious Diseases	Information and resources for healthcare professionals, patients, families, and media regarding the influenza vaccine and related topics

AAP, American Academy of Pediatrics; ACIP, Advisory Committee on Immunization Practices; CDC, Centers for Disease Control and Prevention; H1N1, novel influenza A; H5N1, avian influenza A; IAC, Immunization Action Coalition; IIS, Immunization Information Systems.

2009, reflecting a surge of H1N1 activity in late October and early November. In light of this evidence, support continues to increase for significant prevention strategies against H1N1, such as vaccination.

Challenges in vaccine compliance

Recent studies have addressed increasing trends among parents who are refusing or delaying vaccination for their children. Issues thought to influence parental resistance to vaccines include both the increasing number of available vaccines and lack of perceived threat of the diseases they prevent [14•]. Provider attitudes towards surrounding vaccines may play a large role, as many parents rely heavily on provider counseling regarding vaccine decisions [14•,15,16•,17•,18]. Finally, concerns about safety and risk for adverse events after vaccination continue to mount, as media exposure incites doubt throughout the community [19•].

Vaccine refusal

An increase in the number of parents refusing or delaying vaccines for their children has prompted studies to evaluate the characteristics of vaccine refusers. Gust *et al*. [16•] interviewed a random subset of parents ($n = 3924$) who completed the National Immunization Survey (NIS) by the CDC in 2003 and 2004 to explore just these factors. Approximately 28% of parents surveyed reported some level of doubt about vaccination (13% delayed vaccinations, 9% were unsure, and 6% completely refused vaccinations for their child). Factors associated with vaccine refusal included white race/ethnicity of the mother, age of child under 2 years, and general concern that vaccination may not be safe or may cause serious side effects. In another study [20] of parents who refused immunization for their children ($n = 1249$), investigators found that refusers were more likely to come from high-income and well educated communities, but continued to access the healthcare system.

Trust in vaccine information provided is important in the decision-making process for parents about immunizations. In a small qualitative study [15] of parents who refused vaccination for their children ($n = 25$), patients were again found to be mostly white and highly educated. Parents interviewed expressed distrust of the medical community, and were opposed to vaccine information offered at the time of vaccine administration rather than prior to administration. Many of these parents wished to discuss both risks and benefits with providers in order to address their concerns about vaccine safety. Similar themes were also addressed in a case–control intervention study of parental vaccine refusers, as patients in the case group ($n = 69$) tended to disagree or be neutral about their trust in providers or government agencies regarding vaccine information [17•]. Parents in this group suggested that an informational brochure provided should include honest and balanced information about both risks and benefits of vaccines.

Provider recommendations have been shown to play a large role in parents' decisions on vaccination [14•,15,16•, 17•, 18,21•], yet providers themselves are not always recommending vaccination [22]. A study [22] of pediatric providers ($n = 733$) found that 11% did not fully recommend vaccinations. These physicians were also more likely to report being neutral or agreeing that they have some concerns about immunizations. This raises the question of whether adequate immunization information is disseminated to pediatric providers. Another pilot study [23•] examined physicians' communication strategies in addressing vaccine refusal through the use of standardized patients. Although most of the physicians scored well on listening and spending sufficient time with the standardized patients, lower scores were obtained in validation of the standardized patients' concerns, using open-ended questions, and checking for knowledge or understanding. Additional training on communication for pediatric providers is essential in addressing vaccine refusal with patients.

Vaccine safety controversies

As mentioned above, safety concerns have greatly influenced vaccine acceptance rates among parents. Despite previous research in existence refuting the suggested relationship between measles or measles–mumps–rubella (MMR) vaccines and autism spectrum disorders (ASDs) [24], research continues to emerge in this area. In a case–control study [25] of over 200 vaccinated children in the UK, there was again found to be no difference between ASD patients and controls in measles antibody concentrations or altered immunological response following MMR vaccination. The proposed relationship between thimerosal preservatives in vaccines and ASDs has also been refuted yet again [19•,24,26].

Combination vaccines offer advantages over separate vaccines, including fewer injections and thus better compliance, but their safety has come into question [27]. This past summer, the Advisory Committee on Immunization Practices (ACIP) revised the 1999 recommendations for the use of combination vaccines [28], and this revision is included in the latest 2010 recommended immunization schedule [4••]. The ACIP states that combination vaccines are generally preferred over separate injections of their component vaccines as long as patient choice, provider assessment, and risk of adverse events have been considered. A recent exception to this came in 2008, when a higher incidence of febrile seizures following a MMR–varicella (MMRV) vaccine in the United States (Proquad, Merck & Co. Inc., Whitehouse Station, New Jersey, USA) led the ACIP to declare no preference

between use of the MMRV and the separate MMR and varicella vaccines [29]. In 2009, the ACIP issued further provisional recommendations encouraging providers to address the risks of febrile seizure with parents when considering the use of MMRV for a child's first dose at the age of 12–47 months [30]. For children receiving the first dose at 48 months or older, and for children of any age receiving the second dose, the MMRV vaccine is still considered preferred over its separate components.

Parental refusal of vaccines despite current evidence of their safety continues to show an impact on disease rates and outbreaks. Results of a case–control study [31] of pertussis vaccination and infection rates in Colorado children from 1996 to 2007 ($n = 156$ patients, 595 matched controls) showed that 11% of all pertussis patients were attributed to parental vaccine refusal. Although more research is needed on the epidemiology of disease related to vaccine refusal, it is obvious across the literature that comprehensive patient education by pediatric providers regarding the evidence and myths surrounding vaccine safety is vitally important to improving immunization rates.

Adolescent immunizations

Efforts continue toward bringing adolescents up-to-date for both routine and newly introduced vaccines. Barriers include infrequent preventive visits, incomplete records, lack of awareness about the risk of serious infectious diseases, and lack of coverage for adolescent vaccination [21•,32,33•,34–37]. Several studies over the last year have looked at the influences affecting poor adolescent immunization rates as well as the challenges in improving them.

Visits and venues

Although childhood immunizations occur during routine well child visits, a decrease in the number of preventive visits in adolescence creates a barrier to this process. This is problematic for those behind on childhood vaccines, as well as those who were older than 12 years when routine recommendations for the MCV4, HPV, and tetanus and diphtheria toxoids and acellular pertussis (Tdap) vaccines were released. According to the 2008 NIS-Teen of almost 18 000 US adolescents, coverage rates for these three vaccines had improved but still fell below 50% [38]. One method of addressing this problem is to vaccinate at acute visits whenever possible, although many practitioners currently miss these opportunities. In a large study of adolescents in Massachusetts ($n = 23\,987$), investigators found that missed opportunities for tetanus and diphtheria immunization occurred at 84% of all healthcare visits, mostly associated with nonpreventive visits [39].

Obtaining accurate immunization records for adolescents has also been identified as a barrier to vaccination at nonpreventive visits [21•]. The use of Immunization Information Systems (IIS), also known as immunization registries, has been promoted as a potential solution [21•,33•,34,39]. Current studies [40,41] show promise in the effectiveness of IIS to improve tracking and record keeping and more is sure to emerge in the coming years.

Adolescents may also use alternative sites for healthcare such as school-based health centers or family planning clinics. In a multistate qualitative study [33•] of participants with varying roles associated with adolescent immunization ($n = 49$), many patients discussed the lack of available vaccines in the sites where teens routinely seek care. Participants also raised the related issue of adolescents' ability to consent for vaccines, which is limited in many states. In this study as well as another qualitative interview of US pediatric providers, patients raised concerns that missed opportunities for vaccination increase when teens independently seek care without a parent and are unable to consent to their own immunization [21•,33•].

Perceived risk of disease and safety

The HPV vaccine has particularly highlighted the low perceived threat of disease by adolescent girls and their parents, which studies show plays a role in the decision to be immunized [33•,42–44]. In several international studies, attitudes towards the HPV vaccination revealed a low perceived threat of HPV infection and, therefore, an initial tendency to decline the vaccine. In adolescent girls, most demonstrated a low initial understanding of the threat of HPV but responded positively to vaccination once the risks of genital warts and cancer were explained [42,44,45]. For parents, the low perceived threat of HPV was associated with the belief that their daughters were not or would not soon be sexually active [33•,43,46,47]. Given the most recent ACIP permissive recommendation for administration of quadrivalent HPV vaccine to boys aged 9 through 18 years to lower their risk for acquiring genital warts [48], we will undoubtedly see more research exploring attitudes and beliefs in adolescent boys and their parents on their perceived risk of disease. As administration of the HPV vaccine expands, the need for parent education by providers regarding the role of vaccines in disease prevention once again continues to grow.

Concerns regarding safety for adolescent vaccines have arisen recently as well, particularly with the HPV vaccine. A recent safety surveillance [49•] summarizes reports to the Vaccine Adverse Event Reporting System (VAERS) related to the more than 23 million doses of the quadrivalent HPV vaccine administered between June 2006 and December 2008. Results revealed 12 424 reports of adverse events following HPV immunization, 6% of

which were categorized as serious (although many appeared unrelated to vaccination after investigation). The most commonly reported adverse event was syncope (15%), which was not surprising given that postvaccination syncope reports to VAERS have increased significantly in adolescent girls following the addition of the MCV, Tdap, and HPV to the immunization schedule [50]. Most syncopal events related to vaccination were not serious (95%), although falls accompanied 15% of them, some with head injuries [49•]. For this reason, providers are encouraged to monitor patients for 15 min after vaccination [48].

Financial barriers

The high cost of adolescent vaccines and concerns with reimbursement were also cited as barriers to improving teen immunization rates [33•,34,37]. In the United States, most insurance companies cover recommended adolescent vaccines, and the Vaccines for Children (VFC) program covers low-income and uninsured populations. However, in private practices that do not participate in the VFC program or for older teen patients ineligible for VFC, the cost of these expensive vaccines has become an added barrier [21•,33•,34,36].

Conclusion

As immunization recommendations expand and evolve, the public's perception of their safety and efficacy will also change. Pediatric healthcare providers have a responsibility to continue the efforts toward eliminating vaccine-preventable diseases and deaths by improving the rate of vaccination in children. Future research is needed to evaluate barriers and strategies for successful vaccination in children and adolescents.

Recommendations for improving vaccination efforts in the pediatric office are as follows (see Table 2 for helpful resources):

(1) Stay up-to-date on the latest immunization recommendations and safety data.
   (a) Consult online resources for most current information and post or distribute updates and revisions to other practice providers to ensure consistency.
   (b) Sign up for e-mail alerts and updates for local disease patterns.
(2) Improve patient–parent communication regarding vaccination.
   (a) Allow time to explore and validate parents–patients' concerns regarding vaccines.
   (b) Provide patient education materials and links to reliable websites.
   (c) Discuss risks and benefits as well as vaccine safety prior to vaccine administration.
(3) Avoid missed opportunities for vaccination.
   (a) Consider joining an IIS to consolidate and keep track of patients' immunization records as well as identifying overdue vaccinations.
   (b) Administer vaccinations during any visit (including nonpreventive) when appropriate.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

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Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 000–000).

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