

Immunizations for Preteens

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As a part of health supervision visits, all preteens should receive the combined tetanus, diphtheria, and pertussis vaccine, the meningococcal conjugate vaccine, the human papillomavirus vaccine series, and an annual influenza vaccine. Because levels of vaccine coverage among preteens are generally suboptimal, strategies for improving coverage should be devised and implemented.

Immunizations are a major component of health supervision visits for children and adolescents. Because immunization recommendations change frequently, Bright Futures, an initiative of the American Academy of Pediatrics (AAP) that promotes the health of children and adolescents, has issued guidelines that refer providers to the Web sites of the Centers for Disease Control and Prevention (CDC) [1] and the AAP [2] for the most up-to-date immunization schedules. For no other age group have routine immunization recommendations evolved more rapidly in the past 8 years than for preteens. (See Figure 1 for a list of vaccines recommended for those 11-12 years of age.) This advancement resulted from the development of a number of novel vaccines, including meningococcal conjugate vaccine; tetanus, diphtheria, pertussis vaccine; and human papillomavirus vaccine. In addition, an annual influenza vaccine is now recommended for everyone, including preteens. The discussion that follows will highlight the rationale for recommending vaccines during the preteen period. Challenges for immunizing North Carolina preteens will also be described, and potential strategies for improving preteen vaccine coverage will be considered.

Meningococcal Disease

Meningococcal disease, caused by *Neisseria meningitidis* bacteria, most commonly presents as meningitis but may also present with bacteremia or septicemia. The case-fatality rate of invasive disease is about 10%, and survivors often suffer from such sequelae as hearing loss, limb loss, or neurologic impairment [3]. Disease incidence is highest among children during the first year of life and climbs again during the teenage years. Serogroups C, Y, and W-135 cause about 75% of disease among persons 11 years of age or older [3]. The vast majority of disease among teens can be prevented by vaccination. Prior to 2000, the annual number of reported cases of invasive meningococcal disease in the US ranged from 1,300 to 3,500. Since 2001, the annual number of cases has steadily decreased from 2,333 in 2001 to 833 in

FIGURE 1.
Immunizations Universally Recommended for North Carolina Preteens 11-12 Years of Age

Meningococcal conjugate vaccine
First dose (to be followed by a second dose at age 16 years).
Tetanus, diphtheria, pertussis vaccine
Human papillomavirus vaccine
3 doses
Females - either HPV4 or HPV2
Males - HPV4
Influenza vaccine
Yearly

2010 [3, 4]. In 2010, only 14 cases were reported in North Carolina, and 11 of those cases were caused by serogroups included in the current vaccine [4]. Although meningococcal disease is uncommon, vaccination is critical, because the consequences of infection can be devastating.

In 2005 the US Food and Drug Administration (FDA) approved the first of the 2 currently licensed quadrivalent meningococcal conjugate (MCV4) vaccines, which target serogroups A, C, Y, and W-135. Either of the 2 vaccines can be used to routinely immunize children 11 or 12 years of age. It was subsequently recognized that immunity following a single dose of MCV4 administered at this age is short-lived, leaving some older adolescents unprotected from meningococcal infection when exposed. Therefore, in 2011 the CDC began recommending a second dose of MCV4 vaccine for routine administration starting at age 16 years [5].

Pertussis

Pertussis most frequently manifests in preteens as a prolonged and severe cough illness [6]. The early phase of the illness, characterized by rhinorrhea, low-grade fever, and mild cough, is indistinguishable from upper respiratory infections from other causes. As the illness progresses, the preteen child will typically experience coughing fits and post-tussive emesis. Sleep is often disrupted, and school absenteeism is common. Over the course of many weeks to

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several months, the coughing fits become less frequent and eventually resolve.

A key concern related to pertussis infection in preteens is transmission of infection to school classmates and younger siblings. This may result in classroom and school outbreaks. Furthermore, infected preteens can serve as a reservoir of infection, posing risk to infants and newborns, who are most vulnerable to severe infection.

Since the early 1980s, the incidence of pertussis has gradually increased [4]. A recent outbreak in California resulted in more than 9,000 cases, 809 hospitalizations, and 10 infant deaths [7]. High rates of disease were noted among preteens, and a recent evaluation of data from that outbreak suggests that the protection from disease conferred by a fifth dose of diphtheria, tetanus, and acellular pertussis (DTaP) vaccine is short-lived [8]. Data from the North Carolina Electronic Disease Surveillance System show that 2012 has so far witnessed the largest number of pertussis cases seen in the state during the past 6 years, with the majority occurring in children and adolescents 6-17 years of age, many of whom were appropriately vaccinated (Figure 2).

Current measures for controlling pertussis include vaccination of infants and preschool-age children with DTaP according to the recommended childhood immunization schedule, as well as routine vaccination of preteens and unvaccinated adolescents and adults with tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine. Since 2006, 2 Tdap vaccines have been approved and recommended for preteens 11-12 years of age. In 2008, the state of North Carolina mandated that all children enrolled in public school receive a dose of Tdap vaccine before entering sixth grade, or by age 12 years for those not attending public schools [9]. Further studies are needed to elucidate the optimal timing for pertussis vaccination to

assure protection across the lifespan. Improved vaccines that induce long-lasting protection against pertussis also need to be developed.

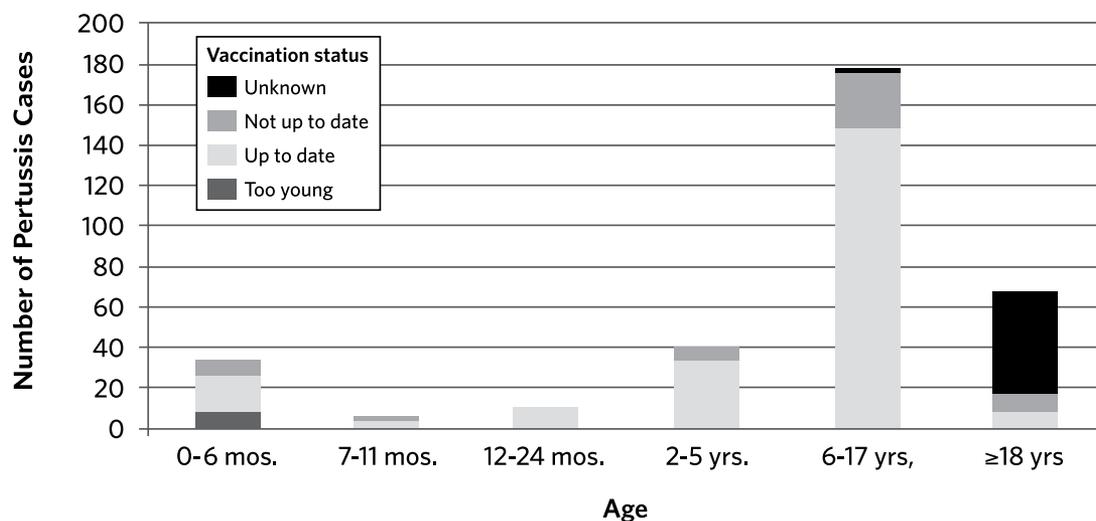
Human Papillomavirus

Human papillomavirus (HPV) infection is the most common sexually transmitted infection in the United States. More than 6 million persons in the United States become infected with HPV each year, with the vast majority of new infections occurring among persons 15-24 years of age [3]. Although infection is typically transient, persistent infection with oncogenic HPV types is the most important risk factor for development of precancerous or malignant lesions of the cervix, anus, or genitals [10]. HPV types 16 and 18 cause approximately 70% of cancers of the cervix, anus, or genitals [3]. There is also increasing recognition that many head and neck cancers are associated with HPV infection [11]. Other HPV types, in particular types 6 and 11, are responsible for 90% of genital warts [3].

In the United States, there are more than 12,000 incident cervical cancer cases and 4,000 deaths due to cervical cancer annually [12]. In North Carolina, the rate of cervical cancer is consistent with the national average, but within the state there are 20 counties with a disease incidence that is higher than the highest rate estimated for any of the 50 states [13]. The best methods of preventing cervical cancer include cervical cancer screening and vaccination. Given pockets of higher disease incidence, more intensive efforts at increasing vaccination and screening in some North Carolina counties is warranted.

A quadrivalent human papilloma virus (HPV4) vaccine was approved by the FDA in 2006 and quickly recommended for routine administration to females starting at age 11-12 years. Although a permissive recommendation for

FIGURE 2.
Pertussis Cases Reported in North Carolina During the First 8 Months of 2012, by Age and Vaccination Status



Source: Data are from the North Carolina Electronic Disease Surveillance System provided by the North Carolina Immunization Branch.

Coping With a Pertussis Outbreak in Alamance County, North Carolina

Kathleen Shapley-Quinn

At its peak prevalence in the United States in the 1930s, pertussis (whooping cough) affected as many as 265,000 people per year, killing thousands of infants [1]. With the introduction of a combination vaccine for diphtheria, pertussis, and tetanus (DPT) in the mid 1940s, the number of annual cases gradually decreased, until fewer than 2,000 were being recorded in the 1970s [1]. Since that time, though, the incidence of pertussis has been on the rise, and more than 30,000 cases were reported during the first 9 months of 2012 [2].

Why the resurgence? DPT vaccine, which contains whole-cell pertussis, is very effective but also has an unacceptable side-effect profile. A newer vaccine, DTaP, which has an acellular pertussis component, began gradually replacing the whole-cell vaccine in the 1990s. Although DTaP has fewer side effects than DPT, the immunity it confers is less durable. The acellular vaccine initially provides 98% protection against disease when it is administered to children 4-5 years of age in a 5-dose series, but protection wanes to 71% over the next 5 years [3]. As a result, children 7-10 years of age become susceptible to pertussis, which is also present in the adult population where it often goes undiagnosed. Communities are therefore at increased risk for outbreaks.

Alamance County, North Carolina, experienced such an outbreak recently. In December 2011, a child attending elementary school was diagnosed with pertussis, and investigation of the child's contacts (schoolmates, fellow school-bus riders, and family members) soon identified many children who had pertussis-like symptoms. Health department nurses spent hundreds of hours talking with families to clarify which children and adults met the case

definition for pertussis. Laboratory testing with culture and/or polymerase chain reaction technology was used whenever possible to confirm diagnoses. Contacts in additional schools were identified, and additional unrelated (not epidemiologically linked) cases of pertussis in the community were found by health care providers. A total of 166 cases were diagnosed between December 2011 and August 2012, most of them children in the Alamance-Burlington school system. A total of 24 schools were affected.

Inadequate vaccination rates are often blamed for such outbreaks, so it is notable that school records showed that 100% of students in the Alamance-Burlington school system had been appropriately vaccinated. Furthermore, among children with proven disease, 100% of those 3-12 years of age were up to date on their vaccinations, as were 93% of those 13-17 years of age.

Initial responses to the outbreak followed Centers for Disease Control and Prevention (CDC) guidelines [4], which call for administration of prophylaxis to all close contacts of each case—that is, household contacts and those who had spent at least 15 minutes within 3 feet of the ill individual. Furthermore, when 2 or more cases of pertussis were identified in a classroom or on a school bus, all of the children in that classroom or on that bus were considered close contacts. Hundreds of courses of prophylactic antibiotics were prescribed during the first weeks of the outbreak.

Our public health partners in the Immunization Branch and the Communicable Disease Branch of the North Carolina Department of Health and Human Services worked closely with us throughout this effort. We were becoming frustrated with the burdensome strategy for containment,

administration of HPV4 to males followed in 2010, a full routine recommendation for its use among males at age 11-12 years did not occur until 2011. In 2010, a bivalent human papilloma virus (HPV2) vaccine was also approved for use in females. Both vaccines are administered in 3 doses over a period of 6 months.

The 2 HPV vaccines differ both in composition and in indications for use. HPV4 contains purified virus-like particles from the major capsid protein of HPV types 6, 11, 16, and 18, whereas HPV2 contains virus-like particles from the major capsid protein of HPV types 16 and 18. Both HPV4 and HPV2 are indicated for the prevention of cervical cancer and precancerous cervical lesions in women. HPV4 is also indicated for prevention of genital warts, anal cancers, and precancerous anal lesions in both males and females. To be most effective, HPV vaccine should be administered prior to acquisition of infection. Because a significant proportion of adolescents will become sexually active during their mid to late teens and the potential risk for HPV exposure is high,

the best time to initiate the vaccine series is during the pre-teen years. Preteen vaccination also assures the best chance for vaccine series completion in order to achieve optimal protection from infection prior to virus exposure [1, 2].

Other Considerations for Vaccination of Preteens

All 3 routinely recommended preteen vaccinations (MCV4, Tdap, and HPV) can be administered at the same health care visit, thereby decreasing the need for additional visits other than those to complete the 3-dose HPV series and to receive the MCV4 booster at age 16. Preteens should also receive an annual influenza vaccine. Although most preteens can receive the intramuscular inactivated influenza vaccine, an alternative for those without underlying long-term health problems such as asthma is the intranasal administration of live attenuated influenza vaccine. The preteen health care visit also provides an opportunity to assess whether or not preteens are up to date for other immunizations. All preteens should have previously received 2 doses

which did not appear to be effective, so our state partners soon linked us with pertussis experts at the CDC, who reviewed our approach.

CDC staff informed us that broad-scale prophylaxis for pertussis is ineffective at curbing outbreaks and that they are therefore developing new guidelines. Alamance County implemented this unofficial guidance from the CDC, which focuses on protection of those at highest risk: close contacts to a pertussis case who have a weakened immune system or chronic lung disease, or who live with a woman who is more than 20 weeks pregnant or an infant who is younger than 12 months. This narrowed focus freed our nursing staff to begin the potentially more effective strategy of widespread pertussis vaccination. We administered Tdap vaccine to thousands of people, including parents and staff members of schools and child care centers, and offered vaccination at multiple community events.

Despite its imperfect nature, vaccination is one of our most effective prevention strategies. North Carolina state law requires DTaP vaccination at the ages of 2 months, 4 months, 6 months, and 15-18 months, with a booster dose at age 4-5 years. In addition, administration of Tdap vaccine, which contains a reduced amount of diphtheria toxin, is now mandated for entrance into the sixth grade and is strongly recommended for every adult.

Immunizing caregivers of infants is especially important. Fewer than 50% of pertussis infections in infants have a known source, but when the source is known, in 80% of cases it is a parent, sibling, or other close family member [3]. Women who are pregnant can be given Tdap vaccine after the 20th week of pregnancy and should receive it immediately after giving birth at the latest. In Alamance County, we partnered with local hospitals and obstetricians to ensure Tdap vaccination of all new mothers, and we also strongly encouraged their family members to be vaccinated.

By October 2012, Alamance County pertussis rates had

returned to baseline. We keep our fingers crossed. Our hope is that other North Carolina counties will undertake robust vaccination programs in order to avoid experiencing a similar outbreak. In addition, local health departments and the North Carolina Division of Public Health should continue to work together to determine optimal responses, including use of new strategies based on emerging information about pertussis control. **NCMJ**

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of vaccine(s) for measles, mumps, rubella, and varicella and 3 doses of hepatitis B vaccine [1, 2].

Teen Vaccination Coverage

In 2011, 77.8% of North Carolina adolescents 13-17 years of age had received Tdap vaccine and 65.9% had received 1 or more doses of MCV4 vaccine as shown in Figure 3 [12]. In addition, 54.4% of females 13-17 years of age had received 1 or more doses of HPV vaccine, but only 32.3% had received the full recommended complement of 3 doses [14]. It is encouraging that state trends in teen vaccine coverage have mirrored national trends by showing steady increases in Tdap and MCV4 coverage over the past 4 years [14-17].

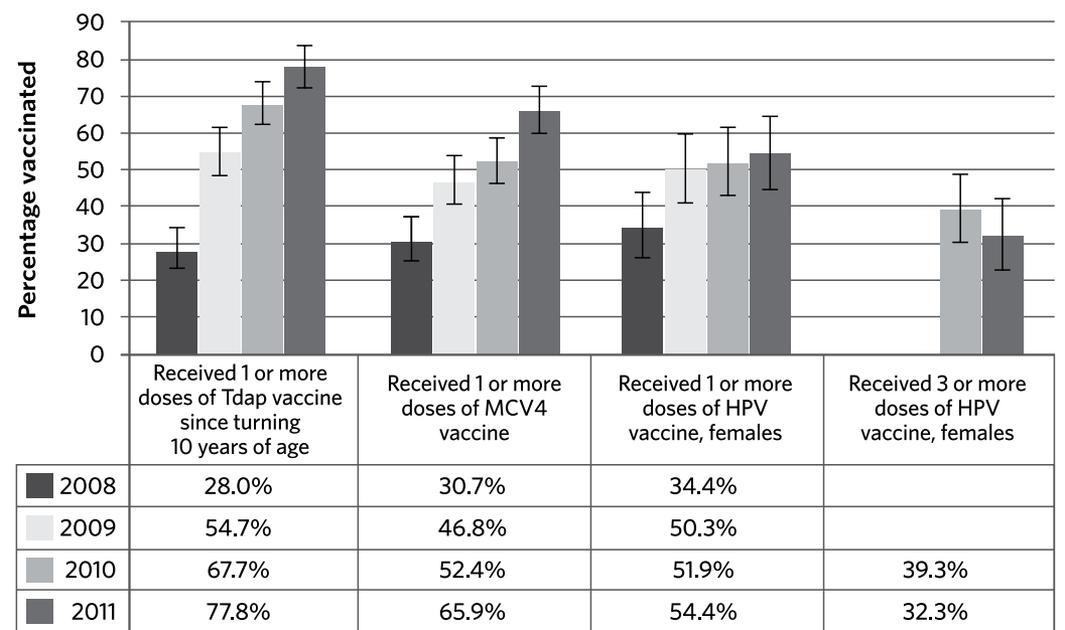
Unfortunately, increases in HPV coverage among adolescent females lag considerably behind those for other teen vaccines. Routine HPV vaccination of males was recommended only recently, so it is too soon to comment on coverage level in that group. National data suggest that younger teens are less likely to have received at least 1 dose

of HPV vaccine. These data reflect the reluctance of many parents to vaccinate their preteens. Some parents prefer to defer vaccination based on their assessment of their child's experience with sexual activity. Likewise, health care providers often reinforce the parents wish to defer vaccination. Providers delay preteen HPV vaccination for a number of different reasons including discomfort discussing sexuality with parents and preteens, a belief that HPV is not a significant health concern for their younger patients, and concern about parental resistance to HPV vaccination [18]. Health care providers should acknowledge the parents' perspectives but also point out that preventive measures such as the HPV vaccine are best implemented well in advance of any potential infectious exposures.

Improving Delivery of Vaccines to Preteens

Although the barriers to preteen vaccination are many, efforts to mitigate these obstacles are similarly numerous [19]. Preteens present for routine care less frequently than

FIGURE 3.
Meningococcal, Pertussis, and Humana Papillomavirus Vaccination Coverage of North Carolina Adolescents 13-17 Years of Age, 2008-2011



Note. The error bars indicate 95% confidence intervals. Tdap, tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine; MCV4, quadrivalent meningococcal conjugate vaccine; HPV, human papillomavirus vaccine (either quadrivalent or bivalent). Source: Data are from the National Immunization Survey-Teen (NIS-Teen), United States, 2008-2011.

do younger children and therefore have fewer opportunities to be immunized in general. The concept of annual health supervision visits for preteens is not as familiar to parents and guardians as the slate of frequent visits that characterize early childhood. In addition, parents may not be aware of the various health needs of preteens or of the existence of a preteen vaccination schedule. These obstacles to immunization may be compounded by the inherent conflict between typical clinical office schedules and the busy lives of preteens and adolescents, who often navigate a variety of obligations related to school, family, and other activities. Shifting services to align with the needs of preteens and adolescents may mitigate these issues but would also require fundamental changes to practice patterns. To help alleviate such obstacles, it may be important to add points of access such as schools or other community settings.

Furthermore, the expanded vaccination platform in the preteen years is still a recent development and may not be implemented seamlessly in some settings. Clinicians often lack awareness of current recommendations regarding the types of immunizations, the numbers of doses recommended, the recommended ages of initiation, and the timing of continuation. Immunizations can and should be offered during any clinical encounter, including acute care visits when possible. Again, doing this may require a shift in fundamental practice patterns, which currently limit immunization efforts to health supervision settings.

Finally, although vaccination mandates are known to be

effective in increasing coverage, neither MCV4 vaccination nor HPV vaccination is mandated in North Carolina. As of this writing, only 12 states mandate receipt of MCV4 vaccine and a single dose of HPV vaccine, whereas 34 have mandates for receipt of Tdap vaccine [20]. This deficit is often compounded by misinformation, particularly about vaccine safety, in the media and among many peers and adults. The value of vaccinations is also often understated, given the general lack of experience with historically devastating illnesses that are now vaccine-preventable. Stigma, particularly related to the HPV vaccine, continues to confound immunization efforts. Finally, cultural and religious exemptions often pose a barrier to extending vaccination coverage. Effective messaging to educate and address the public regarding the benefits of preteen immunizations is needed.

Adolescent vaccination is a constantly evolving and immensely impactful realm of preventive care for young people. Collectively, the 3 vaccinations highlighted in this commentary constitute a tremendous advance in personal and public health. All preteens should receive should receive an annual influenza vaccine, the Tdap vaccine, MCV4, and the 3-dose HPV vaccine series. Female preteens may receive either HPV4 or HPV2 while male preteens should only receive HPV4. The fact that large numbers of adolescents have not received these vaccines is very troubling. Despite various barriers, ongoing efforts to increase vaccine coverage are promising and convey a sense that the future for preteens and adolescents in this regard is indeed bright. NCMJ

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Even healthy kids of any age can get seriously sick from the flu, and they can spread it to family, friends and others.

Everyone 6 months of age and older should get a flu vaccine every year.

Get your kids vaccinated—call their doctor, nurse or clinic.

Spread popcorn. Not flu.

For more information, visit: <http://www.flu.gov>



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