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The recognition that human papillomavirus (HPV) onco-
genic viruses cause cervical carcinoma remains one of the most game-changing medical discoveries of the last century. Improvements in screening options for detecting cervical cancer precursors followed. We now have the ability to detect high-risk HPV subtypes in routine specimens. Finally, a highly effective vaccine was developed that targets HPV types 16 and 18, which are responsible for causing approximately 70% of all cases of cervical carcinoma.

In one of the original vaccines HPV types 6 and 11, responsible for 90% of all genital warts, were also targeted. In 2014, a 9-valent vaccine incorporating an additional 5 HPV strains (31, 33, 45, 52, and 58) was approved and is set to replace all previous vaccine versions. Together, these 7 oncogenic HPV types are responsible for approximately 90% of HPV-related cancers, including cervical, anal, oropharyngeal, vaginal, and vulvar cancer.

By vaccinating boys and girls between ages 9 and 21 (for males) and 9 and 26 (for females), we could effectively eliminate 90% of genital warts and 90% of all HPV-related cancers. So why have we not capitalized on this extraordinary discovery? In 2016, why were only 40% of teenage girls and less than 25% of teenage boys vaccinated against HPV when we are immunizing 80% to 90% of these populations with tetanus, diphtheria, and acellular pertussis (Tdap) and meningococcal vaccines?

**Barriers to HPV vaccination**

When the first HPV vaccine was approved in 2006, cost was a significant factor. Many health insurance plans did not cover this “discretionary” vaccine, which was viewed as a prevention for sexually transmitted infections rather than as a valuable intervention for the prevention of cervical and other cancers. At well over $125 per dose with 3 doses required for a full series, ObGyns were reluctant to stock and provide these expensive vaccines without assurance of reimbursement. The logistics of recalling patients for their subsequent vaccine doses were challenging for offices that were not accustomed to seeing patients for preventive care activities more than once a year. In addition, the office infrastructure required to maintain the vaccine stock and manage the necessary paperwork could be daunting. Finally, the requirement that patients be observed for 15 to 30 minutes in the office after vaccine administration created efficiency and rooming problems in busy, active practices.

Over time, almost all payers covered the HPV vaccines, but the logistical issues in ObGyn practices remain. Pediatric practices, on the other hand, are ideally suited for vaccine administration. Unfortunately, our colleagues delivering preventive care to young teens have persisted in considering the HPV vaccine as an optional adjunct to routine vaccination despite the advice of the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC), which for many years has recommended the HPV vaccine for girls. In 2011, the ACIP extended the HPV vaccine recommendation to include boys beginning at ages 11 to 12.

**New 2-dose HPV vaccine schedule for children <15 years**

In October 2016, 10 years after the first HPV vaccine approval, the ACIP and

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the CDC approved a reduced, 2-dose schedule for those younger than 15. The first dose can be administered simultaneously with other recommended vaccines for 11- to 12-year-olds (the meningococcal and Tdap vaccines) and the second dose, 6 or 12 months later. The 12-month interval would allow administration, once again, of all required vaccines at the annual visit.

**Pivotal immunogenicity study**

The new recommendation is based on robust multinational data (52 sites in 15 countries, N = 1,518) from an open-label trial. Immunogenicity of 2 doses of the 9-valent HPV vaccine in girls and boys ages 9 to 14 was compared with that of a standard 3-dose regimen in adolescents and young women ages 16 to 26. Five cohorts were studied: boys 9 to 14 given 2 doses at 6-month intervals; girls 9 to 14 given 2 doses at 6-month intervals; boys and girls 9 to 14 given 2 doses at a 12-month interval; girls 9 to 14 given the standard 3-dose regimen; and girls and young women 16 to 26 receiving 3 doses over 6 months.

The authors assessed the antibody responses against each HPV subtype 1 month after the final vaccine dose. Data from 1,377 participants (90.7% of the original cohort) were analyzed. Prespecified antibody titers were set conservatively to ensure adequate immunogenicity. Noninferiority criteria had to be met for all 9 HPV types.

**Trial results.** The immune responses for the 9- to 14-year-olds were consistently higher than those for the 16- to 26-year-old age group regardless of the regimen—not a surprising finding since the initial trials for HPV vaccine demonstrated a greater response among younger vaccine recipients. In this trial, higher antibody responses were found for the 12-month dosing interval than for the 6-month interval, although both regimens produced an adequate response.

**Immunogenicity remained at 6 months.** Antibody levels were retested 6 months after the last dose of HPV vaccine in a post hoc analysis. In all groups the antibody titers declined; however, there was no difference between the 2- and 3-dose cohorts. All levels remained above a threshold required for immunogenicity.

**Simplified dosing may help increase vaccination rates**

What does this new dosing regimen mean for practice? It will be simpler to incorporate HPV vaccination routinely into the standard vaccine regimen for preadolescent boys and girls. In addition, counseling for HPV vaccine administration can be combined with counseling for the meningococcal vaccine and routine Tdap booster.

Notably, primary care physicians have reported perceiving HPV vaccine discussions with parents as burdensome, and they tend to discuss it last after conversations about Tdap and meningococcal vaccines. Brewer and colleagues documented a 5% increase in first HPV vaccine doses among patients in practices in which the providers were taught to “announce” the need for HPV vaccine along with other routine vaccines. There was no increase in HPV vaccine uptake among practices in which providers were taught to “discuss” HPV with parents and to address their concerns, or in control practices. Therefore, less conversation about HPV and the HPV vaccine, as distinct from any other recommended vaccines, is better.

With the new 2-dose regimen, it should be easier to convey that the HPV vaccine is another necessary, routine intervention for children’s health. We should be able to achieve 90% vaccination rates for HPV—similar to rates for Tdap.

**References**


