



New Vaccine Developments in 2010 and Beyond

The management of immunization programs in health systems and vaccine-preventable diseases in adults was the subject of one of four CE in the Mornings continuing education activities conducted in early December 2009 at the 44th ASHP Midyear Clinical Meeting and Exhibition in Las Vegas, Nevada. The topic was discussed by Michael D. Hogue, Pharm.D., FAPhA, Director, Experiential Programs, and Associate Professor of Pharmacy Practice, McWhorter School of Pharmacy, Samford University, Birmingham, Alabama.

Attendees submitted questions about unresolved issues and controversies as well as emerging research in adult immunization that were later addressed by the faculty in a live webinar conducted on February 16, 2010. Some of the highlights of the webinar pertaining to the pharmacist's role in improving influenza and pneumococcal vaccination rates were described in a previous newsletter available at www.ashpadvantage.com/cemornings. Highlights of the webinar pertaining to other vaccines are described in this newsletter.

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Human Papillomavirus Vaccine Developments

Two human papillomavirus (HPV) vaccine products are available: a quadrivalent HPV vaccine (Gardasil, Merck) introduced in 2006 and a bivalent HPV vaccine (Cervarix, GlaxoSmithKline) introduced in 2009.¹⁻³ Most (70%) cervical cancers are caused by HPV infection. Cervical HPV infection can result in histologic changes that may be precursors to cervical cancer, and these histologic changes are classified as cervical intraepithelial neoplasias (CIN) grades 1, 2, or 3, depending on the degree of abnormality.¹ The HPV strains most frequently associated with high-grade cervical lesions (CIN 2/3) and cervical cancers are HPV types 16 and 18.⁴ Both the quadrivalent and bivalent vaccine products protect against cervical cancer and high-grade cervical lesions in girls and women 9-26 years of age caused by these types of HPV. The quadrivalent vaccine also protects against genital warts (condyloma acuminata) caused by low-risk HPV types 6 and 11 in this patient population. Use of the quadrivalent product for protection against genital warts recently was extended to boys and men 9-26 years of age. The bivalent vaccine does not provide protection against genital warts in males or females. The vaccines are not interchangeable, so the same product must be used for each dose in the three-dose series required for vaccination.

At its October 2009 meeting, the Centers for Disease Control and Prevention Advisory Committee on

Immunization Practices (ACIP) reviewed comparative data for these two vaccine products in girls, women, boys, and men, including cost-effectiveness data, and made the recommendations in Table 1.⁵ The bivalent and quadrivalent HPV vaccine are considered comparable for prevention of cervical cancer. For prevention of genital warts, only the quadrivalent HPV vaccine should be used. The recommendation pertaining to use of the quadrivalent vaccine in boys and men is for permissive use (i.e., use is based on patient preference, not routinely recommended in the ACIP adult or pediatric immunization schedules).

Table 1. ACIP Recommendations for HPV Vaccine Use⁵

- Quadrivalent HPV vaccine (Gardasil) is recommended for all girls and women 9-26 years of age for prevention of cervical cancer, high-grade cervical lesions, and genital warts
- Quadrivalent HPV vaccine can be used for prevention of genital warts in boys and young men 9-26 years of age (permissive use)
- Bivalent HPV vaccine (Cervarix) is recommended for all girls and women 9-26 years of age for prevention of cervical cancer and high-grade cervical lesions

HPV = human papillomavirus

Most (three of four) new genital HPV infections occur in the age group 15 to 24 years of age, but vaccination may be beneficial for older women because of the possibility that they have not yet been exposed to all of the many viral strains associated with cervical cancer.⁶ Currently no efficacy or safety data are available to support the use of the HPV vaccine in persons more than 26 years of age. Third party payers are not likely to cover vaccine administration in this age group without such data. Studies of the vaccine in women in this age group are underway.

New 2010 Immunization Schedules

Updated immunization schedules for infants, children, adolescents, and adults were released by ACIP in January 2010.⁷⁻⁹ The new schedules are very similar to the 2009 schedules. The primary changes are to the footnotes, which have been revised to clarify when and under what circumstances vaccines should be administered. In the new adult immunization schedule, which applies to persons 19 years of age or older, the footnote pertaining to the HPV vaccine has been revised to reflect the ACIP recommendation for vaccination of females 19-26 years of age (girls 9-18 years of age are excluded from this document only because they are not classified as adults) with either the bivalent or quadrivalent HPV vaccine, and permissive use of the quadrivalent HPV vaccine in males.⁷

Measles, Mumps, and Rubella in Health Care Workers

Health care workers have a greater risk of acquiring measles compared with other adults their own age largely because of their higher likelihood of exposure to the virus.¹⁰ Most patients who contract measles seek medical attention at a health care facility, thereby exposing health care workers to the virus. Nosocomial transmission of measles and mumps in health care facilities has been documented, and the incidence of nosocomial transmission may be increasing.¹¹

Table 2 lists criteria for presumptive evidence of immunity to measles, mumps, and rubella in health care workers. Adults born before 1957 generally are considered immune to measles and mumps, although acceptance of birth before 1957 as evidence of immunity may vary depending on current state and local requirements.^{7,12} The year 1957 is used as a cutoff date for evidence of immunity because persons born prior to that year are presumed to be immune to measles due to natural exposure to the virus.

Table 2. Criteria for Presumptive Evidence of Immunity to Measles, Mumps, and Rubella in Health Care Workers¹²

- Documentation of administration of appropriate vaccination against measles, mumps, and rubella (i.e., administration of the first of two doses of live measles vaccine on or after the first birthday and the second dose at least 28 days later; one dose of live mumps vaccine; and one dose of live rubella vaccine)
- Laboratory evidence of immunity
- Documentation of physician-diagnosed disease for measles and mumps (does not apply to rubella)
- Birth before 1957^a

^aAcceptance of this criterion as evidence of immunity may vary depending on current state and local requirements.

The updated immunization schedule for adults released by ACIP in early 2010 calls for administration of two doses of measles, mumps, and rubella (MMR) vaccine to health care workers born during or after 1957 who do not meet the criteria in Table 2 unless they have a medical contraindication.⁷ One or two MMR vaccine doses should be considered for unvaccinated healthcare personnel born before 1957 who lack laboratory evidence of measles, mumps, and/or rubella immunity or laboratory confirmation of disease (two doses if evidence is lacking for measles or mumps, and one dose if evidence is lacking for rubella), especially during outbreaks of these illnesses.⁷ The minimum interval between two doses of the vaccine is 4 weeks.

The MMR vaccine should be reconstituted with the diluent supplied by the manufacturer because the diluent is free of preservatives and other antiviral substances that might inactivate the vaccine.¹³ The manufacturer of the MMR vaccine should be contacted for a replacement if this diluent is misplaced or contaminated.

It is safe to administer the MMR vaccine to persons with a newborn infant in the household despite the fact that the product contains live, attenuated virus because there is no evidence of transmission of vaccine virus after decades of vaccine use. Similarly, the presence of an immunocompromised person in the household should not deter other members of the household from receiving the MMR vaccine.¹⁴

Herpes Zoster

Increases in the number of senior citizens in the United States and the prevalence of diseases and conditions that disproportionately affect this age group are anticipated in the near future because of the aging of the “baby boom” generation. Herpes zoster (i.e., shingles) characterized by skin eruptions and sometimes ophthalmic involvement and other serious systemic effects is one of these conditions.¹⁵ Herpes zoster sometimes is followed by debilitating postherpetic neuralgia lasting for months or even years, with a substantial adverse economic impact. Herpes zoster is caused by reactivation of the varicella zoster virus associated with chickenpox, and it usually affects older adults. Each year approximately 1 million new cases of herpes zoster occur in the United States. The lifetime risk of herpes zoster is one in three in the general population.¹⁵

In 2006, a vaccine to prevent herpes zoster was introduced for use in persons 60 years of age or older.¹⁶ The zoster vaccine is administered as a single subcutaneous injection using the supplied diluent without a need for serologic testing. The zoster vaccine should not be given to patients with primary or acquired immunodeficiencies, including leukemia, lymphoma, or other malignant neoplasms affecting the bone marrow or lymphatic system; persons with the acquired immunodeficiency syndrome or other clinical manifestations of human immunodeficiency virus infection (e.g., CD4+ T-lymphocyte value ≤ 200 per mm^3); or persons receiving recombinant human immune mediators (e.g., adalimumab, infliximab, etanercept).¹⁵ Additional contraindications to use of the vaccine are listed in the manufacturer’s product labeling.

In the Shingles Prevention Study of more than 38,000 persons 60 years of age or older, the zoster vaccine reduced the incidence of herpes zoster by 51% and the incidence of postherpetic neuralgia by 67%, without causing serious adverse events.¹⁷ The vaccine also reduced the burden of illness due to herpes zoster, a measure that reflects the incidence, severity, and duration of pain and discomfort, by 61%. The vaccine is considered cost-effective because of these findings, the morbidity associated with herpes zoster, and the relatively low cost of the vaccine (\$195-\$250).^{18,19} Assuming a vaccine product cost of \$500, the cost of immunization is roughly \$2000 per quality-adjusted life-year gained, which is well below the customary \$50,000 cutoff value above which interventions are judged not cost-effective.¹⁹

“ The herpes zoster vaccine is cost-effective for older Americans because of the often prolonged suffering from postherpetic neuralgia and the adverse impact on quality of life in this patient population. ”

—Michael D. Hogue, Pharm.D., FAPhA

Research Pipeline

Vaccines are in development to prevent a wide variety of diseases. Table 3 lists vaccine products in development for various infectious diseases.

Promising results have been obtained from studies of a vaccine to protect against infection with *Helicobacter pylori*, a bacterium associated with peptic ulcer disease and gastric cancer.²⁰ The potential economic benefit from such a vaccine, which could become available within the next 5 years, is substantial.²¹

Table 3. Infectious Diseases Targeted by Vaccine Products in Development

- *Helicobacter pylori*
- Malaria
- Hepatitis C
- Human immunodeficiency virus
- Ebolavirus
- Marburg virus
- West Nile virus
- Dengue fever

Preventing malaria is a worldwide priority because of the mortality associated with the disease.²² Although malaria is a larger problem in places such as sub-Saharan Africa than in the United States, many Americans travel frequently to areas where malaria is endemic and are susceptible to the illness. American scientists are involved in research to develop a malaria vaccine.²³

Effective vaccines to protect against hepatitis A and B are available. However, progress in developing a vaccine to protect against hepatitis C remains elusive.²⁴

Developing a vaccine to protect against human immunodeficiency virus is a priority in the United States, but the results of clinical research have been disappointing because of problems in phase II trials.²⁵ Such a vaccine probably is at least 8-10 years away from approval by the Food and Drug Administration.

Web-based CE Activity and More Information

If you missed the CE activity "Preventable Diseases 2010: Implementing Health-System Strategies for Adult Immunization" at the 2009 ASHP Midyear Clinical Meeting and Exhibition and want to learn more about this topic, a web-based activity based on Dr. Hogue's presentation is available until February 28, 2011. One hour (0.1 CEUs) of continuing pharmacy education credit is offered for this activity. To access this activity and obtain more information on this topic and other learning activities in the CE in the Mornings 2010 Educational Initiative, go to www.ashpadvantage.com/cemornings.

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References

1. Markowitz LE, Dunne EF, Saraiya M et al. Quadrivalent human papillomavirus vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2007; 56(RR-2):1-24. <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5602a1.htm>.
2. Gardasil package insert. Whitehouse Station, NJ: Merck & Co., Inc.; October 2009.
3. Cervarix package insert. Research Triangle Park, NC: GlaxoSmithKline; October 2009.
4. Munoz N, Bosch FX, de Sanjose S et al. Epidemiologic classification of human papillomavirus types associated with cervical cancer. *N Engl J Med.* 2003; 348:518-27.
5. Advisory Committee on Immunization Practices. Summary report. October 21-22, 2009. <http://www.cdc.gov/vaccines/recs/acip/downloads/min-oct09.pdf>.
6. Weinstock H, Berman S, Cates W Jr. Sexually transmitted diseases among American youth: incidence and prevalence estimates, 2000. *Perspect Sex Reprod Health.* 2004; 36:6-10.
7. Advisory Committee on Immunization Practices. Recommended adult immunization schedule: United States, 2010. *Ann Intern Med.* 2010; 152:36-9.
8. Advisory Committee on Immunization Practices. Recommended immunization schedule for persons aged 0 through 6 years—United States. 2010. <http://pediatrics.aappublications.org/cgi/data/125/1/195/DC1/1> (2010 Feb 16).
9. Advisory Committee on Immunization Practices. Recommended immunization schedule for persons aged 7 through 18 years—United States. 2010. <http://pediatrics.aappublications.org/cgi/data/125/1/195/DC1/2> (2010 Feb 16).
10. Steingart KR, Thomas AR, Dykewicz CA et al. Transmission of measles virus in healthcare settings during a communitywide outbreak. *Infect Control Hosp Epidemiol.* 1999; 20: 115-19.
11. Centers for Disease Control and Prevention Advisory Committee on Immunization Practices (ACIP). Summary report. Atlanta, GA: June 24-26, 2009. <http://www.cdc.gov/vaccines/recs/acip/downloads/min-jun09.pdf>.
12. Watson JC, Hadler SC, Dykewicz CA et al. Measles, mumps, and rubella—vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 1998; 47(RR-8):1-57.
13. M-M-R II package insert. Whitehouse Station, NJ: Merck & Co., Inc.; September 2009.

14. Advisory Committee on Immunization Practices. MMR vaccine questions and answers. <http://www.cdc.gov/vaccines/vpd-vac/combo-vaccines/mmr/faqs-mmr-hcp.htm> (2010 Feb 16).
15. Harpaz R, Ortega-Sanchez IR, Seward JF. Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2008; 57(RR-5):1-30. <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5705a1.htm>.
16. Zostavax package insert. Whitehouse Station, NJ: Merck & Co., Inc.; December 2009.
17. Oxman MN, Levin MJ, Johnson GR et al. A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. *N Engl J Med*. 2005; 352:2271-84.
18. Coplan PM, Schmader K, Nikas A et al. Development of a measure of the burden of pain due to herpes zoster and postherpetic neuralgia for prevention trials: adaptation of the brief pain inventory. *J Pain*. 2004; 5:344-56.
19. Gilden DH. Varicella-zoster virus vaccine—grown-ups need it, too. *N Engl J Med*. 2005; 352:2344-6.
20. Malfertheiner P, Schultze V, Rosenkranz B et al. Safety and immunogenicity of an intramuscular *Helicobacter pylori* vaccine in noninfected volunteers: a phase I study. *Gastroenterology*. 2008; 135:787-95.
21. Rupnow MF, Chang AH, Schachter RD et al. Cost-effectiveness of a potential prophylactic *Helicobacter pylori* vaccine in the United States. *J Infect Dis*. 2009; 200:1311-7.
22. Centers for Disease Control and Prevention. Malaria worldwide. http://www.cdc.gov/malaria/malaria_worldwide/index.html (2010 Feb 16).
23. National Institute of Allergy and Infectious Diseases. Laboratory of Malaria Immunology and Vaccinology. <http://www3.niaid.nih.gov/labs/aboutlabs/lmiv/> (2010 Feb 16).
24. Anon. HCV vaccine development. http://www.hivandhepatitis.com/hep_c/news/2009/041409_a.html (2010 Feb 16).
25. Buchbinder SP, Mehrotra DV, Duerr A et al. Efficacy assessment of a cell-mediated immunity HIV-1 vaccine (the Step Study): a double-blind, randomised, placebo-controlled, test-of-concept trial. *Lancet*. 2008; 372:1881-93.