

Adverse Effects of Adolescent Immunizations

Natalia Vernon, MD

Pooja Jhaveri, MD

From the Department
of Allergy and Immunology
at the Penn State
Milton S. Hershey
Medical Center.

Financial Disclosures:
None Reported.

Address correspondence to
Natalia Vernon, MD,
Penn State Milton S. Hershey
Medical Center, Department
of Allergy and Immunology,
500 University Dr,
Hershey, PA 17033-2360.

E-mail:
nvernon@hmc.psu.edu



Optimal protection against preventable diseases for adolescents can be provided through routine vaccination. Vaccinations recommended by the Advisory Committee on Immunization Practices of the Centers of Disease Control and Prevention can reduce morbidity and mortality associated with influenza, meningococcal, human papillomavirus, tetanus, diphtheria, and pertussis infections. Most reported adverse reactions to these vaccinations are mild, and the benefits of immunization often outweigh the potential risks. In the present article, the authors discuss adverse events, contraindications, and precautions associated with adolescent immunizations.

J Am Osteopath Assoc. 2014;114(3 suppl 1):S13-S17

doi:10.7556/jaoa.2014.044

This supplement is supported by an independent educational grant from **Merck & Co, Inc.**

Adolescent vaccinations recommended by the American Academy of Pediatrics and the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC) aim to reduce morbidity and mortality from preventable diseases. Current recommendations for the adolescent population (aged 11-18 years) include the tetanus, diphtheria, and acellular pertussis (Tdap) vaccine; meningococcal conjugate vaccine; human papillomavirus (HPV) vaccine; and influenza vaccine.¹ Adverse events have been reported with the administration of these vaccines, but serious, life-threatening reactions are rare.² In the present article, we review the adverse events, contraindications, and precautions associated with administration of the Tdap, meningococcal conjugate, HPV, and influenza vaccines.

Tetanus, Diphtheria, and Acellular Pertussis Vaccine

The Tdap vaccine immunizes against the pathogenic microorganisms of tetanus, diphtheria, and pertussis. There are currently 2 types of Tdap vaccines available in the United States: Adacel (Sanofi Pasteur) and Boostrix (Glaxo-SmithKline).^{3,4} According to the most recent ACIP guidelines, a single Tdap dose should be administered for all adolescents aged 11 to 18 years who have completed the recommended childhood vaccination series.⁵

According to a search we conducted in the Vaccine Adverse Event Reporting System (VAERS; <http://vaers.hhs.gov/data/data>), 16,582 adverse events related to the Tdap vaccine occurred from January 2000 to January 2013, with 6779 adverse events in children aged 6 to 17 years. According to our VAERS search results, less than 1% of these reported adverse events were considered life-threatening reactions. For adolescents aged 11 to 17 years, the most common injection site reactions within 14 days of administration were pain, swelling, and erythema.^{3,4} The most common systemic reactions within 14 days of administration were headache, body ache, and muscle weakness.^{3,4}

A severe allergic reaction (eg, anaphylaxis) after a previous dose of Tdap or any other diphtheria toxoid, tetanus toxoid, and pertussis antigen-containing vaccine is a contraindication to vaccination.^{3,4} If these individuals require further immunization, they should be referred to an allergist for evaluation. Another contraindication is a history of encephalopathy (eg, coma, decreased level of consciousness, prolonged seizures) within 7 days of administration of a previous pertussis antigen-containing vaccine.^{3,4} If Guillain-Barré syndrome (GBS) occurred within 6 weeks of receipt of a previous tetanus toxoid vaccine, the risk of reoccurrence of GBS is high, and the physician must consider the risks and benefits of administering the Tdap vaccine. Also, it is important to remember that the tip caps of the prefilled syringes of Tdap may contain natural rubber latex, which may cause allergic reactions in individuals who are sensitive to latex.^{3,4}

hhs.gov/data/data), 16,582 adverse events related to the Tdap vaccine occurred from January 2000 to January 2013, with 6779 adverse events in children aged 6 to 17 years. According to our VAERS search results, less than 1% of these reported adverse events were considered life-threatening reactions. For adolescents aged 11 to 17 years, the most common injection site reactions within 14 days of administration were pain, swelling, and erythema.^{3,4} The most common systemic reactions within 14 days of administration were headache, body ache, and muscle weakness.^{3,4}

Meningococcal Conjugate Vaccine

The meningococcal conjugate vaccine is indicated for active immunization to prevent invasive meningococcal disease caused by *Neisseria meningitidis* serogroups. In the United States, there are 2 types of meningococcal vaccines available: meningococcal polysaccharide vaccine [Menomune (Sanofi Pasteur)] and meningococcal conjugate vaccine [Menactra (Sanofi Pasteur) and Menveo (Novartis)].⁶⁻⁸ According to the most recent guidelines of the ACIP,⁹ adolescents should receive a single dose of the meningococcal conjugate vaccine (MCV4) at age 11 to 12 years, with a booster dose at age 16 years.

According to a VAERS search we conducted, from January 2000 to January 2013, a total of 9581 adverse events were related to a meningococcal conjugate vaccination, with 7405 adverse events in children aged 6 to 17 years. Only 1% of these reported adverse events were considered life-threatening reactions. The most commonly reported local and systemic adverse reactions in adolescents, aged 11 to 18 years, were injection site pain, headache, and fatigue.⁷ The tip caps of prefilled syringes of the vaccine may contain latex, which can lead to allergic reactions in individuals who are sensitive to latex. A severe allergic reaction (eg, anaphylaxis) after a previous dose of a meningococcal capsular polysaccharide or diphtheria toxoid-containing vaccine is a contraindication to vaccination.⁷ If these indi-

viduals require further immunization, they should be referred to an allergist for evaluation. Persons with previously diagnosed GBS may have an increased risk of GBS after receiving the meningococcal vaccine.⁷ In these circumstances, the physician must consider the potential risks and benefits of administering the meningococcal vaccine.

Human Papillomavirus Vaccine

The HPV vaccine immunizes against several genotypes of HPV associated with cervical and anal cancers, genital warts, and precancerous or dysplastic lesions of the cervix, vulva, vagina, and anus. There are 2 HPV vaccines available in the United States—Gardasil (Merck & Co, Inc) and Cervarix (Glaxo-SmithKline).^{10,11} Gardasil, a quadrivalent vaccine, vaccinates against HPV types 6, 11, 16, and 18, and Cervarix, a bivalent vaccine, against types 16 and 18. The ACIP recommends routine vaccination via a 3-dose series of the HPV vaccine to adolescents aged 11 to 12 years. However, the vaccine series can be started beginning at age 9 years. Females may receive either HPV4 or HPV2, but only HPV4 should be used for males.^{12,13}

According to our search results on VAERS, a total of 16,608 adverse events were reported related to quadrivalent HPV vaccine use from January 2000 to January 2013, with 9652 events in children and adolescents aged 6 to 17 years. Only 1.2% of the reported adverse events were considered life

threatening. Related to the bivalent HPV vaccine, VAERS included 75 events, with 54 events in children and adolescents aged 6 to 17 years.

With quadrivalent HPV vaccine administration, the most common adverse reaction is headache. Patients may also experience fever, nausea, dizziness, and injection-site pain and swelling.¹⁰ Syncope, sometimes associated with tonic-clonic movements, has been reported after quadrivalent HPV vaccination. For this reason, observation for 15 minutes after vaccination is recommended.¹⁰ A severe allergic reaction (eg, anaphylaxis) after a previous dose of the quadrivalent HPV vaccine or to yeast (a vaccine component) is a contraindication to vaccination.¹⁰ If these persons require further immunization, they should be referred to an allergist for evaluation.

With bivalent HPV vaccine administration, the most common local adverse reactions were pain, redness, and swelling at the injection site. The most common general adverse events were fatigue, headache, myalgia, gastrointestinal symptoms, and arthralgia.¹¹ Because syncope may occur, observation for 15 minutes after administration is recommended. The bivalent HPV vaccine is available in 2 types of prefilled syringes, 1 of which has a tip cap that may contain natural rubber latex and may cause an allergic reaction in individuals who are sensitive to latex. A severe allergic reaction (eg, anaphylaxis) after a previous dose of the bivalent HPV vaccine is a contraindication to vaccination.¹¹

Influenza Vaccine

The influenza vaccine is indicated for active immunization against influenza type A and influenza type B viruses that trigger acute respiratory disease. There are 3 main forms of the influenza vaccine: the trivalent inactivated vaccine, the quadrivalent inactivated vaccine, and the live attenuated influenza vaccine. Influenza vaccines available for use in the United States include Afluria (CSL Limited), Agriflu (Novartis), FluLaval (ID Biomedical Corporation of Quebec), Fluarix (GlaxoSmithKline), Flublok (Protein Sciences Corporation), Flucelvax (Novartis), Fluvirin (Novartis), Fluzone (Sanofi Pasteur), and FluMist (MedImmune, LLC). ACIP guidelines recommend routine annual influenza vaccination of all persons aged 6 months or older.¹⁴ Children with chronic underlying medical conditions including diabetes mellitus, asthma (does not have to be uncontrolled) or other chronic disorders of the pulmonary or cardiovascular systems, renal dysfunction, or hemoglobinopathies should not be vaccinated with the live attenuated influenza vaccine.¹⁵ Also, any adolescent female who is pregnant should not receive the live attenuated influenza vaccine.¹⁵ Adolescents through age 17 years who are receiving aspirin or other salicylates should not receive the live attenuated influenza vaccine because of the potential for Reye syndrome.¹⁶ In the United States, the live attenuated vaccine is only available in the intranasal form.

In children aged 6 to 17 years, the most common systemic adverse events after influenza vaccination were fatigue, muscle ache, headache, arthralgia,

and gastrointestinal symptoms. According to our VAERS search results, from January 2000 to January 2013, a total of 63,882 adverse events related to the influenza vaccine were reported to the VAERS, with 8050 events in children aged 6 to 17 years. Less than 1% of the reported events were considered life-threatening. In 1976, the swine influenza vaccine was associated with an increased frequency of GBS, but the risk was lower among persons younger than 25 years. Subsequent studies have not demonstrated an increase in GBS of the same magnitude.¹⁷ However, individuals who developed GBS within 6 weeks of receiving a prior influenza vaccination may have an increased risk of GBS after subsequent vaccination with the influenza vaccine. In those circumstances, the physician must consider the potential risks and benefits of administering the influenza vaccine. Certain multi-dose vial preparations of the inactivated influenza vaccine contain thimerosal, a mercury-containing antibacterial compound used to reduce the likelihood of bacterial growth. Evidence to date shows no increased risks from exposures to thimerosal-containing vaccines.¹⁵ The tip caps of prefilled syringes of the influenza vaccine may contain natural rubber latex, which can lead to allergic reactions in individuals who are sensitive to latex.¹⁸

Patients with egg allergy should receive influenza vaccinations because the benefits outweigh the risks of vaccinating in this population. Persons with a history of suspected egg allergy should be evaluated by an allergist to further clarify the egg allergy, but such an evaluation should not delay the administration of

Table.
Recommendations for Influenza Vaccination for Persons With Reported Food Allergy to Eggs

Reaction	Recommendation
Person eats cooked eggs (eg, scrambled, fried, boiled) but has no adverse reactions	Person may receive the influenza vaccine (inactivated or live attenuated, depending on other comorbidities)
Person has only hives after egg ingestion	Person may receive the inactivated influenza vaccine in a primary care office and should be observed for a minimum of 30 minutes after vaccination
Person has symptoms suggestive of anaphylaxis after egg ingestion	Person may receive the inactivated influenza vaccine in an allergist's office and observed for a minimum of 30 minutes after vaccination

the influenza vaccination. Patients with egg allergy should receive influenza vaccines in a setting where clinicians are experienced in recognizing and treating anaphylaxis and should be observed for 30 minutes after vaccination. Patients with egg allergy and with a history of only hives after egg ingestion can receive the influenza vaccine in a primary care provider's office, provided the appropriate observation and equipment are available. Those with a history of a more severe reaction (eg, anaphylaxis) after egg ingestion should receive their vaccine in an allergist's office (*Table*). All influenza vaccines available in the United States contain low amounts of ovalbumin, including the intranasally administered form. The injectable vaccination is the preferred form of influenza vaccination for patients with egg allergy. For patients with a history of an allergic reaction to the influenza vaccine itself, referral to an allergist for further evaluation, including skin testing with the vaccine and vaccine ingredients, is appropriate.¹⁹

Guillain-Barré Syndrome: Potential Adverse Effect

Guillain-Barré syndrome is a rare autoimmune disorder characterized by inflammatory demyelination of the peripheral nerves. Severe complications include paralysis and death. The condition can be triggered by infection or vaccination.²⁰ Given the potential severity of GBS, it is often viewed as a contraindication to vaccination by physicians. Although cases of GBS have been reported after various vaccinations (hepatitis B; measles, mumps, rubella; meningococcal polysaccharide; tetanus; polio; influenza), a clear association has only been established with the 1976 H1N1 inactivated influenza vaccine.²⁰ For all other vaccines, available data are limited to case reports or small patient clusters, which prevent conclusions about causality.²¹ Numerous studies have shown no evidence of an increased risk of GBS after vaccinations.^{15,20,22} Immunizing individuals with a prior history of GBS requires caution; the benefit of vaccination in preventing disease and re-

ducing morbidity and mortality must be weighed against the potential risk of GBS on an individual patient basis.²¹

Conclusion

Routine immunization of adolescents provides substantial protection from preventable diseases. Individuals who have had adverse reactions to vaccinations might unnecessarily be advised to avoid subsequent immunization. Most reported adverse reactions are mild and do not constitute absolute contraindications to vaccination. Patients who have experienced an apparent allergic or anaphylactic reaction after receiving a vaccination should be referred to an allergist for further evaluation.

References

- Recommended immunizations for children from 7 through 18 years old. Centers for Disease Control and Prevention website. <http://www.cdc.gov/vaccines/who/teens/downloads/parent-version-schedule-7-18yrs.pdf>. Accessed November 1, 2013.
- National Center for Immunization and Respiratory Diseases. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP) [published correction appears in *MMWR Recomm Rep*. 2011;60:993]. *MMWR Recomm Rep*. 2011;60(RR-2):1-64.
- Adacel [package insert]. Swiftwater, PA: Sanofi Pasteur; April 2013. <http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142764.pdf>. Accessed November 1, 2013.
- Boostrix [package insert]. Research Triangle Park, NC: GlaxoSmithKline. <http://www.fda.gov/downloads/BiologicsBloodVaccines/UCM152842.pdf>. Accessed November 1, 2013.
- Centers for Disease Control and Prevention. Updated recommendations for the use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine from the Advisory Committee on Immunization Practices, 2010. *MMWR Morb Mortal Wkly Rep*. 2011;60(1):13-15.
- Menomune [package insert]. Swiftwater, PA: Sanofi Pasteur; October 2012. <http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM308370.pdf>. Accessed November 1, 2013.
- Menactra [package insert]. Swiftwater, PA: Sanofi Pasteur; April 2013. <http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM131170.pdf>. Accessed November 1, 2013.
- Menveo [package insert]. Cambridge, MA: Novartis; August 2013. <http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM201349.pdf>. Accessed November 1, 2013.
- Cohn AC, MacNeil JR, Clark TA, et al; Centers for Disease Control and Prevention. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2013;62(RR-2):1-28.
- Gardasil [package insert]. Whitehouse Station, NJ: Merck & Co, Inc; 2010. <http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM111263.pdf>. Accessed November 1, 2013.
- Cervarix [package insert]. Research Triangle Park: GlaxoSmithKline; 2012. <http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM186981.pdf>. Accessed November 1, 2013.
- Markowitz LE, Dunne EF, Saraiya M, Lawson HW, Chesson H, Unger ER; Centers for Disease Control and Prevention. Quadrivalent human papillomavirus vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2007;56(RR-2):1-24.
- Centers for Disease Control and Prevention. Recommendations on the use of quadrivalent human papillomavirus vaccine in males—Advisory Committee on Immunization Practices (ACIP), 2011. *MMWR Morb Mortal Wkly Rep*. 2011;60(50):1705-1708.
- Centers for Disease Control and Prevention. Advisory Committee on Immunization Practices (ACIP) recommended immunization schedules for persons ages 0 through 18 years and adults aged 19 years and older—United States, 2013 [published correction appears in *MMWR Surveill Summ*. 2013;62(13):256]. *MMWR Surveill Summ*. 2013;62(suppl 1):1-19.
- Committee on Infectious Diseases, American Academy of Pediatrics. Recommendations for prevention and control of influenza in children, 2012-2013 [published online September 10, 2012]. *Pediatrics*. 2012; 130(4):780-792. doi:10.1542/peds.2012-2308.
- Flumist [package insert]. Gaithersburg, MD: MedImmune; 2012. <http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM123743.pdf>. Accessed December 13, 2013.
- Centers for Disease Control and Prevention. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices—United States, 2013-2014 [published correction appears in *MMWR Recomm Rep*. 2013;62(45):906]. *MMWR Recomm Rep*. 2013;62(RR-7):1-43.
- Fluarix Quadrivalent [package insert]. Research Triangle Park, NC: GlaxoSmithKline; 2013. <http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM220624.pdf>. Accessed November 5, 2013.
- Kelso JM, Greenhawt MJ, Li JT, et al. Adverse reactions to vaccines practice parameter 2012 update [published online May 16, 2012]. *J Allergy Clin Immunol*. 2012;130(1):25-43. doi:10.1016/j.jaci.2012.04.003.
- Baxter R, Bakshi N, Fireman B, et al. Lack of association of Guillain-Barré syndrome with vaccinations [published online April 11, 2013]. *Clin Infect Dis*. 2013;57(2):197-204. doi:10.1093/cid/cit222.
- Haber P, Sejvar J, Mikaeloff Y, DeStefano F. Vaccines and Guillain-Barré syndrome [review]. *Drug Saf*. 2009;32(4):309-323. doi:10.2165/00002018-200932040-00005.
- Souayah N, Nasar A, Suri MF, Qureshi AI. Guillain-Barré syndrome after vaccination in the United States: data from the Centers for Disease Control and Prevention/Food and Drug Administration Vaccine Adverse Event Reporting System (1990-2005). *J Clin Neuromuscul Dis*. 2009;11(1):1-6. doi:10.1097/CND.0b013e3181aaa968.

© 2014 American Osteopathic Association