

**CLINICAL REVIEW**

# Update on Adult Immunizations

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**The past few years have seen numerous additions and modifications to the current immunization schedules. Starting with the 2010 to 2011 influenza season, the Centers for Disease Control and Prevention have recommended universal annual influenza vaccination for all persons without a contraindication who are 6 months of age and older, including healthy persons aged 19 to 49 years. Hepatitis B vaccination is now recommended for all susceptible diabetics  $\leq 60$  years of age. One dose of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine, adsorbed, is recommended to replace one tetanus and diphtheria toxoids adsorbed (adult) vaccination for all adults, including those 65 years of age or older, who are anticipating contact with infants and unvaccinated pregnant women (preferably during the second or third trimester). All adult vaccines remain underused. This article will summarize the most recent changes in the adult immunization recommendations of the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention. (J Am Board Fam Med 2012;25:496–510.)**

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Rates of vaccination of adults have consistently fallen behind vaccination rates for children and adolescents. The Centers for Disease Control and Prevention (CDC) analyzed data from the 2010 National Health Interview Survey to assess adult vaccination rates and found them to be low for most routinely recommended vaccines. Rates of the 3 vaccines included in Healthy People (HP) 2020—pneumococcal, herpes zoster, and hepatitis B (for health care personnel [HCP])—were well below the respective target levels: for pneumococcal vaccine, rates in 2010 were 59.7% for persons aged  $>65$  years (HP2020 target of 90%) and 18.5% for per-

sons at high risk aged 18 to 64 years (HP2020 target, 60%); for herpes zoster vaccine, rates were 14.4% for persons aged  $\geq 60$  years (HP2020 target, 30%); and for the hepatitis vaccine for HCP, the rates were 63.2% (HP2020 target, 90%). For adults for whom tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine, adsorbed (Tdap) status could be assessed, coverage was only 8.2%; for HCP Tdap coverage was 20.3%.<sup>1</sup>

The CDC estimated that 40,000 to 50,000 vaccine-preventable deaths occur every year in the United States and estimates the health care burden of vaccine-preventable diseases at \$10 billion.<sup>2</sup> Family physicians are specialists in preventive care and can be leaders in seeing that adult patients get the full benefit of protection against vaccine-preventable diseases. This article summarizes the most significant recent changes in the US adult immunization schedule.

## Influenza Vaccine

### Universal Influenza Immunization

Since the 2010 to 2011 flu season, the CDC has recommended that all persons should be immunized annually against influenza, starting from the age of 6 months, which is the youngest age for which any influenza vaccine is approved. The 2011

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to 2012 US seasonal influenza vaccine virus strains are identical to those contained in the 2010 to 2011 vaccine and includes the 2009 pandemic influenza A (H1N1) vaccine virus strain.<sup>3</sup>

### Available Influenza Vaccines

There are 2 types of influenza vaccine available for administration to adults: the trivalent inactivated influenza vaccine (TIV) and the live attenuated influenza vaccine (LAIV). LAIV is administered intranasally and contains the same influenza viruses as TIV. The live viruses in LAIV are temperature sensitive and do not replicate effectively at the human core body temperature; thus, they cannot produce disease. However, the LAIV viruses are adapted to cold, which enables them to replicate in the slightly cooler temperature of the nasopharyngeal mucosa and produce immunity. A recent meta-analysis comparing TIV with LAIV concluded that LAIV seems to be slightly more effective than TIV in children.<sup>4</sup> Studies comparing TIV with LAIV in adults have shown conflicting results.<sup>5,6</sup> The CDC has stated that both TIV and LAIV have been demonstrated to be effective in children and adults and that there is insufficient data directly comparing the effectiveness of these 2 types of influenza vaccines to identify whether one vaccine might offer a clear advantage over the other in a particular population.<sup>3</sup> LAIV is not approved for adults  $\geq 50$  years of age and may not be given to pregnant women or persons who are immunocompromised, which includes those with chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, neurological/neuromuscular, hematologic, or metabolic (including diabetes) disorders or with immunosuppression (including that caused by medications or HIV).

A new influenza vaccine, trivalent influenza vaccine intradermal (TIVI) (Fluzone Intradermal, Sanofi Pasteur, Swiftwater, PA), was licensed in May 2011. This vaccine is indicated for persons aged 18 through 64 years and is administered intradermally via a single-dose, prefilled microinjection syringe. TIVI contains 9  $\mu\text{g}$  of each flu strain in 0.1 mL total volume versus intramuscular TIV preparations, which contain 15  $\mu\text{g}$  of each strain in 0.5 mL total volume. The preferred site for administration is over the deltoid muscle. The most common adverse reactions are local: erythema, induration, swelling, pain, and pruritus. With the exception of pain, these reactions occurred more frequently than with the intramuscular vaccine

but generally resolved within 3 to 7 days.<sup>7</sup> The CDC has not indicated a preference for this vaccine over other influenza vaccines.<sup>3</sup>

Trivalent influenza vaccine high dose (TIVHD; Fluzone High-Dose, Sanofi Pasteur), available since the 2010 to 2011 influenza season, contains 60  $\mu\text{g}$  of hemagglutinin per vaccine strain (rather than 15  $\mu\text{g}$  per strain as in other TIV preparations). TIVHD is available as an alternative TIV for persons aged  $\geq 65$  years. The rationale for the higher antigen dose is to stimulate a better antibody response in the elderly, who have a weaker response to influenza vaccines because of immunosenescence. The CDC has indicated no preferential recommendation for this vaccine over other influenza vaccines indicated for use in the elderly.<sup>3</sup>

A web page listing influenza vaccines available in the United States for the current influenza season and their age indications is available at <http://www.immunize.org/catg.d/p4072.pdf> (Acquired from Immunization Action Coalition on April 22, 2012); the link is updated continuously to match current recommendations and availability.

### Pneumococcal Polysaccharide Vaccine

Pneumococcal disease causes significant illness and death worldwide. The most serious manifestations of illness are pneumonia, pneumococcal sepsis and meningitis. In 2005 the World Health Organization estimated that 1.6 million persons died of pneumococcal disease throughout the world, mainly the elderly and small children.<sup>8</sup> In 2005 in the United States, more than 40,000 cases and more than 4,400 deaths from invasive pneumococcal disease (IPD; bacteremia and meningitis) were estimated to have occurred. More than half of these cases occurred in adults for whom the pneumococcal polysaccharide vaccine was indicated.<sup>9</sup>

Pneumococcal polysaccharide vaccine (23-valent) (PPSV23; Pneumovax 23, Merck, Whitehouse Station, NJ) was licensed in 1983. It contains antigens against strains that account for 88% of pneumococci that cause sepsis. The vaccine is recommended for all persons 65 years of age and older and also is recommended for certain high-risk groups (see Table 1). In 2008 the CDC added smokers and asthmatics aged 19 to 64 years to the high-risk list because these groups have an increased risk of IPD. Observational studies generally have shown that PPSV23 is 50% to 80% effective

**Table 1. Indications for Pneumococcal Polysaccharide Vaccine (PPV23)**

|  |   |
|--|---|
| Who needs to be vaccinated with PPV23? | <ol style="list-style-type: none"> <li>1. Vaccinate all previously unvaccinated adults aged 65 years and older.</li> <li>2. Vaccinate all adults who smoke cigarettes.</li> <li>3. Vaccinate persons aged 2 to 64 years who: <ul style="list-style-type: none"> <li>● have chronic cardiovascular disease (eg, congestive heart failure, cardiomyopathy); chronic pulmonary disease (eg, chronic obstructive pulmonary disease, emphysema, adults with asthma); or diabetes mellitus or those who are cochlear implant patients.</li> <li>● have chronic liver disease (including cirrhosis), are alcoholic, or have a cerebrospinal fluid leak.</li> <li>● live in special environments or social settings (eg, adults aged 50 to 64 years who are Alaska Natives or certain American Indian populations if recommended by local health authorities).</li> </ul> </li> <li>4. Vaccinate persons aged 2 to 64 years with functional or anatomic asplenia (including persons with sickle cell disease or splenectomy patients).</li> <li>5. Vaccinate immunocompromised persons aged 2 years and older, including those with HIV infection,* leukemia, lymphoma, Hodgkin disease, multiple myeloma, generalized malignancy, chronic renal failure (including dialysis patients), or nephrotic syndrome; those receiving immunosuppressive therapy (including long-term systemic corticosteroids); and those who have received an organ or bone marrow transplant.<sup>†</sup></li> </ol> |
| Who needs a second dose of PPV23?      | <p>A one-time revaccination is indicated for:</p> <ul style="list-style-type: none"> <li>● All adults aged 65 years and older who were previously vaccinated with PPSV before age 65 if <math>\geq 5</math> years have elapsed since the previous dose.</li> <li>● All children and adults who are at the highest risk of serious pneumococcal disease or are likely to have a rapid decline in pneumococcal antibody levels (categories 4 and 5 above) if <math>\geq 5</math> years have elapsed since the previous dose.</li> </ul>   |

\*Persons with asymptomatic or symptomatic HIV infection should be vaccinated as soon as possible after their diagnosis is confirmed (per Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 1997;46(RR-8):1–24).

<sup>†</sup>When cancer chemotherapy or other immunosuppressive therapy is being considered (eg, for patients with Hodgkin disease or those who undergo organ or bone marrow transplantation), PPV23 should be given 2 weeks before or 3 months after immunosuppressive or radiation therapy. Vaccination during chemotherapy or radiation therapy should be avoided (per Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 1997;46(RR-8):1–24).

Adapted with permission from Pneumococcal polysaccharide vaccine (PPSV) CDC answers your questions. From the Immunization Action Coalition, St. Paul, MN. Available online at: [www.immunize.org/catg.d/p2015.pdf](http://www.immunize.org/catg.d/p2015.pdf).

in preventing IPD in immunocompetent adults and that it may reduce the severity of pneumonia in those patients who develop pneumonia after vaccination.<sup>10</sup> Recent studies even have indicated that pneumococcal vaccination may prevent myocardial infarction and stroke by reducing thrombosis caused by inflammation.<sup>11–13</sup>

Persons who are immunocompromised, such as HIV patients or cancer patients undergoing chemotherapy or radiation therapy, have a particularly high rate of IPD. Health care workers administering PPSV23 should be proactive and have patients newly diagnosed with any malignancy vaccinated immediately upon diagnosis because a full immune response to the vaccine requires at least 2 weeks and is weakened by chemotherapy or radiation therapy.<sup>9</sup> If chemotherapy or radiotherapy is initiated less than 2 weeks after administering PPSV23, the CDC recommends that the patient be considered un-

vaccinated, and should be revaccinated at least 3 months after therapy is discontinued if immune competence has been restored.

Persons  $\geq 65$  years of age who have had one prior dose of PPV23 should receive a second dose if  $\geq 5$  years have elapsed since the previous dose. Only one revaccination dose of PPV23 is recommended for certain high-risk persons (see Table 1); a third dose is not presently recommended by the CDC because of a lack of proven efficacy.<sup>9</sup> However, some recent studies have shown a good antibody response to a primary and booster dose of PPSV23.<sup>14–16</sup>

In December 2011, the US Food and Drug Administration (FDA) approved a pneumococcal 13-valent conjugate vaccine (PCV13; Prevnar 13, Wyeth Pharmaceuticals, Radnor, PA) to help protect adults aged 50 and over from pneumococcal pneumonia. At this time the optimal use of PCV13 in adults, alone or in a series with PPV23, has not been determined.<sup>17</sup>

Recognizing the importance of pneumococcal immunizations, the Centers for Medicare & Medicaid Services has added screening for and administration of pneumococcal immunization as a quality measure for hospital inpatients. Beginning January 1, 2012, rates of pneumococcal immunization will be assessed for all inpatients  $\geq 65$  years of age and inpatients 5 to 64 years of age with high-risk conditions.<sup>18</sup> After October 2013, reported data will be available to the public at <http://www.hospitalcompare.hhs.gov/>. (See Table 2 for Level of Evidence [LOE].)

### Herpes Zoster Vaccine

Varicella zoster virus (VZV) causes 2 clinical conditions. The first, varicella (chickenpox), was widespread in childhood before the era of varicella vaccination and has infected 98% of the adult US population. The virus travels through affected sensory nerves to the sensory dorsal root ganglia next to the spinal cord, where it enters a latent phase. The second stage, herpes zoster, occurs when the virus reactivates in one dorsal root ganglion and travels back to the skin, where it causes a localized unilateral vesicular rash.<sup>19</sup> Reactivation seems to be related to declining cell-mediated immunity and is more common with advancing age and in patients with immunosuppressive conditions such as neoplastic disease, organ transplant recipients, persons receiving immunosuppressive medication, and HIV patients.<sup>20</sup> Pain is the most common symptom of herpes zoster, affecting about 75% of cases. Lingering pain after a zoster infection is called post-herpetic neuralgia (PHN) and is commonly defined as pain lasting more than 1 to 3 months after the primary infection. PHN can be excruciatingly painful and can last for months and occasionally for

years. Antiviral therapy after the onset of shingles has not shown efficacy for the prevention of PHN.<sup>21</sup>

The herpes zoster (shingles) vaccine (ZOS; Zostavax, Merck), was approved by the FDA in May 2006 for use in persons  $\geq 60$  years of age. Although the FDA licensed ZOS for use in adults aged 50 to 59 years in March 2011, the Advisory Committee on Immunization Practices (ACIP) so far has declined to extend a formal recommendation for this age range because of concerns about limitations in the vaccine supply and uncertainty about the duration of the vaccine's protection in younger adults.<sup>22</sup> ZOS is similar to the varicella vaccine (VAR; Varivax, Merck); it is made from the live-attenuated Merck-Oka viral strain but contains 14 times as much viral antigen as is present in varicella vaccine. In the Shingles Prevention Study, more than 38,000 adults (median age, 69 years; range, 59–99 years) were followed for a mean of 3.1 years after receiving either vaccine or placebo. Vaccination with ZOS reduced the incidence of herpes zoster by 51% and the incidence of PHN by 66%.<sup>19,23</sup> Side effects were mild, and there was no significant increase in serious adverse events in the vaccine group when compared with the placebo group. A subsequent cohort study found ZOS to be as effective, and in some subpopulations, more effective, than was indicated by the Shingles Prevention Study.<sup>24</sup>

ZOS is recommended by the ACIP for all adults 60 years of age and older (LOE: A; see Table 2).<sup>19</sup> A history of zoster is not a contraindication to vaccination because there is no way to document the level of herpes zoster immunity and vaccine side effects are minimal. In addition, immunization will give additive immunity against shingles; this

**Table 2. Practice Recommendations and Level of Evidence**

| Practice Recommendations  | Level of Evidence | Reference |
|---|-------------------|-----------|
| Give pneumococcal polysaccharide vaccine (PSV23, Pneumovax) for prevention of pneumococcal disease to following persons:                              |                   |           |
| Immunocompetent persons and persons aged $\geq 65$ years of age.  | A                 | 54        |
| Persons aged 2–64 years with chronic cardiovascular disease, chronic pulmonary disease, or diabetes mellitus.   | A                 | 54        |
| Persons aged 2–64 years with alcoholism, chronic liver disease, or cerebrospinal fluid leaks.   | B                 | 54        |
| Give herpes zoster vaccine (Zostavax) for the prevention of herpes zoster and its complications in persons $\geq 60$ years without contraindications. | A                 | 55        |

may be particularly important in view of a recent study indicating higher rates of recurrence of shingles than previously believed.<sup>3</sup> ZOS is an attenuated live-virus vaccine and is not indicated for persons with certain immune-suppressing conditions (see Table 3).

A study showing a reduced VZV antibody response when ZOS was given simultaneously with PSV23 (Pneumovax) led the manufacturer to recommend that these 2 vaccines should not be given simultaneously and that there should be a 4-week interval between administration of the 2 vaccines.<sup>25</sup> However, the CDC continues to recommend that these vaccines be given simultaneously, if indicated, because VZV immunity is cell mediated and does not correlate well with antibody levels.<sup>22,26</sup> This is supported by an observational study published in 2011 that found no evidence that simultaneous administration of the 2 vaccines would impair zoster immunity.<sup>27</sup> (See Table 2 for Level of Evidence.)

### Human Papillomavirus Vaccine

Human papillomavirus (HPV) is estimated to be the most common sexually transmitted disease; more than 80% of sexually active American women will acquire an HPV infection by the age of 50 years with seroprevalence of HPV type 16 (the most carcinogenic type) as high as 41%.<sup>28</sup> HPV is responsible for more than 99% of cervical cancer and is believed to be responsible for 90% of anal cancers and 40% of vulvar, vaginal, or penile cancers.<sup>29</sup> In developed countries, HPV has passed tobacco use to become the major cause of oropharyngeal cancer (found in 45% to 90% of cases).<sup>30</sup> Four HPV types account for the most serious illness: high-risk types 16 and 18 are found in 70% of cervical cancers, and low-risk types 6 and 11 cause 90% of genital warts. HPV type 16 is responsible for >85% of HPV-related head and neck squamous cell cancers.<sup>30</sup> Most HPV infections clear within 8 months to 2 years, but high-risk HPV subtypes are more likely to persist and lead to precancer and cancer. Progression from high-grade precancerous lesions to cancer is estimated to take 10 years.<sup>31</sup>

Two vaccines are available to prevent HPV infections. HPV4 (Gardasil, Merck) contains types 16 and 18 (high risk) and types 6 and 11 (low risk). HPV2 (Cervarix, GlaxoSmithKline, Research Triangle Park, NC) contains types 16 and 18 (high

risk). Both HPV2 and HPV4 are composed of virus-like particles prepared from the recombinant L1 capsid protein of HPV—neither is a live vaccine. Both vaccines have shown efficacy well over 90% for preventing precancerous cervical lesions.<sup>32</sup>

HPV4 vaccine is licensed for girls and young women 9 through 26 years of age for the prevention of cervical, vulvar, vaginal, and anal cancers caused by HPV types 16 and 18; genital warts caused by HPV types 6 and 11; and precancerous or dysplastic lesions caused by HPV types 6, 11, 16, and 18. As of October 2011, HPV4 also is recommended by the ACIP for boys and men 9 through 21 years of age for the prevention of anal cancer caused by HPV types 16 and 18; for the prevention of anal dysplasias and precancerous lesions caused by HPV types 6, 11, 16, and 18; and for the prevention of genital warts caused by HPV types 6 and 11. The ACIP also recommends HPV4 for previously unvaccinated men 22 to 26 years of age who are immunocompromised, who test positive for HIV infection, or who have sex with men. However, any man may receive the vaccine through age 26 if desired. The HPV2 vaccine is licensed for girls and women ages 10 through 25 years for the prevention of cervical cancers and precancers. The ACIP recommends the same age range, 9 to 26 years of age, for both HPV2 and HPV4. If a man or woman reaches age 27 before the vaccination series is complete, the vaccine series may still be completed if it had been started before the 27th birthday.<sup>32</sup> The ACIP recommends the same 3-dose schedule for either vaccine. Each dose is 0.5 mL and is administered intramuscularly. The second dose is administered 1 to 2 months after the first dose, and the third dose is administered 6 months after the first dose. The ACIP has not expressed a preference for one HPV vaccine over the other for vaccination of women.

Although HPV vaccines are not recommended to be given during pregnancy, testing for pregnancy is not necessary before giving the vaccine, and no intervention is needed if a patient is found to be pregnant after receiving HPV vaccine. Women receiving the HPV vaccine should be counseled to continue routine Papanicolaou screening for cervical cancer according to existing guidelines. Although it is biologically plausible that HPV2 and HPV4 could prevent oropharyngeal cancers, it may take several decades before this effect could be detectable in population studies<sup>30</sup> (see the box titled, “Can HPV

**Table 3. Adult Immunization Table**

| Vaccine Name and Route   | For Whom Vaccination Is Recommended   | Schedule for Vaccine Administration*  | Contraindications and Precautions†   |
|--|---|---|--|
| Influenza<br>TIV (give IM)<br>LAIV (give intranasally)                       | <ul style="list-style-type: none"> <li>● Vaccination is recommended for all adults. (This includes healthy adults aged 19–49 years without risk factors.)</li> <li>● LAIV is only approved for healthy nonpregnant people aged 2–49 years.</li> <li>● Adults aged 18–64 years may be given any intramuscular TIV product or, alternatively, the intradermal TIV product (Fluzone Intradermal).</li> <li>● Adults ages 65 years and older may be given standard-dose TIV or, alternatively, the high-dose TIV (Fluzone High-Dose).</li> </ul> <p>Note: LAIV may not be given to some adults; see contraindications and precautions listed in far right column.</p> | <ul style="list-style-type: none"> <li>● Give 1 dose every year in the fall or winter. Begin vaccination services as soon as vaccine is available and continue until the supply is depleted.</li> <li>● Continue to give vaccine to unvaccinated adults throughout the influenza season (including when influenza activity is present in the community) and at other times when the risk of influenza exists.</li> <li>● If 2 or more of the following live virus vaccines are to be given—LAIV, MMR, varicella, or yellow fever—they should be given on the same day; otherwise space them apart by at least 28 days.</li> </ul> | <p>Contraindications:</p> <ul style="list-style-type: none"> <li>● Previous anaphylactic reaction to this vaccine or to any of its components. Egg allergy is no longer a contraindication for TIV.</li> <li>● For LAIV only: pregnancy; chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, neurological/neuromuscular, hematologic, or metabolic (including diabetes) disorders; immunosuppression (including that caused by meds or HIV)</li> </ul> <p>Precautions:</p> <ul style="list-style-type: none"> <li>● Moderate or severe acute illness.</li> <li>● History of Guillain-Barré syndrome within 6 weeks after previous influenza vaccination.</li> <li>● For LAIV only: close contact with an immunosuppressed person when the person requires protective isolation or receipt of specific antivirals (ie., zanamivir or oseltamivir) 48 hours before vaccination. Avoid use of these antiviral drugs for 14 days after vaccination.</li> </ul> |
| Human papillomavirus<br>HPV2 (Cervarix; give IM)<br>HPV4 (Gardasil; give IM) | <p>HPV2 or HPV4:</p> <ul style="list-style-type: none"> <li>● All previously unvaccinated women through age 26 years</li> <li>● HPV4 only: <ul style="list-style-type: none"> <li>● All previously unvaccinated men through the age of 21 years and previously unvaccinated men 22–26 years who are immunocompromised, who test positive for HIV infection, or who have sex with men</li> </ul> </li> </ul> <p>Note: any man may receive the HPV4 through age 26 if desired</p>   | <ul style="list-style-type: none"> <li>● Give 3 doses on a 0, 2, and 6 month schedule.</li> <li>● There must be at least 4 weeks between doses 1 and 2 and at least 12 weeks between doses 2 and 3. Overall, there must be at least 24 weeks between doses 1 and 3. If possible, use the same vaccine product for all 3 doses.</li> </ul>   | <p>Contraindication:</p> <ul style="list-style-type: none"> <li>● Previous anaphylactic reaction to this vaccine or to any of its components.</li> </ul> <p>Precautions:</p> <ul style="list-style-type: none"> <li>● Moderate or severe acute illness.</li> <li>● Data on vaccination in pregnancy are limited. Vaccination should be delayed until after completion of the pregnancy.</li> </ul>   |
| Pneumococcal polysaccharide (PSV23; give IM or SC)                           | See Table 1   | See Table 1   | <p>Contraindication: Previous anaphylactic reaction to this vaccine or to any of its components.</p> <p>Precaution: Moderate or severe acute illness.</p>  |

*Continued*

**Table 3. Continued**

| Vaccine Name and Route     | For Whom Vaccination Is Recommended   | Schedule for Vaccine Administration*  | Contraindications and Precautions†   |
|----------------------------|---|---|--|
| Td, Tdap (give IM)         | <ul style="list-style-type: none"> <li>All adults who lack written documentation of a primary series of at least 3 doses of tetanus and diphtheria toxoid vaccine.</li> <li>A booster dose of tetanus- and diphtheria toxoid-containing vaccine may be needed for wound management as early as 5 years after last dose; consult ACIP recommendations<sup>‡</sup>.</li> <li>During pregnancy, when indicated, give Td or Tdap in second or third trimester. If not administered during pregnancy, give Tdap in immediate postpartum period.</li> </ul> <p>For Tdap only:</p> <ul style="list-style-type: none"> <li>Adults &lt;65 years who have not already received Tdap.</li> <li>Adults of any age, including adults ≥65 years in contact with infants &lt;12 months (eg, parents, grandparents, childcare providers) who have not received a dose of Tdap should be prioritized for vaccination.</li> <li>Health care personnel of all ages.</li> <li>Adults aged ≥65 years without a risk indicator (eg, not in contact with an infant) may also be vaccinated.</li> </ul> | <ul style="list-style-type: none"> <li>For people who are unvaccinated or behind, complete the primary Td series (spaced at 0, 1- to 2-month, 6- to 12-month intervals); substitute a one-time dose of Tdap for one of the doses in the series, preferably the first.</li> <li>Give Td booster every 10 years after the primary series has been completed.</li> <li>Tdap should be given regardless of interval since previous Td.</li> </ul> | <p><b>Contraindications:</b></p> <ul style="list-style-type: none"> <li>Previous anaphylactic reaction to this vaccine or to any of its components.</li> <li>For Tdap only, history of encephalopathy not attributable to an identifiable cause, within 7 days after DTP/DTaP.</li> </ul> <p><b>Precautions:</b></p> <ul style="list-style-type: none"> <li>Moderate or severe acute illness.</li> <li>Guillain-Barré syndrome within 6 weeks after previous dose of tetanus toxoid-containing vaccine.</li> <li>For Tdap only, progressive or unstable neurologic disorder, uncontrolled seizures, or progressive neuropathy until a treatment regimen has been established and the condition has stabilized.</li> <li>History of arthus reaction after a prior dose of tetanus- or diphtheria toxoid-containing vaccine; defer vaccination until at least 10 years have elapsed since the last tetanus toxoid-containing vaccine.</li> </ul> |
| Zoster (shingles; give SC) | <ul style="list-style-type: none"> <li>People aged ≥60 years</li> </ul> <p>Note: Zoster is FDA-approved for persons 50 years and older, but is not CDC recommended for this age group and therefore may not be covered by some insurers for persons aged 50–59 years</p>  | <ul style="list-style-type: none"> <li>Give one-time dose if unvaccinated, regardless of previous history of herpes zoster (shingles) or chickenpox.</li> <li>If 2 or more of the following live virus vaccines are to be given—MMR, zoster, or yellow fever—they should be given on the same day. If they are not, space them by at least 28 days.</li> </ul>  | <p><b>Contraindications:</b></p> <ul style="list-style-type: none"> <li>Previous anaphylactic reaction to this vaccine or to any of its components</li> <li>Primary cellular or acquired immunodeficiency</li> </ul> <p><b>Pregnancy</b></p> <p><b>Precautions:</b></p> <ul style="list-style-type: none"> <li>Moderate or severe acute illness.</li> <li>Receipt of specific antivirals (ie, acyclovir, famciclovir, or valacyclovir) 24 hours before vaccination, if possible; delay resumption of these antiviral drugs for 14 days after vaccination.</li> </ul>   |

*Continued*

**Table 3. Continued**

| Vaccine Name and Route   | For Whom Vaccination Is Recommended  | Schedule for Vaccine Administration*  | Contraindications and Precautions†  |
|--|--|---|---|
| Meningococcal<br>Meningococcal conjugate<br>vaccines (MCV4; give<br>IM)<br>Menactra, Menveo<br>Meningococcal<br>polysaccharide vaccine<br>(MPSV4; give SC) | <p>For people through age 18 years, consult “Summary of Recommendations for Child/Teen Immunization” at <a href="http://www.immunize.org/catg.d/p2010.pdf">www.immunize.org/catg.d/p2010.pdf</a>.</p> <ul style="list-style-type: none"> <li>● People with anatomic or functional asplenia or persistent complement component deficiency.</li> <li>● People who travel to or reside in countries in which meningococcal disease is hyperendemic or epidemic (eg, the “meningitis belt” of Sub-Saharan Africa).</li> <li>● Microbiologists routinely exposed to isolates of <i>Neisseria meningitidis</i></li> <li>● First-year college students through age 21 years who live in residence halls (see fifth bullet in the column to the right for details).</li> </ul> | <ul style="list-style-type: none"> <li>● Give 2 initial doses of MCV4 2 months apart to adults ≤55 years with risk factors listed in first bullet in column to left or to adults with HIV in this age group.</li> <li>● Give one initial dose to all other adults with risk factors (see second through fourth bullets in column to left).</li> <li>● Give booster doses every 5 years to adults with continuing risk (see the first through third bullets in column to left).</li> <li>● MCV4 is preferred over MPSV4 for people ≤55 years old unless contraindicated; use MPSV4 <i>only</i> if age ≥56 years</li> <li>● For first-year college students aged 19–21 years living in residence halls, give one dose if unvaccinated plus booster dose if most recent dose was given when &lt;16 years.</li> </ul> | <p>Contraindication:</p> <ul style="list-style-type: none"> <li>● Previous anaphylactic reaction to this vaccine or to any of its components</li> </ul> <p>Precaution:</p> <ul style="list-style-type: none"> <li>● Moderate or severe acute illness</li> </ul> |
| Hepatitis A<br>Hepatitis B<br>MMR<br>Varicella<br>Polio  | <p>Refer to the Summary of Recommendations for Adult Immunization table at the Immunization Action Coalition (IAC) website at <a href="http://www.immunize.org/adultrules">www.immunize.org/adultrules</a></p>   |   |   |

\*Any vaccine can be given with another.

†Mild illness is not a contraindication.

Adapted with permission from Summary of Recommendations for Adult Immunization, Immunization Action Coalition, St. Paul, MN (2011). The original table is adapted from the recommendations of the Advisory Committee on Immunization Practices (ACIP) and is updated regularly at [www.immunize.org/adultrules](http://www.immunize.org/adultrules).

CDC, Centers for Disease Control and Prevention; FDA, US Food and Drug Administration; IM, intramuscularly; LAIV, live attenuated influenza vaccine; MMR, measles–mumps–rubella; SC, subcutaneously; Td, tetanus–diphtheria; acellular pertussis; TIV, trivalent inactivated influenza vaccine.



Vaccination Prevent Cancer of the Head and Neck?”). Information about administration, precautions, and contraindication are listed in Table 2.

### **Tetanus–Diphtheria–Pertussis Vaccine**

Tetanus and diphtheria have become rare in the United States, and most cases occur in adults who have not completed a primary immunization series. However, pertussis, a coughing illness caused by the bacteria *Bordetella pertussis*, remains an endemic disease, with the true number of cases estimated to be between 800,000 and 3.3 million annually in the United States.<sup>40</sup> Pertussis incidence has been increasing gradually since the early 1980s. More than 25,000 cases were reported in 2004, the largest number since 1959.<sup>41</sup> In 2010, 9,143 cases of pertussis (including 10 infant deaths) were reported throughout California. This is the most cases reported in 63 years, when 9,394 cases were reported in 1947.

Adolescents and adults serve as a reservoir of disease because pertussis immunity wanes 4 to 12 years after the completion of childhood vaccination.<sup>42</sup> Giving a booster dose of pertussis vaccine to adults is considered essential to reduce the burden of disease and protect newborns from infection, especially during the vulnerable first 2 months of life before the first pertussis vaccination.

Vaccines containing acellular pertussis were first licensed for use in adolescents and adults in 2005. Tdap is written with small *d* and *p* letters to indicate that the dose of diphtheria and acellular pertussis toxoid in the vaccine has been reduced in the adolescent/adult formulations to minimize the incidence of adverse effects. Two Tdap vaccines are currently available. Boostrix (GlaxoSmithKline) is approved for persons 10 through 64 years of age. Adacel (Sanofi Pasteur) is approved for persons 11 through 64 years of age. In response to the 2010 pertussis epidemic in California, the ACIP voted on October 27, 2010, to approve the off-label use of Tdap in adults aged  $\geq 65$  years who anticipate contact with children aged  $\leq 12$  months to protect both themselves and the infant.<sup>43</sup>

The ACIP recommends that Tdap should replace a single dose of the tetanus–diphtheria vaccine (Td) for adults aged  $\geq 19$  years or older who have not previously received a dose of Tdap. Tdap also can be substituted for any Td dose in the 3-dose primary series. A dose of Tdap is recom-

mended for pregnant women (preferably given in the third or late second trimester), postpartum women, those with close contacts with infants aged  $< 12$  months, and all HCP with direct patient contact if they have not previously received Tdap. When giving Tdap to protect an infant, no minimum interval needs to be adhered to; a dose of Tdap can be given immediately after a dose of Td in such cases.<sup>44</sup> Ideally, these adults should receive Tdap at least 2 weeks before they are in close contact with the infant. Tdap, if given during pregnancy, preferably should be administered during the third or late second trimester (after 20 weeks' gestation). If not administered during pregnancy, Tdap should be administered immediately postpartum.<sup>43</sup>

### **Meningococcal/Varicella/Measles–Mumps–Rubella/Polio/Hepatitis A/Hepatitis B**

Some adults will require catch-up vaccination with these vaccines, particularly HCP and travelers. A summary of ACIP recommendations for immunization of HCP can be found in Table 4.<sup>45</sup> Key updates are given below.

#### ***Meningococcal***

Two quadrivalent meningococcal conjugate vaccines (MCV4) are now available: Menactra (Sanofi Pasteur), for persons aged 2 to 55 years, and Menveo (Novartis, East Hanover, NJ), for persons aged 11 to 55 years. A quadrivalent meningococcal polysaccharide vaccine (MPSV4), Menomune (Sanofi Pasteur), still is available for use in adults  $\geq 56$  years of age.

The ACIP now recommends revaccination with MCV4 after 5 years for adults previously vaccinated with MCV4 or MPSV4 who remain at increased risk for infection (eg, adults with anatomic or functional asplenia or microbiologists or travelers with prolonged exposure). Either MCV4 vaccine may be used to revaccinate people aged 11 to 55 years who need a second dose, regardless of which vaccine was used for the first dose.<sup>46</sup> In addition, the ACIP has now recommends a booster dose 5 years after the first MCV4 dose for those who received their initial dose at ages 13 to 15.<sup>47</sup> These changes were made because antibody levels were found to decline over time, and people ages 16 to 21, particularly college freshmen living in dormitories, are considered to be at increased risk for

**Table 4. Summary of Main Changes\* from 1997 Advisory Committee on Immunization Practices/Hospital† Infection Control Practices Advisory Committee Recommendations for Immunization of Health Care Personnel**

|               |  |
|---------------|--|
| Hepatitis B   | HCP and trainees in certain populations at high risk for chronic hepatitis B (eg, those born in countries with high and intermediate endemicity) should be tested for HBsAg and anti-HBc/anti-HBs to determine infection status.   |
| Influenza     | Emphasize that all HCP, not just those with direct patient care duties, should receive an annual influenza vaccination.<br><br>Comprehensive programs to increase vaccine coverage among HCP are needed; influenza vaccination rates among HCP within facilities should be measured and reported regularly.  |
| MMR           | History of disease is no longer considered adequate presumptive evidence of measles or mumps immunity for HCP; laboratory confirmation of disease was added as acceptable presumptive evidence of immunity. History of disease has never been considered adequate evidence of immunity for rubella.<br><br>The footnotes have been changed regarding the recommendations for personnel born before 1957 in routine and outbreak contexts. Specifically, guidance is provided for 2 doses of MMR for measles and mumps protection and 1 dose of MMR for rubella protection. |
| Pertussis     | HCP, regardless of age, should receive a single dose of Tdap as soon as feasible if they have not previously received Tdap.<br><br>The minimal interval was removed, and Tdap now can be administered regardless of interval since the last tetanus- or diphtheria-containing vaccine.<br><br>Hospitals and ambulatory care facilities should provide Tdap for HCP and use approaches that maximize vaccination rates.   |
| Varicella     | Criteria for evidence of immunity to varicella were established. For HCP they include:<br>Written documentation with 2 doses of vaccine;<br>Laboratory evidence of immunity or laboratory confirmation of disease;<br>Diagnosis of history of varicella disease by health care provider or diagnosis of history of herpes zoster by health care provider.  |
| Meningococcal | HCP with anatomic or functional asplenia or persistent complement component deficiencies should now receive a 2-dose series of meningococcal conjugate vaccine. HCP with HIV infection who are vaccinated should also receive a 2-dose series.<br><br>Those HCP who remain in groups at high risk are recommended to be revaccinated every 5 years.  |

\*Updated recommendations made since publication of the 1997 summary of recommendations (CDC Immunization of health-care workers: recommendations of the Advisory Committee on Immunization Practices [ACIP] and the Hospital Infection Control Practices Advisory Committee [HICPAC]. MMWR 1997;46[No. RR-18]).

†Is now “Healthcare.”

CDC, Centers for Disease Control and Prevention; HBsAg, hepatitis B surface antigen; anti-HBc, hepatitis B core antibody; anti-HBs, hepatitis B surface antibody; HCP, health care personnel; MMR, measles, mumps, rubella; Tdap, tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine, adsorbed.

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meningococcal disease. However, college freshmen who were vaccinated at age  $\geq 16$  years do not need revaccination unless they are also in a high-risk category.

### **Varicella**

All healthy adults should be assessed for varicella immunity. Evidence of immunity includes documentation of age-appropriate vaccination, laboratory evidence of immunity (or confirmation of disease), or diagnosis of varicella or zoster by a health care provider. Birth in the United States before 1980 is considered evidence of immunity, except for HCP, pregnant women, and immunocompromised persons, who require other evidence of immunity. Those who do not have evidence of immu-

nity should receive 2 doses of single-antigen varicella vaccine 4 to 8 weeks apart. Varicella vaccination should be considered for HIV-infected adults with a CD4<sup>+</sup> T-lymphocyte count of  $\geq 200$  mm<sup>3</sup>; these individuals should receive 2 doses separated by 3 months.<sup>48</sup> Pregnant women should be screened for varicella immunity; one dose given postpartum when indicated, with a second dose 4 to 8 weeks later.

### **Hepatitis A**

A hepatitis A/hepatitis B combination vaccine—Twinrix (GlaxoSmithKline)—can be given in an accelerated 4-dose schedule to protect travelers who need to depart in less than 1 month. Doses are given at 0, 7, and 21 days and 12 months.<sup>49</sup>

**Table 5. Keeping Current with Vaccines**

Family physicians who wish to stay current with the most recent updates in vaccine recommendations can get up-to-date information at these sites:

|                               |   |  |
|-------------------------------|---|--|
| CDC                           | The Healthcare Professional website of the National Immunization Program of the CDC has extensive current information on immunizations and has an Adult Immunization Scheduler program available for free download.   | <a href="http://www.cdc.gov/vaccines/hcp.htm">www.cdc.gov/vaccines/hcp.htm</a>                       |
| Immunization Action Coalition | The Immunization Action Coalition is a nonprofit organization based in St. Paul, Minnesota. Their website contains extensive, easy-to-access informational materials for providers and patients, and features IAC Express, a free weekly email immunization newsletter for health professionals.  | <a href="http://www.immunize.org/">www.immunize.org/</a>   |
| SHOTS by STFM                 | The Group on Immunization Education of the Society of Teachers of Family Medicine (STFM) created the SHOTS program, developed with support from the CDC.<br>SHOTS by STFM is a free point-of-care immunization information system that can be accessed online or as a stand-alone program compatible with iPhone, Android, and Blackberry. SHOTS contains the complete immunization schedules for children, adults, and persons with special medical conditions. In addition, information can be quickly viewed for each individual vaccine regarding immunization basics, high-risk indications, adverse reactions, contraindications, administration, and catch-up schedules. | <a href="http://www.immunizationed.org/ShotsOnline.aspx">www.immunizationed.org/ShotsOnline.aspx</a> |

CDC, Centers for Disease Control and Prevention.

For unvaccinated adults who are acutely exposed to the hepatitis A virus or are traveling to areas of high prevalence who do not have time to complete a 2-dose hepatitis A vaccine series, a single dose of hepatitis A vaccine now can be used as an alternative to immunoglobulin. For adults younger than age 40, vaccine is preferred; for persons  $\geq 40$  years of age, immunoglobulin is preferred but vaccine is acceptable. Older adults, immunocompromised persons, and persons with chronic liver disease or other chronic medical conditions planning to depart in  $\leq 2$  weeks should receive the initial dose of vaccine and immunoglobulin can be administered simultaneously (0.02 mL/kg) at a separate anatomic injection site.<sup>50</sup>

The CDC recommends hepatitis A vaccination for all previously unvaccinated persons who anticipate close personal contact (eg, household contact or regular babysitting) with an international adoptee from a country of high or intermediate endemicity during the first 60 days after arrival of the adoptee in the United States. The first dose of the 2-dose hepatitis A vaccine series should be administered as soon as adoption is

planned, ideally  $\geq 2$  weeks before the arrival of the adoptee.<sup>51</sup>

### **Hepatitis B**

#### *Hepatitis B Vaccination for Diabetics $\geq 60$ Years Old*

In December 2011 the ACIP recommended that all previously unvaccinated adults aged 19 to 59 years with diabetes mellitus (both type 1 and type 2) be vaccinated against hepatitis B as soon as possible after a diagnosis of diabetes is made.<sup>52</sup> The rationale was the finding that diabetics have approximately double the risk of acquiring a new hepatitis B infection; this increased risk seems to be associated with assisted blood glucose monitoring (when equipment is shared and adequate hand hygiene procedures are not used). Although the risk also is present for diabetics  $\geq 60$  years old, hepatitis B vaccination is less cost-effective in this age range. The CDC notes that a health care provider may still wish to vaccinate a diabetic  $\geq 60$  years of age after assessing their risk, particularly regarding the patient's need for assisted blood glucose monitoring in long-term care facilities and the likelihood of experiencing chronic sequelae if infected with the hepatitis B virus.<sup>52</sup>

### Persons at High Risk for Sexual Transmission of Hepatitis B

The most common source of hepatitis B infection in the United States is sexual contact. Heterosexual transmission accounts for 39% of new cases, and men who have sex with men account for 24%, whereas intravenous drug use accounts for 16% of new cases of hepatitis B infection. The CDC recommends that persons with multiple sexual partners (eg, persons with more than one sex partner during the previous 6 months), men who have sex with men, and all persons seeking evaluation of or treatment for sexually transmitted diseases should be vaccinated against hepatitis B.<sup>53</sup> Serologic testing before vaccination only is recommended for adult populations with a prevalence of hepatitis B virus infection of >20% (eg, injection-drug users, incarcerated persons, men who have sex with men, and persons born in countries with high levels of endemic hepatitis B virus infection). Prevacination testing can be done with a single test, hepatitis B core antibody (anti-HBc) or with a panel of tests (eg, hepatitis B surface antigen and hepatitis B surface antibody [anti-HBs]). The CDC does not recommend delaying vaccination until the test results are reviewed; the first vaccine dose typically should be administered immediately after collection of the blood sample for serologic testing.<sup>53</sup>

#### Keeping Current with Vaccines

To help providers keep current with changing immunization recommendations, a number of regularly updated web-based resources are available: see Table 5.

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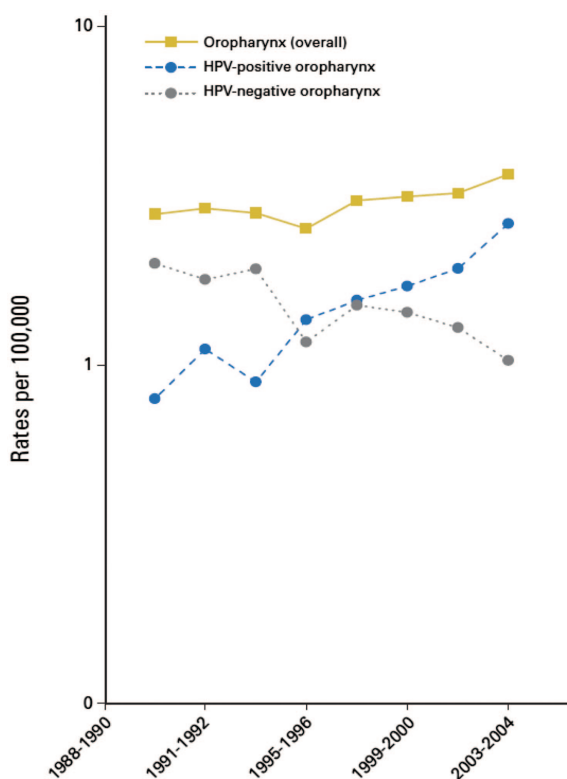
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## Can HPV Vaccination Prevent Cancer of the Head and Neck?

There is mounting evidence that HPV causes not only cervical and anal cancer but also is responsible for ~25% of head and neck squamous cell carcinoma (HNSCC). The majority of these HPV-associated HNSCCs are oropharyngeal (tonsillar and base of tongue) squamous cell cancers (OSCCs), and in developed countries HPV is detected in 45% to 90% of these cases.<sup>30</sup> There is strong evidence connecting HPV as a cause of these tumors, both on a molecular level and in epidemiologic studies showing a strong connection between OSCC, rates of oral HPV, and HPV sexual exposure.<sup>30,33</sup> Of HPV-positive OSCC, ~90% are positive for high-risk HPV type 16, the type responsible for the majority of cervical cancers.<sup>34</sup> Whereas HPV-negative OSCC has been steadily declining in the United States, paralleling the decline in smoking, HPV-positive OSCC has been steadily rising and parallels the rise in rates of oral sex and oral HPV exposure (Figure 1).<sup>35</sup>

**Figure 1. Incidence rates for overall oropharyngeal cancer, human papillomavirus (HPV)-positive oropharyngeal cancers, and HPV-negative oropharyngeal cancers during 1988 to 2004 in Hawaii, Iowa, and Los Angeles. (From Chaturvedi AK, Engels EA, Pfeiffer RM et al Human papillomavirus and rising oropharyngeal cancer incidence in the united states. J Clin Oncol 2011;29:4294-301 (Ref. 49). Reprinted with permission.)**



There are significant differences between HPV-positive and HPV-negative OSCC. Patients with HPV-positive OSCC tend to be younger by about 10 years, usually are nonsmokers, have higher numbers of vaginal and oral sex partners, and have a much better response to treatment.<sup>36,37</sup> A recent study showed that HPV-positive patients had a 69% reduction in risk of death compared with HPV-negative patients, with a mean survival of 131 versus 20 months.<sup>35</sup> The incidence of both HPV-associated and HPV-unassociated HNSCC is more than 2-fold higher among men than women, with a ratio from 2:1 to 5:1. The prevalence of oral HPV infection in a US study was approximately 3-fold higher in men than women (10.1% vs 3.6%) and HPV-16 prevalence was more than 5-fold higher, which could explain the higher incidence of HPV-positive OSCC among men.<sup>38</sup> Possible reasons for this difference include higher risk of HPV acquisition from oral sex on women versus men and higher rates of systemic antibody response to HPV genital infection in women versus men.<sup>38</sup>

By 2020, the number of HPV-positive OSCCs is projected to surpass the number of cervical cancers.<sup>35</sup> Clinical studies to evaluate the effectiveness of HPV vaccines to prevent OSCC are in developmental stages.

<sup>39</sup> It is highly likely that as these studies are completed and as surveillance rates monitor OSCC incidence in HPV-vaccinated populations, prevention of head and neck cancers may prove to be an additional benefit of HPV vaccination, particularly for men, who are at higher risk.