

## PREVENTION OF SECONDARY DISEASE: PREVENTIVE MEDICINE

### I. IMMUNIZATIONS

Immunizations against infectious diseases are a cornerstone of preventive medicine and are an extremely important component of care for immunosuppressed patients. Concerns regarding vaccinations in HIV-infected individuals include:

- The potential danger from live virus vaccines
- The ability of HIV-infected patients to mount an appropriate immune response to vaccine.

In general, the more intact the immune system is, the more effective and safe the vaccines are. Live virus vaccines are generally only used when 1) an inactivated version does not exist, and 2) the risk of the disease clearly outweighs the theoretical risk of vaccination.

#### A. Recommended Immunizations for Non-Pregnant HIV-Infected Adults

TABLE 1 RECOMMENDED IMMUNIZATIONS FOR NON-PREGNANT HIV-INFECTED ADULTS		
Vaccine	Indications	Schedule
<b>Tetanus, Diphtheria, and Pertussis (Tdap),* and Tetanus-Diphtheria (Td)*</b>	For patients who have not received the primary series	Administer 1 dose of Tdap, followed by a dose of Td at 1 month and a second dose of Td 6-12 months later
	For patients who have already received the primary series	Administer 1 dose of Tdap booster every 10 years
<b>Influenza</b>	For all patients	Administer 1 annual dose. Do not use FluMist because it contains live virus.
<b>Pneumococcal polysaccharide</b>	For all patients	Administer 1 dose followed by one revaccination after 5 to 6 years (or more) have elapsed since initial vaccination
<b>Hepatitis A*</b>	All HIV-infected patients who are negative for HAV IgG	Administer 2 doses (0 and 6-12 months)
<b>Hepatitis B*</b>	For patients without serologic evidence of prior HBV infection or who have not previously received the complete series of HBV vaccination	Strongly encourage the vaccine series—3 doses (0, 1 to 2, and 6 months)
<b>Measles, Mumps, Rubella (MMR)*</b>	For all asymptomatic HIV-infected patients who do not have evidence of severe immunosuppression and who are seronegative for antibody to MMR	Administer 1 dose
	For patients with severe immunosuppression (<200 cells/mm <sup>3</sup> )	Do not administer vaccine

<b>Human Papillomavirus (HPV)</b>	For women between the ages of 9 and 26 years	Administer 3 doses (at 0, 2, and 6 months)
<b>Varicella*</b>	For persons who are susceptible	Consider administering 2 doses (at 0 and 4-8 weeks)

For other vaccines, see CDC recommendations. Available at: [www.cdc.gov/vaccines](http://www.cdc.gov/vaccines)

\* Covered by the Vaccine Injury Compensation Program. For information on how to file a claim, call 1-800-338-2382, or visit [www.hrsa.gov/Vaccinecompensation](http://www.hrsa.gov/Vaccinecompensation). To file a claim for vaccine injury write: U.S. Court of Federal Claims, 717 Madison Place, N.W., Washington D.C. 20005, (202) 219-9657.

**Tetanus, Diphtheria, and Pertussis:** *MMWR Recomm Rep* 2006;55(RR-15):1-48. Available at: [www.cdc.gov/mmwr/preview/mmwrhtml/rr5515a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5515a1.htm)

**Influenza:** *MMWR Recomm Rep* 2002;51(RR-3):1-31. Available at: [www.cdc.gov/mmwr/preview/mmwrhtml/rr5103a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5103a1.htm)

**Pneumococcal:** Vaccination effectiveness improves when CD4 count is >200 cells/mm<sup>3</sup>. *MMWR Recomm Rep* 1997;46(RR-8):1-24. Available at: [www.cdc.gov/mmwr/preview/mmwrhtml/00047135.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/00047135.htm)

**Hepatitis A:** Persons at higher risk for HAV infection should receive postvaccination antibody testing to verify vaccine efficacy and to identify patients who might benefit from vaccine boosting. Patients at risk include those with chronic liver disease (e.g. hepatitis B or C); men who have sex with men; travelers to countries with high endemicity of infection; persons who live in a community experiencing an outbreak of HAV infection; illicit drug users, particularly injection drug users; persons who have clotting-factor disorders; persons at occupational risk for infection. For persons who are susceptible to both hepatitis A and hepatitis B, the combined hepatitis A and B vaccine can be used: 3 doses at 0, 1, and 6 months.

**Hepatitis B:** For persons who are susceptible to both hepatitis A and hepatitis B, the combined hepatitis A and B vaccine can be used: 3 doses at 0, 1, and 6 months.

**MMR:**

*Measles component:* Adults born before 1957 may be considered immune to measles. Adults born after 1957 should receive at least one dose of MMR unless they are severely immunosuppressed, [*MMWR Recomm Rep* 1998;47(RR-8):1-57. Available at: [www.cdc.gov/mmwr/preview/mmwrhtml/00053391.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/00053391.htm)], or there is documentation of at least one dose or other acceptable evidence of immunity (e.g., titers). A second dose of MMR is recommended for adults who were recently exposed to measles or in an outbreak setting; were previously vaccinated with killed measles vaccine; were vaccinated with an unknown vaccine between 1963 and 1967; are students in post-secondary educational institutions; work in healthcare facilities; plan to travel internationally. Foreign-born patients who have never received the vaccine should receive the full series. Consider administering 2 doses to persons with occupational, geographic, or other risk (optional). (Recommended Immunizations for Adults with Medical Conditions; Recommendations of the Advisory Committee on Immunization Practices, CDC, October 2002.)

*Mumps component:* 1 dose of MMR should be adequate for protection. (Recommended Immunizations for Adults with Medical Conditions; Recommendations of the Advisory Committee on Immunization Practices, CDC, October 2002.)

**HPV:** Protects against HPV types 6, 11, 16, and 18. HPV testing is not required before administration of the vaccine. The vaccine has been demonstrated to produce high levels of neutralizing antibody for 5 years. HPV vaccine is most effective in women who are not yet sexually active. However, most women, regardless of whether they are sexually active, may benefit from vaccination. In clinical trials, only 1 in 1,000 women showed evidence of exposure to all four types of HPV prevented by the vaccine. Gardasil may also provide some cross-protection against HPV genotypes other than 6, 11, 16, and 18. However, additional data are required before the vaccine can be recommended for the prevention of cross-reactive HPV types. Clinicians should continue to perform regular cervical screening with Pap tests and visual inspection of the vulva and vagina during annual pelvic examinations in women who have received the HPV vaccine. Most of the data regarding HPV vaccine safety and efficacy are derived from studies in non-HIV-infected females. Immune response to the vaccine may be decreased in the setting of HIV infection. Studies are currently underway to provide more extensive data regarding the safety and efficacy of the vaccine in the HIV-infected population. There currently are no recommendations to vaccinate men against HPV.

**Varicella:** Varicella vaccine may be considered for asymptomatic HIV-infected persons with CD4 percentages ≥25% and who do not have reliable clinical history of varicella infection, or serologic evidence of varicella zoster virus (VZV) infection. *Note:* Greater than 90% of US-born adults are immune to VZV.

## **B. RECOMMENDED IMMUNIZATIONS FOR PREGNANT HIV-INFECTED ADULTS**

### **RECOMMENDATIONS:**

**Routine pregnancy testing of women of childbearing age before administering a live-virus vaccine is not recommended.<sup>1</sup>**

**Clinicians should avoid administering immunizations late in the third trimester to avoid the theoretical possibility of the vaccines causing increased viral load levels at the time of delivery.**

**Because of the importance of protecting women of childbearing age against rubella, clinicians should adopt the following practices in any immunization program:**

- **Ask women if they are or could be pregnant or intend to become pregnant within the next 4 weeks**
- **Explain the potential risk of vaccination to the fetus to women who state that they are not pregnant**
- **Counsel women who are vaccinated to avoid pregnancy during the 4 weeks after MMR vaccination.<sup>1-3</sup>**
- **Do not vaccinate women who state that they are pregnant; administer rubella vaccine immediately after delivery in rubella-susceptible HIV-infected women with CD4 counts  $>200$  cells/mm<sup>3</sup>**
- **Test pregnant women for rubella immunity at the first antepartum visit**

**Clinicians should counsel pregnant women who are inadvertently vaccinated or who become pregnant within 4 weeks after MMR or varicella vaccination about the theoretical risk to the fetus; however, exposure to MMR or varicella vaccines during pregnancy generally is not a reason to terminate a pregnancy.<sup>1,4</sup>**

Risks from vaccination of the mother during pregnancy to the developing fetus are primarily theoretical. No direct evidence exists of risk from vaccinating pregnant women with inactivated virus or bacterial vaccines or toxoids.<sup>5,6</sup> Benefits of vaccinating pregnant women usually outweigh potential risks when the likelihood of disease exposure is high, when infection would pose a risk to the mother or fetus, and when the vaccine is unlikely to cause harm.

Pregnancy is a contraindication for measles, mumps, rubella, and varicella vaccines. Although there is a theoretical risk to the fetus, in large follow-up studies, there were no cases of congenital rubella syndrome, congenital varicella, or abnormalities attributable to fetal infection among infants born to women who received rubella or varicella vaccines during pregnancy.<sup>1,7</sup> All women should be tested for rubella immunity at the first antepartum visit. Rubella vaccine should be administered immediately after delivery in all rubella-susceptible women who have not undergone permanent sterilization unless they have CD4 counts  $<200$  cells/mm<sup>3</sup>. For women who are severely immune compromised, the potential risks of receiving the vaccine should be weighed against the potential for the patient to become pregnant again before receiving appropriate ARV therapy to treat the HIV infection.

Table 2 lists recommendations for immunizations in HIV-infected pregnant women.

<b>TABLE 2 RECOMMENDED IMMUNIZATIONS FOR PREGNANT HIV-INFECTED ADULTS</b>		
<b>Vaccine</b>	<b>Indications</b>	<b>Recommendations</b>
<b>Tetanus</b>	<p>For women who have not received Td vaccination in last 10 years but have been previously immunized</p> <p>For women who have never been immunized or have only been partially immunized</p> <p>For women for whom the vaccine is indicated but who do not receive the complete 3-dose series during pregnancy</p>	<p>Administer Td booster</p> <p>Administer the complete primary series, including Tdap (see Table 1)</p> <p>Follow up after delivery to ensure that the series is completed</p>
<b>Influenza</b>	For all pregnant women	Administer vaccine during influenza season, regardless of stage of pregnancy
<b>Hepatitis A</b>	For pregnant women at increased risk for hepatitis A*	Offer hepatitis A vaccine series
<b>Hepatitis B</b>	<p>For all pregnant women who are HBsAg, HBsAb, and HBcAb IgG negative</p> <p>For pregnant women who are HBsAg-positive</p>	<p>Administer hepatitis B vaccine</p> <p>Ensure that 1) the infant receives HBIG and that the hepatitis B vaccine series is initiated within 12 hours after birth, and 2) the recommended hepatitis B vaccine series is completed in the infant</p>
<b>Pneumococcal polysaccharide</b>	For pregnant women who have not received the vaccine within the last 6 years	Administer vaccine
<b>MMR</b>	<p>For pregnant women or women intending to become pregnant in the next 4 weeks</p> <p>For pregnant women who are rubella-susceptible</p> <p>For household contacts of pregnant women</p>	<p>Do not administer vaccine</p> <p>Administer vaccine immediately after delivery</p> <p>Administer vaccine when indicated</p>
<b>Varicella</b>	<p>For all pregnant women</p> <p>For household contacts of pregnant women</p>	<p>Do not administer vaccine</p> <p>Administer vaccine when indicated</p>

	For women who are exposed to varicella at any point during pregnancy with no history of previous varicella	Perform antibody testing for previous varicella exposure. If exposure is negative, administer varicella zoster immune globulin (VZIG)
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Data are from Refs 1-4, 7-11.

\* Persons with chronic liver disease (e.g. hepatitis B or C); travelers to countries with high endemicity of infection; persons who live in a community experiencing an outbreak of HAV infection; illicit drug users, particularly injection drug users; persons who have clotting-factor disorders; persons at occupational risk for infection.

**Notes**

**Influenza:** It has been shown that women in the second and third trimesters of pregnancy are at an increased risk for hospitalization from influenza.

**Hepatitis A and B:** No known risk exists for the fetus from passive immunization of pregnant women with immune globulin preparations.

**MMR:** Persons who receive MMR vaccine do not transmit the vaccine viruses to contacts.<sup>1</sup>

**Varicella:** Transmission of varicella vaccine virus to contacts is rare.<sup>4</sup>

**C. CONCURRENT ADMINISTRATION OF ANTIMICROBIAL AGENTS AND VACCINES**

**RECOMMENDATION:**

**Clinicians should discontinue antiviral drugs active against herpesviruses  $\geq 24$  hours before administration of varicella vaccine.**

With limited exceptions, using an antibiotic is not a contraindication to vaccination.

Antimicrobial agents have no effect on the response to live attenuated vaccines, except live oral Ty21a typhoid vaccine, and have no effect on inactivated, recombinant subunit, or polysaccharide vaccines or toxoids.<sup>12</sup>

Antiviral drugs used for treatment or prophylaxis of influenza virus infections have no effect on the response to inactivated influenza vaccine.<sup>9</sup> Antiviral drugs active against herpesviruses (e.g., acyclovir or valacyclovir) might reduce the efficacy of live attenuated varicella vaccine. These drugs should be discontinued  $\geq 24$  hours before administration of varicella vaccine, if possible.

**D. VACCINES AND ALLERGENS**

**RECOMMENDATIONS:**

**Before administering the influenza vaccine, clinicians should ask patients whether they are able to eat eggs without adverse effects. Clinicians should not administer the influenza vaccine to patients who have a history of anaphylactic or anaphylactic-like allergy to eggs.**

**Clinicians should use extreme caution when administering vaccines that contain gelatin to persons who have a history of anaphylactic reaction to gelatin or gelatin-containing products.**

The most common animal protein allergen is egg protein, which is found in vaccines prepared by using embryonated chicken eggs (influenza and yellow fever vaccines). Persons who are able to

eat eggs or egg products can generally receive these vaccines safely; persons with histories of anaphylactic or anaphylactic-like allergy to eggs or egg proteins should not be administered these vaccines.

Previously, it was thought that patients with a history of anaphylactic reactions following ingestion of eggs were at increased risk for serious reactions following measles- or mumps-containing vaccines because they are grown in chick embryo fibroblast tissue culture. However, the risk for serious allergic reactions such as anaphylaxis following administration of measles- or mumps-containing vaccines is actually extremely low in this population.<sup>1</sup> Therefore, skin-testing or desensitization to egg protein is not required before administering MMR in patients who are allergic to eggs. Rubella and varicella vaccines are grown in human diploid cell cultures and can safely be administered to persons with histories of severe allergy to eggs or egg proteins.<sup>13</sup>

The rare serious allergic reaction after measles or mumps vaccination or measles, mumps, and rubella (MMR) is not believed to be caused by egg antigens, but by other components of the vaccine (e.g., gelatin). MMR, its component vaccines, and other vaccines contain hydrolyzed gelatin as a stabilizer. Extreme caution should be exercised when administering vaccines that contain gelatin to persons who have a history of an anaphylactic reaction to gelatin or gelatin-containing products. Before administering gelatin-containing vaccines to such persons, skin testing for sensitivity to gelatin can be considered. However, no specific protocols for this approach have been published.<sup>14-17</sup>

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