CME CREDIT ***EDUCATIONAL OBJECTIVES:*** Readers will vaccinate patients in special populations according to guidelines

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Vaccinating adults who are pregnant, older, or immunocompromised, or have chronic kidney disease

ABSTRACT

Patients who have special vaccination needs include pregnant women, people over age 60, people with kidney disease, people with compromised immunity due to underlying illness or medications, and international travelers. By being aware of these needs and implementing a strategy for vaccination, physicians can reduce the rate of vaccine-preventable infections. This article reviews the vaccine requirements in these groups.

KEY POINTS

Avoid live-attenuated vaccines (influenza, varicella, zoster, measles-mumps-rubella, and yellow fever) in immunocompromised patients.

Tetanus, diphtheria, and acellular pertussis (Tdap) vaccine is now recommended for pregnant women during each pregnancy, preferably at 27 to 36 weeks of gestation.

Zoster vaccine is recommended for patients age 60 and older, regardless of earlier episodes of herpes zoster.

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Most vaccinations are given during childhood, but some require boosting during adulthood or are indicated for specific patient populations such as international travelers or those with certain medical conditions. Although generally safe, some vaccines contain live, attenuated organisms that can cause disease in immunocompromised patients. Thus, knowledge of the indications for and contraindications to specific vaccinations is critical to protect adults in special circumstances who are at risk.

See related commentary, page 348

Vaccines have helped eliminate or significantly reduce the burden of more than a dozen illnesses.[1–3] The Advisory Committee on Immunization Practices (ACIP) of the US Centers for Disease Control and Prevention (CDC) makes recommendations about vaccinations for normal adults and children as well as for certain groups at high risk of vaccine-preventable infections.[4] **TABLES 1 AND 2** summarize the recommendations for vaccination by medical condition.[4] In addition, several applications are available online, including downloadable apps from the (**www.cdc.gov/vaccines/schedules/Schedulers/adult-scheduler.html**) and the American College of Physicians (**http://immunization.acponline.org/app/**).

HUMANITY'S GREATEST ADVANCES IN PREVENTING INFECTIOUS DISEASE

Immunization and improved sanitation are humanity's greatest advances in preventing sickness and death from infectious diseases. Since Jenner's discovery in 1796 that milk-

TABLE 1

Inactivated vaccines based on underlying medical condition or special circumstances

Inactivated vaccine	Special population [a]					
	Pregnancy	Immunocompromised (not HIV)	HIV, CD4 count ≥ 200/μL	HIV, CD4 count < 200/μL	Age 60 or older	Chronic kidney disease
Pneumococcal 13-valent conjugate (PCV13)	Safety not established	One dose [b]	One dose [b]	One dose [b]	Indicated for patients age 65 or older [b]	One dose (chronic kidney disease or nephrotic syndrome) [b]
Pneumococcal polysaccharide (PPSV23)	Safe in 2nd or 3rd trimester [c]	One or two doses [b]	One or two doses [b]	One or two doses [b]	Indicated for patients age 65 or older [b]	One or two doses (chronic kidney disease or nephrotic syndrome) [b]
Inactivated influenza	One dose annually	One dose annually	One dose annually	One dose annually	One dose annually	One dose annually
Hepatitis B	Three-dose (Recombivax) or four-dose (Engerix) series [c,d]	Three-dose (Recombivax) or four-dose (Engerix) series [c,d]	Three-dose (Recombivax) or four-dose (Engerix) series [d]	Three-dose (Recombivax) or four-dose (Engerix) series [d]	Three-dose (Recombivax) or four-dose (Engerix) series [c,d]	Three-dose (Recombivax) or four-dose (Engerix) series [b,d]
Tetanus, diphtheria, acellular pertussis (Td/Tdap)	One dose in each pregnancy preferably during 27–36 weeks of gestation	One-time dose of Tdap for Td booster, then Td every 10 years	One-time dose of Tdap for Td booster, then Td every 10 years	One-time dose of Tdap for Td booster, then Td every 10 years	One-time dose of Tdap for Td booster, then Td every 10 years	One-time dose of Tdap for Td booster, then Td every 10 years
***Haemophilus influenzae* type b**	No recommendation	Asplenia, post-HCT recipients only [b]	Three doses if other risk factors present [c]	Three doses if other risk factors present [c]	Three doses if other risk factors present [c]	Three doses if other risk factors present [c]
Meningococcal	One or more doses [c]	Two-dose series for asplenia; otherwise one or more doses based on risk factors [b, c]	One or more doses based on other risk factors [b, c]	One or more doses based on other risk factors [b, c]	One or more doses based on other risk factors [b, c]	One or more doses based on other risk factors [b, c]
Human papillomavirus	Not recommended	Indicated through age 26	Indicated through age 26	Indicated through age 26	Not recommended	Indicated through age 26

[a] See text for immunizing immunocompromised international travelers and household members of immunocompromised patients.
[b] See text for details.
[c] Recommended in the presence of other comorbidities and risk factors including occupational, lifestyle, or travel exposure.
[d] Given to nonimmune patients without past or present hepatitis B infection.

HCT = hematopoietic stem cell transplantation; HIV = human immunodeficiency virus

TABLE 2

Live vaccines, based on underlying medical condition or special circumstances

	Special population [a]					
Live vaccines	**Pregnancy**	**Immunocompromising condition (not HIV)[b,c]**	**HIV, CD4 count ≥ 200/µL, asymptomatic**	**HIV, CD4 count < 200/µL**	**Age 60 and older**	**Chronic kidney disease**
Live-attenuated influenza	Contraindicated	Contraindicated	Contraindicated	Contraindicated	Not approved	Contraindicated in kidney failure
Varicella	Contraindicated	Contraindicated	Indicated if no evidence of previous infection or vaccination	Contraindicated	Indicated if no evidence of previous infection or vaccination	Indicated if no evidence of previous infection or vaccination
Zoster	Contraindicated	Contraindicated	No recommendation	Contraindicated	One dose [c]	Indicated if over age 60
Measles-mumps-rubella	Contraindicated	Contraindicated	Indicated if no evidence of previous infection or vaccination	Contraindicated	Consider patient immune if born before 1957	Indicated if no evidence of previous infection or vaccination
Yellow fever	Use caution May be given in high-risk exposure [c]	Contraindicated	Use caution May be given in high-risk exposure [c]	Contraindicated	Indicated in high-risk exposure	No data, use caution

[a] See text for immunizing immunocompromised international travelers and household members of immunocompromised patients.
[b] Patients with asplenia may receive live vaccines if other requirements are met.
[c] See text for details.
HIV = human immunodeficiency virus

maids who had contracted cowpox (vaccinia) were immune to smallpox, vaccination has eliminated smallpox, markedly decreased the incidence of many infectious diseases, and, most recently, shown efficacy in preventing cervical cancer (with the human papillomavirus vaccine) and hepatocellular cancer (with the hepatitis B vaccine).[1–3]

Unfortunately, vaccination rates remain low for most routine vaccinations indicated for adults. For example, about 60% of adults over age 65 receive pneumococcal vaccination, and fewer than 10% of black patients over age 60 receive zoster vaccination.[5] Various factors may account for these low rates, including financial disincentives.[6]

Nevertheless, vaccination remains one of medicine's most effective defenses against infectious diseases and is especially important in the special populations discussed below. By being steadfast proponents of vaccination, especially for the most vulnerable patients, physicians can help ensure the optimum protection for their patients.

VACCINATING PREGNANT PATIENTS

When considering vaccination during pregnancy, one must consider the risk and benefit of the vaccine and the risk of the disease in both the mother and the child.

In general, if a pregnant woman is at high

risk of exposure to a particular infection, the benefits of vaccinating her against it outweigh the risks. Vaccinating the mother can also protect against certain infections in early infancy through transfer of vaccine-induced immunoglobin G (IgG) across the placenta.[7] In general, inactivated vaccines are considered safe in pregnancy, while live-attenuated vaccines are contraindicated.[4] Special considerations for pregnant women include:

Tetanus, diphtheria, and acellular pertussis (Tdap). One dose of Tdap vaccine should be given during each pregnancy, preferably at 27 to 36 weeks of gestation, regardless of when the patient received a previous dose.[8]

Inactivated influenza vaccine should be given as early as possible during the influenza season (October to March) to all pregnant women, regardless of trimester.

Inactivated polio vaccine may be considered for pregnant women with known exposure to polio or travel to endemic areas.

Hepatitis A, hepatitis B, pneumococcal polysaccharide, meningococcal conjugate, and meningococcal polysaccharide vaccines can be given to women at risk of these infections. If a pregnant patient requires pneumococcal polysaccharide vaccine, it should be given during the second or third trimester, as the safety of this vaccine during the first trimester has not been established.[9]

Give inactivated influenza vaccine to all pregnant women as early as possible in the season, regardless of trimester

Smallpox, measles-mumps-rubella, and varicella-containing vaccines are contraindicated in pregnancy. Household contacts of a pregnant woman should not receive smallpox vaccine, as it is the only vaccine known to cause harm to the fetus.[10]

Human papillomavirus vaccination is not recommended during pregnancy.

Yellow fever live-attenuated vaccine. The safety of this vaccine during pregnancy has not been established, and it is in the US Food and Drug Administration (FDA) pregnancy category C. However, this vaccine is required for entry into certain countries, and it may be offered if the patient is truly at risk of contracting yellow fever. Because pregnancy may affect immunologic response, serologic testing is recommended to document an immune response. If the patient's itinerary puts her at low risk of yellow fever, then writing her a vaccine waiver letter can be considered.[11]

VACCINATING IMMUNOCOMPROMISED PATIENTS (NON-HIV)

People who do not have human immunodeficiency virus (HIV) but have a condition such as functional asplenia (sickle cell disease), anatomic asplenia, or complement component deficiency are at higher risk of infection with the encapsulated bacteria *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type b.

Corticosteroids, chemotherapy, radiation for hematologic or solid-organ malignancies, and immune modulators can alter the immune system and pose a risk with the use of live-attenuated vaccines. A corticosteroid dosage equivalent to 2 mg/kg of body weight per day or higher or 20 mg/day of prednisone or higher is generally considered immunosuppressive.

Candidates for organ transplantation should receive vaccinations as early as possible during the disease course leading to transplantation. Vaccinations should be given as soon as the decision is made that the patient is a candidate for transplantation, which could be years or months before the patient actually receives the transplant. In addition to reviewing previously administered vaccinations, pretransplant serologic testing for hepatitis B, varicella, measles, mumps, and rubella antibodies helps to evaluate the need for vaccination.[12]

Recipients of hematopoietic stem cell transplantation are at risk of infections with encapsulated bacteria and certain other vaccine-preventable infections. Antibody titers are significantly reduced after stem cell transplantation because of ablation of bone marrow, and thus certain vaccines should be readministered 3 to 6 months after transplantation (eg, influenza, pneumococcal, and *H influenzae* vaccines). If the recipient is presumed to be immunocompetent, then varicella or measles-mumps-rubella vaccine can be given 24 months after transplantation.[13]

Apart from adhering to the routine vaccination schedule and avoiding live-attenuated vaccines, specific recommendations apply to persons with immunocompromising conditions[14]:

Quadrivalent meningococcal conjugate vaccine should be given to adults of all ages with asplenia or complement component de-

ficiency. The schedule includes two doses at least 2 months apart initially and then revaccination every 5 years.

***H influenzae* type b vaccine** should be given to people with asplenia and recipients of hematopoietic stem cells. One dose is recommended for those with asplenia (functional, anatomic, or elective splenectomy) or sickle cell disease if they have not already received it. A three-dose schedule is considered for hematopoietic stem cell transplant recipients 6 to 12 months after successful transplantation.

Pneumococcal conjugate (PCV13) and pneumococcal polysaccharide (PPSV23) vaccinations are recommended for people who have immunocompromising conditions. PCV13, the newer pneumococcal vaccine, was approved by the FDA in 2010 for use in children and was recommended by the ACIP in 2012 for adults age 19 and older with immunocompromising conditions.

People who have not previously received either of these vaccines and are age 19 or older with immunocompromising conditions including asplenia, chronic renal failure, nephrotic syndrome, cerebrospinal fluid leakage, or cochlear implant should receive a single dose of PCV13 followed by a dose of PPSV23 at least 8 weeks later. One-time revaccination 5 years after the first dose of PPSV23 is recommended for patients with immunocompromising conditions.

For those who have previously been vaccinated with PPSV23, a dose of PCV13 can be given 1 or more years after the last dose of PPSV23. These dosing intervals are important, as lower opsonophagocytic antibody responses have been noted if repeat doses of either pneumococcal vaccine are given sooner than the recommended interval.[15]

Inactivated influenza vaccine is recommended annually, except for patients who are unlikely to respond or those who have received anti-B-cell antibodies within 6 months. Live-attenuated influenza vaccine should not be given to immunocompromised patients.

VACCINATING PATIENTS WHO HAVE HIV

People with HIV should be routinely screened for immunity against certain infections and should be offered vaccination if not immune. The response to vaccines may vary depending on the CD4 count, with a good response in patients whose infection is well controlled with antiretroviral agents and with a preserved CD4 count.[16] Special considerations for HIV patients include the following:

Hepatitis A vaccine may be offered to all HIV patients who have no evidence of immunity against hepatitis A, with negative anti-hepatitis A total and IgG antibodies.

Human papillomavirus vaccine is recommended for men and women with HIV through age 26.

Varicella and measles-mumps-rubella are live-attenuated vaccines and may be considered in patients who are nonimmune and with CD4 counts of 200 cells/μL or higher. However, the ACIP does not make a recommendation regarding the **zoster** vaccine in HIV patients with CD4 cell counts of 200 cells/μL or higher. In general, live-attenuated vaccines should be avoided in patients with CD4 counts less than 200 or with severe immunocompromised status because of risk of acquiring severe, life-threatening infections.

Pneumococcal vaccine should be given to HIV patients if they have not received it before. The schedule is one dose of PCV13, followed by a dose of PPSV23 at least 8 weeks later. If a patient has been previously vaccinated with PPSV23, then PCV13 is recommended at least 1 year after PPSV23.

Antibody responses are lower if pneumococcal vaccine doses are repeated too soon

Inactivated influenza vaccine is recommended annually. Live-attenuated influenza vaccine should not be given.

Hepatitis B vaccine should be given to nonimmune patients without past or present hepatitis B infection. These patients require higher doses of hepatitis B vaccine (40 μg/mL) than immunocompetent patients, who receive 20 μg/mL. The options include Recombivax HB 40 μg/mL given on a three-dose schedule at 0, 1, and 6 months, and Engerix B, two 20-μg/mL injections given simultaneously on a four-dose schedule at 0, 1, 2, and 6 months.

Meningococcal vaccine. HIV infection is not an indication for meningococcal vaccine unless the patient has other risk factors, such as anatomic or functional asplenia, persistent complement component deficiency, occupational exposure, and travel to endemic areas.

VACCINATING PATIENTS WHO ARE OLDER THAN 60

The immune system deteriorates with age, as does immunity gained from previous vaccinations. Vaccination in this age group reduces the risk of illness and death.[17]

Zoster vaccine should be offered to people age 60 and older regardless of previous episodes of herpes zoster unless there is a contraindication such as severe immunodeficiency. The zoster vaccine can reduce the incidence of postherpetic neuralgia by 66.5% and herpes zoster by 51% in patients over age 60.[18]

Pneumococcal conjugate vaccine. PCV13 should be offered to all adults age 65 or older. If a person age 65 or older has not received any pneumococcal vaccine before then, PCV13 should be given first, followed by a dose of PPSV23 at least 6 to 12 months after PCV13.

Pneumococcal polysaccharide vaccine. If PPSV23 was given before age 65 for another indication, a dose of PCV 13 should be given at age 65 or later, as long as 6 to 12 months have passed since the previous dose of PPSV 23. The patient should receive the last dose of PPSV23 vaccine 5 years after the first dose of PPSV23.[4]

Offer zoster vaccine to patients older than 60 years, regardless of prior episodes

Influenza vaccine. People 65 or older are at higher risk of complications from influenza, and vaccine should be offered annually. High-dose inactivated influenza vaccine can be used in this age group.[4]

Tdap. If never given before, Tdap is recommended regardless of the interval since the most recent Td vaccination, followed by a Td booster every 10 years.

VACCINATING PATIENTS WHO HAVE CHRONIC KIDNEY DISEASE

Patients with chronic kidney disease are at risk of certain infections, so vaccination is an important preventive measure.[19] Immunizations should be offered to all patients with chronic kidney disease regardless of the disease stage, but they are recommended during the early stages of progressive renal disease to increase the likelihood of vaccine-induced immunity.[20]

Pneumococcal conjugate vaccine. PCV13 is recommended for adults 19 or older with chronic renal disease or nephrotic syndrome. One dose of PCV13 should be given, followed by a dose of PPSV23 at least 8 weeks later. If the patient has been previously vaccinated with PPSV23, then PCV13 at least 1 year after PPSV23 is recommended.

Hepatitis B vaccine should be given to nonimmune patients without past or present hepatitis B infection. Adult patients on hemodialysis require higher doses of hepatitis B vaccine. The options include Recombivax HB 40 µg/mL given on a three-dose schedule at 0, 1, and 6 months, and Engerix B, two 20-µg/mL injections given simultaneously on a four-dose schedule at 0, 1, 2, and 6 months.

Influenza vaccine should be offered annually to patients with chronic kidney disease.

VACCINATING IMMUNOCOMPROMISED INTERNATIONAL TRAVELERS

International travel for business or pleasure is increasingly common, and immunocompromised patients require specific attention as they may face unanticipated pathogens or have special requirements. Transplant recipients should ideally receive routine and travel-related vaccines as early as possible before transplantation. Vaccination is generally avoided in the first 6 months after organ transplantation to avoid confusion with early graft dysfunction or rejection.[21] However, it should be considered as soon as a patient develops an illness that might lead to transplantation.

Evaluation of patients for vaccination should include an assessment of the travel-specific epidemiologic risk, the nature of the vaccine (live-attenuated or other), and the immune status. As discussed above, live-attenuated vaccines should be avoided in immunocompromised patients, and thus the injectable typhoid vaccine should be given in lieu of the attenuated oral vaccine.

Yellow fever vaccine is required before entrance to certain countries but should not be given to immunocompromised patients, although it can probably be given to asymptomatic HIV-infected adults with a CD4 count higher than 200 cells/µL who are exposed to substantial risk.[22] For patients who cannot receive the vaccine, some governments will accept a physician's letter stating the patient has a contraindication to vaccination.

VACCINATING HOUSEHOLD MEMBERS OF IMMUNOCOMPROMISED PATIENTS

Protecting immunocompromised patients from infectious diseases involves vaccinating not only the patient but also household members so that they do not acquire infections and then bring them into the household. Immunocompetent members of a household can receive inactivated vaccines based on the recommended ACIP schedule.

Annual inactivated influenza vaccination is recommended, although the live-attenuated influenza virus vaccine can be substituted if the immunocompromised patient is not within 2 months of hematopoietic stem cell transplantation, does not have graft-vs-host disease, and does not have severe combined immune deficiency.

Other live-attenuated vaccines can usually be given if indicated, including measles-mumps-rubella vaccine, rotavirus vaccine in infants, varicella vaccine, and zoster vaccine.[14]

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