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# Immunizations in adult immunocompromised patients: Which to use and which to avoid

## ABSTRACT

Immunization is important to protect immunocompromised patients from preventable infectious disease but is often underused. Although live vaccines are contraindicated for most immunocompromised patients, many killed or component vaccines are safe and recommended. Vaccines may sometimes induce suboptimal immunogenicity, but even partial protection may benefit severely ill patients.

## KEY POINTS

Vaccines against *Streptococcus pneumoniae* and influenza are strongly recommended for most immunosuppressed patients.

When possible, immunization series should be completed before procedures that require or induce immunosuppression, such as organ transplantation or chemotherapy. If this is not possible, the patient may mount only a partial immune response, but even this partial response can be beneficial.

Patients who undergo allogeneic bone marrow transplantation lose preexisting immunities against a variety of diseases and should be revaccinated.

In many situations, family members should be vaccinated to protect the patient. However, oral live polio vaccine should be avoided because it may carry the risk of infecting the patient.

**I**MMUNOCOMPROMISED PATIENTS are particularly susceptible to infectious diseases, but they may not always receive the vaccines they need for protection. Reasons for underuse of vaccination include concerns about possible adverse effects, higher priority placed on managing active clinical problems than on prevention, and a belief that vaccination is not worthwhile because immunocompromised patients often respond only partially to vaccination.

But in fact, many killed vaccines or vaccines made from pathogen components are safe, well tolerated, and highly recommended for those with compromised immunity (TABLE 1). In some situations in which patients cannot receive a certain vaccine (TABLE 2), the risk of disease can be reduced by immunizing family members and health-care workers. Postexposure prophylaxis may also be indicated for many immunocompromised patients (TABLE 3). For patients in whom immunosuppression is planned, immunizations can be given in advance.

This article is a brief discussion of a complex topic. For greater detail, consult recent comprehensive review articles<sup>1-4</sup> and guidelines on immunizations<sup>5,6</sup> and vaccine adverse effects<sup>7</sup> from the Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices. Comprehensive recommendations for vaccination and postexposure prophylaxis are also found in the American Academy of Pediatrics' *Red Book*<sup>8</sup> and the American Public Health Association's *Control of Communicable Diseases Manual*.<sup>9</sup> Also helpful are recent recommendations for

TABLE 1

**General vaccinations recommended for immunocompromised adults**

VACCINE	SCHEDULE	CANDIDATES
Influenza	Yearly	All patients
Pneumococcal	Every 2–5 years*†	All patients
Tetanus-diphtheria toxoid	Booster every 10 years	All patients
<i>Hemophilus influenzae</i> B	Single dose†	Patients with asplenia, HIV, Hodgkin disease
Hepatitis A	2-dose series	High-risk patients; patients during outbreaks; travelers
Hepatitis B	3-dose series	At-risk or pretransplant patients
Meningococcal	Single dose†	Patients with asplenia, terminal complement deficiencies; travelers; college students

\*Some clinicians follow current recommendations for nonimmunocompromised adults (every 6 years); give one dose at least 2 weeks before splenectomy if possible

†Titers may be followed in high-risk patients

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**Most killed, inactivated, component, and recombinant vaccines are safe**

immunizations in dialysis patients<sup>10</sup> and for revaccination of patients after bone marrow transplantation.<sup>11</sup>

#### ■ KILLED VACCINES ARE GENERALLY SAFE

Killed, inactivated, component, and recombinant vaccines cannot cause infection and are generally safe for immunocompromised patients. Anecdotal reports and small case series of flares of preexisting rheumatologic disease or new onset of rheumatologic disease after vaccination have not been substantiated in larger studies.<sup>4</sup>

In contrast, live vaccines are almost always contraindicated in immunocompromised patients. Live vaccines include the oral polio, measles-mumps-rubella (MMR), varicella, and oral typhoid vaccines and the *Bacillus Calmette-Guérin* (BCG) vaccine for tuberculosis.

However, there are three primary exceptions to the general contraindication of live vaccines in immunocompromised patients:

- The CDC recommends the MMR vaccine for some patients with human immunode-

ficiency virus (HIV) infection.<sup>6</sup>

- The CDC also recommends that bone marrow transplant recipients be revaccinated with the MMR 24 months or more after the transplantation if they have no graft-versus-host disease and are not receiving immunosuppressive therapy.<sup>11</sup>
- Children can receive live virus vaccines during corticosteroid treatment if they are receiving less than 2 mg/kg/day of prednisone, or less than 20 mg/day if they weigh more than 10 kg, according to the American Academy of Pediatrics' *Red Book*.<sup>8</sup>

#### ■ SUBOPTIMAL RESPONSES MAY STILL BE HELPFUL

Patients receiving immunosuppressive therapies such as cytotoxic chemotherapy, steroids in high doses, or cyclosporine may mount a suboptimal response to certain vaccines. For this reason, candidates for transplants or chemotherapy should have their vaccine series completed or updated beforehand if possible.



TABLE 2

### Vaccines not currently recommended for immunocompromised patients

VACCINE	COMMENTS
Adenovirus	Used in military recruits
Bacillus Calmette-Guérin	
Live oral typhoid (Ty21a)	
Measles-mumps-rubella	May be given to some patients with HIV and children on lower-dose steroids*; indicated for revaccinating bone marrow transplant patients
Live oral polio	Also contraindicated for household contacts, who should receive inactivated polio vaccine†
Smallpox (Vaccinia)	
Varicella	May be given to children receiving low doses of steroids* or those with early HIV
Yellow fever	

\*Less than 2 mg/kg/day prednisone, or less than 20 mg/day in patients weighing more than 10 kg

†If oral polio vaccine is inadvertently given to a household contact, then close contact between the vaccine recipient and the immunocompromised person should be minimized for 4 to 6 weeks<sup>9</sup>

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### Live vaccines are usually contraindicated

However, even partial protection can be useful in fragile, severely immunocompromised patients. In addition, to protect the patient, health care workers and household contacts must also be vaccinated against easily transmissible diseases such as influenza.

#### VACCINES AGAINST BACTERIAL PATHOGENS

##### Pneumococcal vaccine: Strongly recommended

**Vaccine type.** The pneumococcal vaccine is a component vaccine composed of the capsular polysaccharides of the 23 most common serotypes of *Streptococcus pneumoniae*.

**In immunocompromised patients,** vaccination against *S pneumoniae* is critical for three reasons:

- These patients are at high risk for pneumococcal diseases, which include severe pneumonia, meningitis, bacteremia, and occasionally other focal infections such as empyema, pericarditis, and endocarditis.
- Patients with asplenia or B-cell or plasma

cell disorders and bone marrow transplant recipients are particularly susceptible.

- The prevalence of antibiotic resistance among pneumococcal organisms is increasing, so it may be difficult to treat an infection once the patient has contracted it.

**Frequency of administration.** The effectiveness of any vaccine can be estimated by measuring antibody titers. Pneumococcal titers wane with time,<sup>12,13</sup> and current recommendations are to repeat a dose every 6 years in adults. Because titers may wane more rapidly in immunocompromised recipients,<sup>1</sup> some clinicians recommend repeating the pneumococcal vaccine every 2 to 3 years in these patients. The *Red Book*<sup>8</sup> recommends repeating it every 3 to 5 years in patients at high risk, although controlled data for this strategy are lacking. Revaccination of bone marrow transplant recipients is recommended.<sup>11</sup>

**Efficacy is variable.** Studies of immunogenicity in immunocompromised patients have found generally good but sometimes suboptimal responses. The CDC recommends the vaccine be given, even though the response

**TABLE 3****Postexposure prophylaxis for immunocompromised patients**

DISEASE	PROPHYLAXIS
<i>Hemophilus influenzae</i> B invasive infection	Rifampin 20 mg/kg/day (maximum 600 mg/day) for 4 days
Hepatitis A	Immune globulin 0.02 mL/kg intramuscularly within 2 weeks of exposure May give hepatitis A vaccine simultaneously at a separate site
Hepatitis B	For percutaneous exposure: hepatitis B immune globulin 0.06 mL/kg or 5 mL for adults as a single intramuscular dose within 24 hours in conjunction with first dose of hepatitis B vaccine; if hepatitis B vaccine cannot be given, a second dose of immune globulin should be given 1 month after the first dose For sexual contact: hepatitis B immune globulin 0.06 mL/kg as a single intramuscular dose within 14 days of contact
Influenza A	Oral amantadine or rimantadine 100 mg twice a day (less frequently for the elderly or those with renal dysfunction); indicated during outbreaks or within 48 hours of symptoms
Measles	Intramuscular immune globulin 0.5 mL/kg up to 15 mL within 6 days (0.25 mL/kg for non-immunocompromised patients)
Meningococcal disease	Rifampin 600 mg every 12 hours for 2 days Or ciprofloxacin 500 mg (single dose) Or ceftriaxone 250 mg (single intramuscular injection)
Rabies	Human rabies immune globulin 20 IU/kg in a single dose; if possible, half the dose should be infiltrated around the wound and the other half given intramuscularly The human diploid cell rabies vaccine is given concomitantly
Tetanus	Tetanus immune globulin 250 U by intramuscular injection for tetanus-prone wounds in patients who have not completed a primary series or whose vaccination has expired Used in conjunction with tetanus-diphtheria booster or primary series
Varicella	Varicella-zoster immune globulin 125 U/10 kg up to 625 U intramuscularly as soon as possible within 96 hours

Specific recommendations for postexposure prophylaxis after inadvertent administration of live-virus vaccines to an immunocompromised person are not available; consultation with the Centers for Disease Control and Prevention may be helpful (1-404-639-3311 or 1-404-332-4555)

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**After sexual contact, give hepatitis B immune globulin 0.06 mL/kg IM within 2 weeks**

may not be optimal in all patients. For patients at very high risk, such as bone marrow transplant recipients and those without a spleen, specific pneumococcal titers may be measured to assess response and may be followed over time.<sup>14</sup>

To avoid suboptimal responses, it is important to give the pneumococcal vaccine 2 weeks or more before a scheduled splenectomy.<sup>8</sup> If, however, splenectomy must be done with less than 2 weeks' notice, it is still helpful to give the pneumococcal vaccine, as many



splenectomized adults and children without underlying cancer can develop adequate titers.<sup>1</sup> A checklist for splenectomy patients has been recommended to assure that vaccination occurs in a timely fashion.<sup>15</sup>

Similarly, patients with Hodgkin disease should receive the vaccine at least 1 and preferably 2 weeks before starting chemotherapy.<sup>8</sup>

Indirect evidence for the vaccine's efficacy in immunocompromised patients was provided by a study showing that the rare cases of pneumococcal sepsis that occurred in vaccinated patients were caused by unusual serotypes that had not been included in the vaccine.<sup>16</sup> However, splenectomized patients, even those who are fully vaccinated, should be advised to seek medical treatment promptly for any febrile illness, as vaccination is not a guarantee against overwhelming postsplenectomy sepsis.<sup>8</sup>

**In the general population,** patients who should receive the pneumococcal vaccine include:

- The elderly (age 65 and over)
- Patients with chronic heart or lung disease
- Patients with anatomic or functional asplenia caused by factors such as sickle cell disease
- Alcoholic patients
- Others with risk factors for severe pneumococcal infection.

#### ***Haemophilus influenzae* type B vaccine:** Recommended for some patients

**Vaccine type.** The vaccine is a conjugated polysaccharide vaccine.

**In immunocompromised patients.** Although most adults already have antibodies against *Haemophilus influenzae* type B (HIB), this vaccination is helpful in certain groups, as immunocompromised patients occasionally develop invasive HIB disease. Asplenic patients, patients with B-cell or plasma cell disorders, and bone marrow transplant recipients are particularly susceptible to infections from encapsulated organisms such as *H influenzae* and *S pneumoniae*. The HIB vaccine should be given to adults as part of a revaccination program after allogeneic bone marrow transplantation<sup>11</sup> and is also recommended for patients with functional asplenia, HIV infec-

tion, and Hodgkin disease (at least 1 to 2 weeks before chemotherapy if possible).<sup>1</sup> Some clinicians give HIB vaccine in addition to the pneumococcal vaccine before splenectomy.<sup>1,8</sup>

**Frequency of administration.** The optimal interval for revaccination in adults at high risk is not known; some clinicians follow titers as a guide to revaccination.

**In the general population,** HIB vaccination is of crucial importance in infants. Invasive HIB disease in children has decreased sharply since the advent of universal infant vaccination. However, vaccination is not generally performed in healthy adults because most are already seropositive for HIB, and most *H influenzae* disease in adults is caused by nontypable strains against which the HIB vaccine does not protect.

#### **Meningococcal vaccine:** Recommended for some patients

**Vaccine type.** This component vaccine is made from capsular polysaccharides of several organism strains.

**In immunocompromised patients,** meningococcal vaccine has traditionally been indicated for asplenic patients and patients with deficiencies of the terminal components of complement. Recently, clinicians have recommended giving meningococcal vaccine to immunocompromised college students or others who may be at increased risk of exposure.

Some clinicians give meningococcal vaccine 2 weeks before a scheduled splenectomy, as they do for pneumococcal vaccine. The *Red Book*<sup>8</sup> recommends vaccinating previously unimmunized splenectomized children against meningococcus if they are older than 2 years. In patients with Hodgkin disease, the vaccine should preferably be given at least 1 to 2 weeks before starting chemotherapy to optimize the response.

**Frequency of administration.** Revaccination in 3 to 5 years may be required if antibody titers decline, but controlled data are lacking.

**In the general population,** meningococcal vaccine is indicated for travelers to endemic areas, military recruits, and people at risk during outbreaks. New guidelines were published in 2000, which recommend it for college freshmen, as well.<sup>17</sup>

**Meningococcal vaccine is indicated for asplenic patients**



### **Tetanus-diphtheria vaccine is safe**

**Vaccine type.** The tetanus-diphtheria (Td) vaccine is a toxoid (inactivated bacterial toxin).

**In immunocompromised patients,** the tetanus-diphtheria vaccine appears to be safe, well tolerated, and relatively immunogenic. Anecdotal reports of rejection in solid-organ transplant recipients have not been substantiated in larger studies. All immunocompromised patients, like healthy adults, should receive booster doses of tetanus-diphtheria vaccine at least every 10 years to maintain immunity. Revaccination of bone marrow transplant recipients is recommended.<sup>11</sup>

**In the general population.** Tetanus still occurs in the United States, though uncommonly, and remains endemic in many parts of the world. Outbreaks of diphtheria have occurred recently in various areas, including the countries of the former Soviet Union. Cutaneous diphtheria outbreaks have occurred among crowded and indigent populations in the United States.

The diphtheria, tetanus, and pertussis vaccines are combined for administration to children. Adults who have completed a primary series should receive the tetanus-diphtheria booster every 10 years, whereas adults who have never received this vaccine should be given a three-dose series. People with deep, tetanus-prone wounds should receive a booster if they have not had one within 5 years, or a series along with tetanus immune globulin if they have never been vaccinated or if their previous vaccination has lapsed.

### **Lyme disease vaccine:**

#### **Unknown risks and benefits**

**Vaccine type.** Lyme disease vaccine is a recombinant vaccine.

**In immunocompromised patients,** the safety and efficacy of the Lyme disease vaccine are unknown. Data are too preliminary to make a specific recommendation. Immunocompromised patients should be counseled to avoid tick-infested areas and to wear protective clothing and insect repellent in wooded or grassy areas.

**In the general public,** the vaccine appears to be safe and at least moderately effective in healthy persons who live and work in high-risk areas (tick-infested wooded or grassy

areas), particularly those with outdoor occupations. It may be given to patients who have had previously resolved episodes of Lyme disease, because they may not have developed protective immunity. However, it is not recommended for patients with treatment-refractory Lyme arthritis who may have increased immunologic reactivity to the Osp-A protein, which forms the basis for the vaccine.<sup>8</sup>

## **■ VACCINES AGAINST VIRAL PATHOGENS**

### **Influenza vaccine: Strongly recommended**

**Vaccine type.** This inactivated component vaccine is prepared each year from components of the two types of influenza A and one type of influenza B predicted to be most prevalent that year.

**In immunocompromised patients.** Influenza can be devastating or even fatal in fragile patients, especially the elderly and those who have received solid organ or bone marrow transplants. Vaccination is thus strongly recommended in immunocompromised people.

**Frequency of administration.** Patients should receive it at least once a year. Some may need two doses: patients at high risk may experience waning immunity, and if they are immunized early in the flu season (which runs from October through March), a second dose may be considered later in the season. One study found that a three-dose series improved vaccine response in heart transplant recipients.<sup>18</sup> Yearly influenza vaccinations should resume at 6 months or more after bone marrow transplantation.<sup>11</sup>

**Vaccinating family members.** Unfortunately, the response to influenza vaccination may not be optimal, particularly in transplant recipients.<sup>19</sup> Therefore, potential contacts, including family members, must be immunized as well. Health care workers should be strongly encouraged to receive the vaccine if they are caring for immunocompromised patients.

**Refuting myths about influenza vaccination.** Although it is safe, important, and effective, influenza vaccination is the subject of myths, which physicians should try to dispel. Encouragement and education are necessary. Patients are much more willing to be vaccinated if their health care providers recommend it.<sup>20</sup>

**Influenza vaccines do not cause flulike illness**



- *Myth: Vaccination will give you the flu.* Even seasoned health care providers have been known to refuse vaccination for fear of developing flulike illness, a concern for which there is no rational basis. Health care providers, patients, and family members must be educated to understand that the vaccine does not cause influenza, and that upper respiratory infections or other viral illnesses occurring after influenza vaccination are not a consequence of the vaccine.
- *Myth: The vaccine is ineffective.* Failure to prevent the common cold or other noninfluenza flulike illnesses does not constitute evidence of vaccine failure.
- *Myth: The vaccine causes Guillain-Barré syndrome.* The association of the 1976 swine flu vaccine with Guillain-Barré syndrome heightened public awareness and concern about possible vaccine side effects. However, no subsequent influenza vaccine preparations have been shown to increase the risk of Guillain-Barré.
- *Myth: Vaccination causes flare-ups of rheumatologic diseases.* Although case reports and small series suggested that influenza vaccination may be associated with flares of underlying or new rheumatologic disease, larger studies have not suggested significant excess risk.<sup>4</sup> Considering the morbidity and mortality that can be prevented by influenza vaccination, the risk-benefit balance appears to favor immunization in rheumatologic patients.

#### **Varicella vaccine: Not recommended for most immunocompromised patients**

**Vaccine type.** This is a live attenuated vaccine.

**In immunocompromised patients,** the varicella vaccine is currently not recommended in most cases, since it is a live-virus vaccine.<sup>8</sup> For many patients, this is not a problem, because approximately 90% of the general adult population is seropositive for varicella and is therefore immune.

Unfortunately, adults who are seronegative for varicella, even if not immunosuppressed, are at higher risk for severe disease than are healthy children. In addition, seronegative immunocompromised patients who acquire primary varicella are subject to

even more severe disease, including pneumonia, encephalitis, and cutaneous and visceral dissemination, with a high mortality rate.<sup>21</sup> An additional problem is that giving varicella-zoster immune globulin after exposure may not be completely protective.<sup>21</sup> Prophylactic use of acyclovir in immunocompromised patients exposed to varicella is supported by small series,<sup>22</sup> but there are no data from controlled trials.

As varicella vaccine is generally not safe for immunocompromised patients, transplantation candidates who are seronegative for varicella should receive this vaccine before transplantation or onset of immunosuppression if at all possible.

**In children.** Although the varicella vaccine is a live vaccine, it was originally tested in children with leukemia in remission, and some studies have suggested that it is safe and effective in some groups of immunocompromised children.<sup>23,24</sup> In fact, the American Academy of Pediatrics states that varicella vaccination should be considered for children with mild HIV (class I) with a CD4 lymphocyte percentage of 25% or greater, and for children who are receiving low doses of steroids.

**Vaccinating the family.** Family members of immunocompromised patients can safely receive the varicella vaccine.<sup>8,9</sup> A seropositive immunocompromised patient (other than a bone marrow transplant recipient) is considered to have lifelong immunity and is not at risk from varicella exposures nor from exposure to a person who has received the vaccine. There may be a very small theoretical risk of transmission from a vaccinated household contact to a seronegative immunocompromised person, especially if the vaccinated person develops a rash, as 7% to 8% do. However, the benefits of protecting the vaccine recipient and the immunocompromised family member outweigh this theoretical consideration, and the American Academy of Pediatrics recommends that the vaccine be given to the family member.<sup>8</sup> It does not recommend giving varicella-zoster immune globulin to the seronegative immunocompromised person if a rash develops in the vaccinated household contact, since transmission would be unlikely and disease would likely be mild.<sup>8</sup> Some clinicians would consider giving acyclovir prophylactically

**Family members can safely receive the varicella vaccine**



cally to the immunocompromised patient in this situation. There is no evidence that exposure to vaccinated persons causes shingles (varicella-zoster) in the varicella-seropositive immunocompromised person.

### **Polio vaccines: Oral is contraindicated; inactivated is safe but rarely needed**

**Vaccine type.** There are two types, the oral polio vaccine, which is a live vaccine and is contraindicated in immunocompromised persons, and the inactivated polio vaccine.

**In immunocompromised patients,** the inactivated polio vaccine appears to be safe and effective, but adults would be unlikely to require a polio booster unless traveling to endemic areas overseas. Revaccination after bone marrow transplantation is recommended.<sup>11</sup>

**Vaccinating the family.** Transmission of vaccine strains of virus from the oral live vaccine to household contacts has also been documented, and therefore household contacts of immunocompromised persons should receive the inactivated polio vaccine rather than the oral vaccine.

**In the general population.** The Advisory Committee on Immunization Practices recommended last year that the inactivated vaccine replace the oral polio vaccine for everyone (except in specific situations such as polio outbreaks)<sup>25</sup>; therefore, the transmissibility of live oral vaccine strains should no longer be an issue.

### **Hepatitis A vaccine: Recommended for some patients**

**Vaccine type.** There are currently two hepatitis A vaccines, both of which are inactivated.

**In immunocompromised patients,** these vaccines are safe, but immunogenicity may be less than optimal in certain immunocompromised patients, including patients with advanced chronic liver disease and particularly liver transplant patients.<sup>26</sup> If possible, patients with liver disease should be vaccinated early in the course of the disease, when response is likely to be better.

Patients with chronic liver disease are at particular risk for fulminant disease if they contract hepatitis A<sup>27</sup> and therefore should be targeted for vaccination. It may also be desir-

able to vaccinate patients who are candidates for other solid organ transplants if they are not already seropositive.

Travelers to endemic areas of the world should also receive hepatitis A vaccine. If travel is to occur in less than 4 weeks, or if postexposure prophylaxis is needed, intramuscular gamma globulin has generally been used.

### **Hepatitis B vaccine: Recommended, especially for dialysis patients and solid organ recipients**

**Vaccine type.** Hepatitis B vaccine is a recombinant vaccine.

**In immunocompromised patients.** The vaccine is effective in healthy persons but may produce a suboptimal response in patients who are immunocompromised, undergoing dialysis, alcoholic, or diabetic. Enhanced-potency vaccines and, in some cases, additional doses may produce better results.<sup>1,4,28-34</sup> Some studies found the response rates before transplantation to be better than after transplantation,<sup>33</sup> but others found no difference between the effectiveness of vaccination during end-stage liver disease and after transplantation.<sup>34</sup>

**In transplant recipients.** Hepatitis B is of particular concern for patients scheduled to receive transplants of solid organs other than the liver. Recipients who are hepatitis B-seronegative may be offered an organ from a donor who is negative for hepatitis B surface antigen but positive for core antibody. All potential recipients should be vaccinated well beforehand to make it safe for them to receive such organs.

Hepatitis B core antibody-positive donor livers are not used for transplantation, but it is desirable for seronegative liver transplant candidates to become immune to hepatitis B in any case. Dialysis patients have traditionally had a high risk for hepatitis, though modern infection control practices have diminished the risk, and ideally, dialysis patients who are seronegative should be immunized, possibly with an enhanced-potency hepatitis B vaccine.<sup>1,10</sup> In patients at high risk, titers should be monitored periodically, and revaccination considered when necessary.<sup>10</sup>

Other immunocompromised patients may also benefit from the hepatitis B vaccine, espe-

**Oral polio vaccine is contraindicated in immunocompromised persons and their families**



TABLE 4

### Vaccines for immunocompromised patients who plan international travel

VACCINE	COMMENTS*
Inactivated polio	Primary series or booster
Hepatitis A	2-dose series
Hepatitis B	3-dose series; especially for patients planning long-term residence overseas
Meningococcal	At-risk areas
Vi polysaccharide typhoid	At-risk areas
Rabies	At-risk areas
Plague	At-risk areas (unusual)
Anthrax	At-risk areas (unusual)
Japanese encephalitis	At-risk areas

\*Specific recommendations vary with the individual and the destination; consult a travel medicine clinic or the Centers for Disease Control and Prevention for vaccinations, malaria prophylaxis, and other advice

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cially if they are likely to receive blood products frequently. Travelers to endemic areas for more than short visits should receive hepatitis B vaccine. Reimmunization after bone marrow transplantation is recommended.<sup>11</sup>

**Adverse effects.** Adverse effects of hepatitis B vaccine have included rare cases of erythema nodosum and reactive arthritis.<sup>4</sup> Recently, three cases of possible vaccine-associated vasculitis were reported,<sup>35</sup> but the causal relationship is not proven, and they have not led to changes in current recommendations for the hepatitis B vaccine.

Two recent large studies showed that hepatitis B vaccine does *not* increase the risk of developing multiple sclerosis or of flares in patients with preexisting multiple sclerosis.<sup>36,37</sup>

#### Measles-mumps-rubella vaccine: Contraindicated, with several exceptions

**Vaccine type.** The MMR is a live vaccine.

**In immunocompromised patients,** this vaccine is not recommended, with the following exceptions: patients with early HIV,<sup>6</sup> bone marrow transplant recipients without graft-versus-host disease at 24 months, and children

who are receiving low doses of corticosteroids (prednisone < 2 mg/kg/day or < 20 mg/day if weight is > 10 kg).<sup>6-8</sup> Unlike oral polio vaccine strains, MMR strains are not transmitted to household contacts of the vaccine recipient, so it is not necessary for household contacts of immunocompromised patients to postpone MMR vaccination.<sup>7,8</sup>

**Adverse effects.** Adverse effects of the rubella vaccine have generated interest because of cases of vaccine-associated arthritis reported in women.<sup>38</sup> However, the devastating consequences of congenital rubella syndrome have continued to provide a strong reason for maintaining high levels of immunity to rubella in the general population.

**Postexposure prophylaxis.** If a nonimmune immunocompromised patient is exposed to measles, postexposure prophylaxis with intramuscular immune globulin is indicated within 6 days of exposure.<sup>9</sup>

### VACCINES FOR INTERNATIONAL TRAVEL

Immunocompromised patients considering international travel should visit a travel clinic well before the planned trip. A thorough discussion may reveal that the risks outweigh the benefits for a given patient, which may lead to a change in travel plans. A pretravel visit will also allow the travel physician to design an individualized immunization and prophylaxis program. Counseling on issues such as malaria prophylaxis, food and water precautions, insect repellent, and drug interactions is extremely important.<sup>39</sup> Patients should be given a printed summary of their medical history to take on the trip, as well as a list of medical facilities in the area they plan to visit.

In addition to those already mentioned, there are special vaccine recommendations for immunocompromised patients who travel abroad (TABLE 4):

**Yellow fever vaccine** is a live vaccine and is contraindicated for these patients.

**Typhoid.** Immunocompromised patients should not receive the live oral typhoid vaccine but should receive the Vi capsular polysaccharide vaccine.<sup>8</sup>

**Plague and anthrax vaccines** are unlikely to be necessary for routine travelers but may become more important in an era of height-



ened concern about biological warfare. Neither of these are live vaccines, and so both could in theory be given to immunocompromised patients.

The most common **rabies** vaccine is the human diploid cell vaccine, which is inactivated and thus in theory is safe for immunocompromised patients. It is indicated as part of pre-exposure and postexposure prophylaxis for persons at risk of contacting rabid animals through work or travel.

**Japanese B encephalitis** vaccine is an inactivated vaccine that may be recommended for travelers to certain areas of Asia.

**Bacillus Calmette-Guérin (BCG)** vaccine against tuberculosis is a live vaccine and should not be given to immunocompromised persons, who may develop disseminated mycobacterial infection.

## CONCLUSION

Many vaccines are safe and at least moderately effective in immunocompromised persons, but are underutilized. Education of clinicians and the general public can help to increase vaccination use for protection of these fragile patients.

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