Vaccines for International Travel
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Abstract

The pretravel management of the international traveler should be based on risk management principles. Prevention strategies and medical interventions should be based on the itinerary, preexisting health factors, and behaviors that are unique to the traveler. A structured approach to the patient interaction provides a general framework for an efficient consultation. Vaccine-preventable diseases play an important role in travel-related illnesses, and their impact is not restricted to exotic diseases in developing countries. Therefore, an immunization encounter before travel is an ideal time to update all age-appropriate immunizations as well as providing protection against diseases that pose additional risk to travelers that may be delineated by their destinations or activities. This review focuses on indications for each travel-related vaccine together with a structured synthesis and graphics that show the geographic distribution of major travel-related diseases and highlight particularly high-risk destinations and behaviors. Dosing, route of administration, need for boosters, and possible accelerated regimens for vaccines administered prior to travel are presented. Different underlying illnesses and medications produce different levels of immunocompromise, and there is much unknown in this discipline. Recommendations regarding vaccination of immunocompromised travelers have less of an evidence base than for other categories of travelers. The review presents a structured synthesis of issues pertinent to considerations for 5 special populations of traveler: child traveler, pregnant traveler, severely immunocompromised traveler, HIV-infected traveler, and traveler with other chronic underlying disease including asplenia, diabetes, and chronic liver disease.
Influenza is the most common VPD of travelers, especially for those on cruise ships and those going to mass-gathering events such as the Hajj pilgrimage; risk is present at all destinations during transmission season at the destination.20-23,78,79 The rate of serologically confirmed influenza cases has been estimated at 8.9 per 100 person-months of travel.20,79 For other VPDs, the risk for nonimmune travelers to developing countries is most significant for symptomatic hepatitis A (HA), at an estimated attack rate of 3.5 cases per 100,000 travelers to high or intermediate endemic regions.16,78 The rate of serologically confirmed influenza cases has been estimated at 8.9 per 100 person-months of travel.20,79 For other VPDs, the risk for nonimmune travelers to developing countries is most significant for symptomatic hepatitis A (HA), at an estimated attack rate of 3.5 cases per 100,000 travelers to high or intermediate endemic regions.16,78 The risk of symptomatic hepatitis B (HB) is most significant for long-stay travelers and expatriates, at 25 to 420 cases per 100,000 travelers.18 Enteric fever (typhoid and paratyphoid) has a risk of 3 cases per 100,000 travelers per month on the Indian subcontinent and is 10 times lower in Africa and parts of Latin America.78 Among Swedish residents who traveled abroad, measles and pertussis incidence are estimated at about 3 cases per 100,000 travelers per month each. Risk of yellow fever (YF) may be high in an area with current epidemic transmission; at least 10 unvaccinated foreign travelers to Brazil acquired YF during a 2018 outbreak in Brazil. At the same time, the overall risk varies greatly between destinations encompassed by the endemic area map. The risk of meningococcal meningitis, rabies, cholera, polio, varicella, and Japanese encephalitis in travelers is not well characterized but is thought to be small even for travel to highly endemic areas.78 Travelers visiting friends and relatives in their country of origin are a group of travelers with especially high risk, particularly from malaria and typhoid; these travelers require special attention to illness prevention and education. The worldwide epidemiology of travel-related diseases is constantly changing. Online and print resources (Table 3) should be consulted frequently to keep current. Finally, additional considerations are required for special populations such as child travelers, pregnant travelers, immunocompromised travelers, HIV-infected travelers, and travelers with other underlying health conditions including...
The risk of infection is based on the estimated prevalence rate of antibody to hepatitis A virus (anti-HAV), a marker of previous HAV infection among population. This marker is based on limited data and may not reflect current prevalence.

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

A Hepatitis A

Incidence rate (per 100,000 py)

- <20
- 20-49.9
- 50-99.9
- 100-199.9
- 200-499.9
- 500+

The map shows the distribution of diseases preventable with travel vaccines, including Hepatitis A and Typhoid fever. The legend indicates the incidence rates per 100,000 population (py).

B Typhoid fever

FIGURE 2. Distribution of diseases preventable with travel vaccines. A, Hepatitis A. B, Typhoid fever. C, Japanese encephalitis. D, Tickborne encephalitis. E, Yellow fever, Africa. F, Yellow fever, Americas. G, Rabies. H, African meningitis belt. From the World Health Organization (A); Am J Trop Med Hyg (B); the Centers for Disease Control and Prevention (C); the European Centre for Disease Prevention and Control (D); the Centers for Disease Control and Prevention (E and F); the World Health Organization (G); and the Centers for Disease Control and Prevention (H).
C Japanese encephalitis

D Tickborne encephalitis

FIGURE 2. Continued
G Rabies

Level 1, no risk: No risk, no pre-exposure prophylaxis
Level 2, low risk: Pre-exposure prophylaxis recommended for people likely to have regular, direct contact with bats and wild carnivores
Level 3, moderate risk: Pre-exposure prophylaxis recommended for travellers to remote areas and people likely to have contact with bats and other wildlife
Level 4, high risk: Pre-exposure prophylaxis recommended for travellers and people with occupational risks likely to have contact with rabid domestic animals, particularly dogs, bats and wild carnivores

Data Source: World Health Organization
Map Production: Control of Neglected Tropical Diseases (NTD)
World Health Organization

H Meningitis Belt of Africa

FIGURE 2. Continued
asplenia, diabetes, and chronic liver disease (Table 4).  

RISK ASSESSMENT FOR VACCINE SELECTION  
The choice of vaccines for an individual traveler is based on risk of exposure to VPDs on the chosen itinerary; the severity of disease, if acquired; and any risks presented by the vaccine itself. Risk of infection often varies within a risk country so that an exact itinerary needs to be ascertained during the pretravel consultation. Detailed references may need to be consulted (Table 3) for many itineraries. Specific risk and risk-taking behaviors related to travel style, type of accommodation, food, use of repellents, sexual behavior, and outdoor activities also affect risk of infection. Travel medicine physicians as well as travelers differ in their perception and tolerance of risk. Requests for immunization against diseases that are actually of negligible risk to the traveler but have the potential for poor outcome if acquired are often difficult for the physician to refuse because sporadic travel-related cases do occur each year.

ADMINISTRATION OF TRAVEL VACCINES  
General best practices for adult vaccines are found elsewhere in this Mayo Clinic Proceedings vaccine thematic series. Several best practices are specific to travel vaccines. Testing may be useful to assess immunity to HA or HB virus in persons from countries with high endemicity or in persons with a history of jaundice or to assess immunity to measles, mumps, and rubella (MMR) in someone lacking documentation. This scenario must be weighed against cost factors and possible loss to follow-up in those busy preparing for travel. Different brands of HA, HB (except Heplisav-B; Dynavax Technologies Corporation), rabies, and meningococcal ACYW-135 vaccine are interchangeable for subsequent doses if necessary. Acyclovir and related drugs and influenza antivirals (neuraminidase and polymerase inhibitors) preclude concomitant use of live attenuated varicella and zoster vaccines and influenza vaccines, respectively, but not YF vaccine. Antibacterial drugs should not be given within 3 days of a dose of live oral typhoid or 14 days prior to oral cholera vaccine. Anaphylactic egg allergy precludes administration of YF and MMR vaccines, which contain more egg protein than influenza vaccines. No current vaccine contains penicillin. Women who are breastfeeding newborns and infants should avoid YF vaccination but not other travel vaccines. Translations of VPD terms in multiple languages are available when travelers provide foreign-language vaccine records.

An interruption in a vaccination schedule generally does not require restarting the entire vaccine series, nor does it require the addition of extra doses. The series should be continued with the next dose in the series, and any subsequent doses should be administered at the same interval as if the series had not been interrupted. Rabies and oral typhoid vaccines present exceptions to this rule but still have some overall flexibility. All currently used immunizations may be given at the same time and in any combination. If 2 live viral antigens are not administered on the same day, they must be spaced by a month. Live oral vaccines (typhoid, cholera, polio) can be administered at any interval with respect to any live virus vaccine. Baseline purified protein derivative skin tests or interferon-γ release assays, often done in the pretravel setting, can be given on the day that live virus vaccines are administered or else must be done more than 4 weeks later.

ROUTINE VACCINES OFTEN ADMINISTERED IN THE TRAVEL CLINIC  
This section considers routine vaccines that are normally readministered at regular intervals or vaccine series that need to be finished in a healthy adult regardless of the current plans for international travel and when there are no specific medical or behavioral risk factors. The text of this and the next 2 sections provides general information on vaccine indications and logistic issues that arise in the clinic and
TABLE 1. Highlights of Vaccines for International Travel Noting Trip Characteristics Putting Travelers at Particularly High Risk and Examples of Recent Outbreaks With Implications for Travelers

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Trip characteristics suggesting particularly high risk</th>
<th>Recent outbreaks or new findings with impact on travelers</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholera</td>
<td>Destination with poor hygiene and sanitation where cholera is endemic; humanitarian aid work; some VFR travelers</td>
<td>Haiti, Somalia, Yemen</td>
<td>14</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Destinations with poor hygiene and sanitation practices; adventurous eating habits; men who have sex with men</td>
<td>Widespread</td>
<td>15-17</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Adventure travel; medical tourism; health condition that may require medical intervention; injections or infusions; possibility of sexual contact at destination</td>
<td>None</td>
<td>18,19</td>
</tr>
<tr>
<td>Influenza (+ avian influenza)</td>
<td>Mass gatherings; cruise ships; exposure to live poultry</td>
<td>Saudi Arabia, China, Vietnam, Indonesia</td>
<td>20-23</td>
</tr>
<tr>
<td>Japanese encephalitis</td>
<td>Adventure travel in agricultural areas; open-air accommodations; rural home stays; some VFR travelers</td>
<td>Bali, China, Thailand</td>
<td>24-26</td>
</tr>
<tr>
<td>Measles, mumps, rubella</td>
<td>Mass gatherings; travel to one of many areas with current outbreaks; travel to areas with antivaccine community</td>
<td>Venezuela, Brazil, Democratic Republic of the Congo, Europe (England, France, Greece, Italy, Romania, Serbia, Ukraine), Indonesia, Philippines</td>
<td>2-4, 27</td>
</tr>
<tr>
<td>Meningococcal, quadrivalent ACYW-135</td>
<td>Mass gatherings; sub-Saharan Africa</td>
<td>Saudi Arabia</td>
<td>28, 29</td>
</tr>
<tr>
<td>Poliovirus</td>
<td>Endemic destinations with low vaccine coverage or disruption in health care infrastructure; humanitarian aid work</td>
<td>Afghanistan, Nigeria, Pakistan, Papua New Guinea, Somalia, Democratic Republic of Congo</td>
<td>30</td>
</tr>
<tr>
<td>Rabies</td>
<td>Remote destinations in areas with high incidence of canine rabies; behaviors with close contact with canines, wildlife, and bats</td>
<td>Indonesia (Bali), Malaysia (Sarawak), India, Thailand</td>
<td>31-35</td>
</tr>
<tr>
<td>Tetanus diphtheria pertussis (Tdap) or tetanus diphtheria (Td)</td>
<td>Tetanus: participating in injury-prone activities such as cycling, riding motorcycle, construction</td>
<td>Diphtheria: Haiti, Venezuela, Bangladesh, Thailand, South Pacific, Vanuatu, Pertussis: exposure occurs widely</td>
<td>36-38</td>
</tr>
<tr>
<td>Tick-borne encephalitis</td>
<td>Hiking; camping; consuming unpasteurized dairy products</td>
<td>Austria, Czech Republic, Finland, Germany, Latvia, Norway, Sweden, Switzerland…</td>
<td>39-43</td>
</tr>
</tbody>
</table>

Continued on next page
complement the information in Table 2. Full details of routine adult immunization are found elsewhere in this Mayo Clinic Proceedings vaccine thematic series.94 Verification and update of these routine vaccines, regardless of itinerary, is part of the pretravel consultation. However, for many VPDs, the risk of disease is also increased in developing countries.

### Tetanus-Diphtheria—Acellular Pertussis

If no adult doses of tetanus-diphtheria—acellular pertussis have ever been given, a dose is indicated regardless of the time elapsed since the last tetanus-diphtheria vaccination, but travelers to remote areas where tetanus toxoid (indicated in cases of dirty trauma) will be inaccessible should get boosters at 5-year intervals. Trauma during travel is common, and unsafe needles or uncertain vaccine quality at the destination is another reason for assuring immunity pretravel. Although immunity to tetanus after a primary childhood vaccination series tends to be very long-lived, the short-lived immunity to diphtheria and pertussis conferred by vaccination mandates strict validation of vaccine history and booster doses according to schedule. Evidence indicates that pertussis immunity, at least in children and adolescents, is significantly shorter than the standard 10-year interval, but no special accelerated dosing guidelines for travelers at very high risk of pertussis exposure exist.72

### Varicella

Varicella, which is highly contagious, is primarily a disease of adolescents and young adults in tropical, nonindustrialized countries.97 Two doses of varicella vaccine, administered at least 4 weeks apart, should be considered for adult travelers without evidence of varicella immunity. Adults born before 1980 in the United States are considered immune.

### Zoster

Data are lacking to determine whether travel poses additional risk for shingles due to reactivation of varicella zoster virus. The newly approved recombinant zoster vaccine should be given to all adults aged 50 years and older regardless of travel plans and regardless of having received a previous dose of the live zoster vaccine.98

### Pneumococcal

Travelers are at increased risk of all types of respiratory infections. Healthy travelers who are 65 years of age or older should be current with pneumococcal vaccination with sequential doses of PCV13 and PPSV23. Beginning in 2019, ACIP no longer recommends routine (now optional) PCV13 for healthy nontraveler adults 65 years and older. Travelers may face PCV13 strains at their destinations making travel an indication for PCV13 in this age cohort. A minimum interval of 8 weeks (as used for patients with underlying medical conditions) between a dose of Pneumovax 23 (Merck & Co, Inc) (if indicated) and a
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Vaccine type (specific type)</th>
<th>Adult dose</th>
<th>Pediatric dose</th>
<th>Route</th>
<th>Standard schedule of immunization</th>
<th>Accelerated schedule for series</th>
<th>Estimated duration of protection</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholera</td>
<td>Live</td>
<td>1 Sachet</td>
<td>NA</td>
<td>Oral</td>
<td>1 Dose</td>
<td>NA</td>
<td>3-6 mo</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td>Not live (inactivated virus)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Not live (inactivated virus)</td>
<td>1 mL</td>
<td>Age $\geq$12 mo: 0.5 mL</td>
<td>IM</td>
<td>2 Doses: days 0, 6-12 mo</td>
<td>Traveling children aged $\geq$6 mo should receive 1 dose pretravel and receive 2 doses of hepatitis A at age $\geq$12 mo Available in combined hepatitis A and B formulation: days 0, 7, 21 and 12 mo</td>
<td>$&gt;$25 y based on seropositivity; $&gt;$40 y based on anti-body modeling</td>
<td>50-54</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>From birth: 0.5 mL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Not live (recombinant hepatitis B surface antigen)</td>
<td>1 mL</td>
<td>From birth: 0.5 mL</td>
<td>IM</td>
<td>3 Doses: days 0, 1 mo, and 6 mo</td>
<td>Various options including: (1) days 0, 7, 21 and 12 mo; (2) days 0, 1, 2 and 12 mo</td>
<td>$&gt;$30 y</td>
<td>55, 56</td>
</tr>
<tr>
<td>Hepatitis B-CpG</td>
<td>Not live (recombinant hepatitis B with adjuvant)</td>
<td>0.5 mL</td>
<td>NA</td>
<td>IM</td>
<td>2 Doses: day 0, 1 mo</td>
<td>NA</td>
<td>No data, but appears noninferior to standard hepatitis B vaccine</td>
<td>57, 58</td>
</tr>
<tr>
<td>Combined</td>
<td>Not live (inactivated virus and recombinant viral antigen)</td>
<td>1 mL</td>
<td>NA in US (pediatric formulation licensed in Canada, Europe, and other countries)</td>
<td>IM</td>
<td>3 Doses: day 0, 1 mo, and 6 mo</td>
<td>4 Doses: days 0, 7, 21 and 12 mo</td>
<td>$&gt;$20 y based on seropositivity and anamnestic response; $&gt;$40 y based on mathematical modeling</td>
<td>52</td>
</tr>
<tr>
<td></td>
<td>hepatitis A and B</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Influenza</td>
<td>Not live (inactivated virus, trivalent or quadrivalent)</td>
<td>0.5 mL</td>
<td>Age $\geq$6 mo but dose varies per product. Age 6-35 mo: 0.25 mL or 0.5 mL Age $\geq$36 mo: 0.5 mL</td>
<td>IM</td>
<td>1 Dose (children $&lt;$8 y require 2 doses administered $\geq$4 wk apart with a first receipt of influenza vaccination)</td>
<td>NA</td>
<td>1 y</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td>Not live (inactivated high-dose trivalent)</td>
<td>0.5 mL</td>
<td>(age $\geq$65 y)</td>
<td>NA</td>
<td>IM</td>
<td>1 Dose</td>
<td>NA</td>
<td>1 y</td>
</tr>
<tr>
<td></td>
<td>Not live (inactivated virus, adjuvanted trivalent)</td>
<td>0.5 mL</td>
<td>(age $\geq$65 y)</td>
<td>NA</td>
<td>IM</td>
<td>1 Dose</td>
<td>NA</td>
<td>1 y</td>
</tr>
<tr>
<td></td>
<td>Live (attenuated virus, quadrivalent)</td>
<td>Intranasal spray</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

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TABLE 2. Continued

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Vaccine type (specific type)</th>
<th>Adult dose</th>
<th>Pediatric dose</th>
<th>Route</th>
<th>Standard schedule of immunization</th>
<th>Accelerated schedule for series</th>
<th>Estimated duration of protection</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>JEV</td>
<td>Not live (recombinant, trivalent)</td>
<td>0.5 mL (age ≥18 y)</td>
<td>NA</td>
<td>IM</td>
<td>1 Dose</td>
<td>NA</td>
<td>1 y</td>
<td>60-62</td>
</tr>
<tr>
<td>JEV</td>
<td>Not live (cell culture–based inactivated virus, trivalent)</td>
<td>0.5 mL</td>
<td>Age ≥4 y: 0.5 mL</td>
<td>IM</td>
<td>1 Dose</td>
<td>NA</td>
<td>1 y</td>
<td></td>
</tr>
<tr>
<td>Japanese encephalitis, tissue culture–derived</td>
<td>0.5 mL</td>
<td>Age ≥2 mo through 2 y: 0.25 mL</td>
<td>IM</td>
<td>2 Doses: days 0, and between 7-28</td>
<td>1-2 y (booster with third dose leads to seropositivity for ≥6 y)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles, mumps, rubella</td>
<td>Live (attenuated virus)</td>
<td>0.5 mL</td>
<td>Age ≥12 mo: 0.5 mL</td>
<td>SC</td>
<td>2 Doses: day 0, 4 wk</td>
<td>Traveling children aged ≥6 mo who are not yet vaccinated should receive 1 dose pretravel and receive 2 doses at age ≥12 mo</td>
<td>Lifelong after 2 doses (third dose may be recommended for contacts during mumps outbreaks)</td>
<td>63, 64</td>
</tr>
<tr>
<td>Meningococcal, quadrivalent ACYW-135</td>
<td>Not live (bacterial polysaccharide, conjugated)</td>
<td>0.5 mL</td>
<td>Age ≥2 mo for MenACYW-CRM, ≥9 mo for MenACYW-D, 0.5 mL</td>
<td>IM</td>
<td>2 Doses in adolescents: age 11-12 y, then age 16-18 y</td>
<td></td>
<td>65, 66</td>
<td></td>
</tr>
<tr>
<td>Poliovirus</td>
<td>Not live (inactivated virus)</td>
<td>0.5 mL</td>
<td>Age ≥2 mo: 0.5 mL</td>
<td>SC</td>
<td>1 Dose in those with primary childhood series</td>
<td>NA</td>
<td>Lifelong, after primary series plus an adult (age ≥18 y) booster</td>
<td>48</td>
</tr>
<tr>
<td>Rabies</td>
<td>Not live (inactivated virus, human diploid cell)</td>
<td>1 mL</td>
<td>From birth: 1 mL</td>
<td>IM</td>
<td>3 Doses preexposure: days 0, 7 and 21 or 28</td>
<td>Abbreviated course days 0, 7, 21 or 28 “Boostable” lifelong; 2 additional doses are required on days 0 and 3 after rabies exposure</td>
<td></td>
<td>62,67-71</td>
</tr>
<tr>
<td>Vaccine</td>
<td>Vaccine type (specific type)</td>
<td>Adult dose</td>
<td>Pediatric dose</td>
<td>Route</td>
<td>Standard schedule of immunization</td>
<td>Accelerated schedule for series</td>
<td>Estimated duration of protection</td>
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<tr>
<td>Not live (inactivated virus, purified chick embryo)</td>
<td>1 mL</td>
<td>From birth: 1 mL</td>
<td>IM</td>
<td>3 Doses preexposure: days 0, 7 and 21 or 28</td>
<td>Abbreviated course days 0, 7 dosing proposed by WHO SAGE, under evaluation by ACIP</td>
<td>“Boostable” lifelong; 2 additional doses are required on days 0 and 3 after rabies exposure</td>
<td>62,67-71</td>
<td></td>
</tr>
<tr>
<td>Tetanus, diphtheria, pertussis (Td) or tetanus, diphtheria (Td)</td>
<td>0.5 mL</td>
<td>Age ≥2 mo: 0.5 mL</td>
<td>IM</td>
<td>1 Dose in those with primary childhood series; boost with Tdap if no previous dose of Tdap</td>
<td>NA</td>
<td>10 y</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>Tick-borne encephalitis</td>
<td>0.5 mL</td>
<td>Age 3-16 y: 0.25 mL dose 1 followed by 0.5 mL</td>
<td>IM</td>
<td>3 Doses: day 0, 1-3 mo, and 5-12 mo</td>
<td>3 Doses: days 0, 7, 21</td>
<td>3 y</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td>Typhoid</td>
<td>0.5 mL</td>
<td>Age ≥2 y: 0.5 mL</td>
<td>IM</td>
<td>1 Dose</td>
<td>NA</td>
<td>2 y</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td>Live (attenuated bacteria)</td>
<td>4 Capsules</td>
<td>Age ≥6 y: 4 capsules</td>
<td>Oral</td>
<td>4-Capsule series, 1 every other day</td>
<td>NA</td>
<td>5 y</td>
<td>75-77</td>
<td></td>
</tr>
</tbody>
</table>

**TABLE 2. Continued**

<table>
<thead>
<tr>
<th>Vaccine</th>
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<th>Estimated duration of protection</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yellow fever</td>
<td>Live (attenuated virus)</td>
<td>0.5 mL</td>
<td>Age ≥9 mo: 0.5 mL</td>
<td>SC</td>
<td>1 Dose</td>
<td>NA</td>
<td>Lifelong</td>
<td>75-77</td>
</tr>
</tbody>
</table>

*ACIP = Advisory Committee on Immunization Practices; IM = intramuscular; NA = not applicable; SC = subcutaneous; US = United States; VPD = vaccine-preventable disease; WHO SAGE = World Health Organization Strategic Advisory Group of Experts.

*bSee respective ACIP recommendations*; only the most recent relevant ACIP publications are listed in the References column.
previously given dose of Prevnar 13 (Pfizer Inc) may be used to ensure optimal immunity of healthy travelers 65 years of age and older needing maximal protection prior to the trip.80 No data support an advantage of the current 1-year over an 8-week PCV13 to PPSV23 interval in healthy individuals; the 1-year interval was introduced solely for a number of logistic considerations.88

Human Papillomavirus
Substantial evidence of increased rates of sexual activity, often unplanned, during travel exists. No specific indication for travelers has been studied or recommended, but all travelers in the indicated age groups (now includes optional vaccination for males and females age 27-45) for human papillomavirus vaccination should be fully immunized according to standard schedules.

Routine Adult Vaccines with Additional Travel Indications

Measles–Mumps–Rubella
Imported measles and mumps have caused travel-related outbreaks in the United States, and nonimmune adult US travelers are at significant risk, including in Western Europe and Mexico.3,4 Persons (except traveling health care workers) born in the United States before 1957 or born at any time in the developing world are considered immune to measles; other adult travelers should have received a lifetime total of at least 2 doses of live measles-containing vaccine during their life, unless measles immunity can be documented (definitive laboratory evidence of acute infection or current antibody titers). Two doses of MMR should be considered for health care or humanitarian workers without other evidence...
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Consideration of contraindications/precautions for special populations</th>
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<th>Special indication beyond general ACIP recommendations</th>
<th>Attention to dosing recommendations for specific populations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholera</td>
<td>C: no data for &lt;18 y P: vaccine strain may be shed in stool for ≥7 d, with a potential to transmit the vaccine strain to infant during vaginal delivery I: no data for immunocompromised individuals O: no contraindication for asplenia, despite this being a live vaccine</td>
<td>Hydrolyzed casein, dried lactose</td>
<td>None</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>P: no contraindication; may be used based on risk vs benefit</td>
<td>Aluminum, formalin, MRC-5 cells, nonviral proteins, neomycin sulfate, bovine albumin</td>
<td>I: specifically recommended especially with transplant H: specifically recommended O: specifically recommended for liver disease, diabetes mellitus</td>
<td>C: different pediatric dose (vs adult dose); administer noncountable dose at age 6-11 mo if travelling I: 1 dose provides suboptimal serologic response; administer ≥2 doses pre-travel, consider second dose 1 mo after first dose for imminent travel or supplemental immunoglobulin O: chronic liver disease dose as per I</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>P: no contraindication; may be used if indicated</td>
<td>Yeast protein, Saccharomyces cerevisiae cell line</td>
<td>I: specifically recommended especially with transplant H: specifically recommended O: specifically recommended for liver disease, diabetes mellitus, renal failure</td>
<td>C: different pediatric dose (vs adult dose) O: use double-dose formulation for dialysis patients</td>
</tr>
<tr>
<td>Influenza</td>
<td>P: live-attenuated vaccine contraindicated; nonlive vaccines are recommended I: live-attenuated vaccine contraindicated; nonlive vaccines are recommended O: no contraindication for asplenia</td>
<td>For inactivated quadrivalent or trivalent; β-propiolactone or formaldehyde in different formulations, thimerosal in multidose vials Check package insert because different cell lines used (embryonated chicken eggs, Madin-Darby Canine Kidney cells, Spodoptera frugiperda): -/+ baculovirus and insect cell proteins and DNA; ovalbumin, neomycin, polymyxin B, non-HA protein, MDCK cell protein/</td>
<td>P: specifically recommended I: specifically recommended H: specifically recommended O: specifically recommended for all those with underlying chronic diseases</td>
<td>C: children aged 6 mo through 8 y who are receiving their initial influenza vaccination should receive 2 doses &gt;4 wk apart</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Additives/residuals/cell lines highlighting substances with potential sensitivity concerns</th>
<th>Special indication beyond general ACIP recommendations</th>
<th>Attention to dosing recommendations for specific populations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japanese encephalitis, tissue culture—derived</td>
<td>DNA, polysorbate 80, gentamicin sulfate, Aluminum, formaldehyde, bovine serum albumin, Vero cells, host cell DNA, host cell proteins</td>
<td>None</td>
<td>C: different pediatric dose for children &lt;3 y</td>
</tr>
<tr>
<td>Measles, mumps, rubella</td>
<td>Hydrolyzed gelatin, chick embryo cell culture, WI-38 cells, recombinant human albumin, neomycin, bovine serum albumin</td>
<td>C: specifically recommended for traveling children ≥6 mo who are not yet vaccinated</td>
<td>C: traveling children ≥6 mo should receive 1 dose pretravel, and receive 2 doses at ≥12 mo</td>
</tr>
<tr>
<td>Meningococcal, quadrivalent ACYW-135, conjugated</td>
<td>Diphtheria toxoid protein, formaldehyde</td>
<td>C: specifically recommended for age 2-23 mo if at increased risk (complement deficiency, asplenia, outbreak setting, travel)</td>
<td>C: if at increased risk, administer either 4-dose series starting at 8 wk or 2-dose series depending on product and age at initial dose</td>
</tr>
<tr>
<td>Pneumococcal, 13-valent conjugated (PCV13) and/or 23-valent polysaccharide (PPSV23)</td>
<td>PCV13: CRM197 carrier protein, aluminium phosphate adjuvant; PPSV23: phenol</td>
<td>I: Both PCV13 and PPSV23 are recommended for immunocompromised individuals</td>
<td>I: PCV13 followed by PPSV23 with an interval of 8 wk; additional dose of PPSV23 recommended 5 y after initial dose for immunocompromised individuals</td>
</tr>
<tr>
<td>Poliovirus, inactivated</td>
<td>2-Phenoxyethanol, formaldehyde, neomycin, streptomycin, polymyxin B, calf serum protein, Vero cells</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Rabies</td>
<td>Human diploid cell vaccine: MRC-5 cells, human serum albumin, neomycin chicken fibroblasts,</td>
<td>None</td>
<td>I: additional PEP dose recommended</td>
</tr>
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<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Consideration of contraindications/ precautions for special populations</th>
<th>Additives/residuals/cell lines highlighting substances with potential sensitivity concerns</th>
<th>Special indication beyond general ACIP recommendations</th>
<th>Attention to dosing recommendations for specific populations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovalbumin, neomycin, chlortetracycline, amphotericin B</td>
<td>- P: no contraindication</td>
<td>- Alum or aluminum, formaldehyde</td>
<td>- P: Tdap specifically recommended every pregnancy</td>
<td>- None</td>
</tr>
<tr>
<td>Tick-borne encephalitis</td>
<td>- P: precaution</td>
<td>- FSME-Immun: aluminum, human albumin</td>
<td>- None</td>
<td>- None</td>
</tr>
<tr>
<td>Typhoid</td>
<td>- P: live-attenuated vaccine contraindicated; may consider polysaccharide vaccine</td>
<td>- Amino acid mixture</td>
<td>- None</td>
<td>- None</td>
</tr>
<tr>
<td>Yellow fever</td>
<td>- C: contraindicated age &lt;6 mo; precaution age 6-8 mo</td>
<td>- Gelatin, chicken embryo</td>
<td>- None</td>
<td>- C: additional dose recommended if vaccinated previously at age &lt;5 y P: additional dose recommended if vaccinated previously during pregnancy I: additional dose recommended for those with prior yellow fever vaccination before hematopoietic stem cell transplant and who are at risk for yellow fever but are now immunocompetent H: additional dose recommended if vaccinated previously while HIV infected</td>
</tr>
</tbody>
</table>

ACIP = Advisory Committee on Immunization Practices; C = child traveler; H = HIV-infected traveler; I = severely immunocompromised traveler; O = traveler with other chronic underlying disease including asplenia, diabetes, and chronic liver disease; P = pregnant traveler; PEP = postexposure prophylaxis.

*See references 80 through 93 in addition to those listed in Table 2.

*Data from Plotkin’s Vaccines* and manufacturer’s vaccine package inserts for cholera (Vaxchora; PaxVax, Inc), meningococcal conjugate (Menactra; Sanofi Pasteur Inc), pneumococcal conjugate (Prevnar; Pfizer Inc), pneumococcal polysaccharide (Pneumovax; Merck & Co, Inc), and tick-borne encephalitis (FSME-Immun; Pfizer Inc).
of immunity. A third lifetime dose of MMR vaccine may be given during specific mumps outbreak situations. Many persons born in the United States before 1970 have not been vaccinated with MMR at all, and many born in the 1970s have not received the second dose in the series, which has been in the guidelines only since 1990. Children who are 6 to 11 months of age need one dose of MMR prior to travel regardless of destination country. This dose is noncountable, and 2 doses still should be given at the recommended ages (at least 28 days apart).

**Hepatitis B**

Travelers born in the United States after 1992 will most often already have received an HB vaccine series. For previously nonimmune travelers, pretravel HB vaccination is indicated for all nonvaccinated travelers with standard indications, such as health care workers, and also for all longer-stay travelers who will be visiting or residing in high- or moderate-risk areas. Transmission via routes such as sexual contact, blood transfusions, contaminated medical equipment, body piercing, tattooing, and acupuncture is difficult to control or predict in the context of travel. Vaccination is usually advocated for short-term travelers, especially younger travelers and those anticipating close contact with local populations, even if they have no specific risk factors. Adventure travelers who are by definition at high risk of injury, as well as backpackers and those with underlying medical conditions, are more likely to require contact with the medical system. Business and other frequent travelers who take multiple short trips have a cumulative risk that increases with time, and such individuals should receive the HB vaccine. Persons likely to engage in future international travel should consider a vaccine that confers lifelong protection.

Accelerated and hyperaccelerated schedules (Table 2) are used widely in travel medicine practice and are approved in many countries. These schedules are not as well known among pharmacists and primary care clinicians, so travelers in whom an accelerated series is initiated may have difficulty completing them when seeking subsequent doses at a location other than a dedicated travel clinic. For conventional HB vaccines, all 3 primary doses before travel are necessary for high assurance of protection. A newly licensed HB vaccine, Heplisav-B, which is not yet widely integrated into clinical practice, produces protection with a standard schedule of 2 doses spaced by 1 month, making it especially convenient for travelers. With the overlap of indications for use of the individual vaccines, the combined HA and HB vaccine provides convenience for travelers and has a licensed accelerated 3-week schedule (Table 2).

**Influenza**

Influenza is the most common VPD of travelers, especially those on cruise ships and those going to mass-gathering events such as the Hajj pilgrimage. Vaccination clearly protects against influenza complications such as pneumonia, hospitalization, or death even if some breakthrough respiratory illness does occur. Influenza virus circulates year-round in tropical and subtropical regions, and influenza season occurs in winter in temperate regions in the Southern Hemisphere (which is summer in the Northern Hemisphere). All travelers visiting the tropics at any time of year and visiting temperate countries where it is currently winter should be current on the most recent influenza vaccine available at home before the trip. Vaccine will not protect for at least 1 week postimmunization. Recent evidence suggests that travelers immunized with the current vaccine formulation more than 6 months earlier may consider revaccination because immunity clearly declines to close to zero by this time. Data supporting revaccination is limited but enticing.

Travelers may consider baloxavir or oseltamivir as standby therapy, especially for those who are at high risk for complications from influenza or who are inadequately vaccinated. Travelers who carry baloxavir or oseltamivir should be advised to make every effort to institute therapy only under medical advice. This advice could be obtained at the
destination or after telephone consultation with the prescribing physician at home. In China and Southeast Asia, avoiding poultry markets and farms may decrease risk of avian influenza such as H7N9, H5N1, and H5N6, against which currently available vaccines are ineffective; in vitro data indicate efficacy of baloxavir against all the aforementioned avian influenza strains.

**Meningococcal**

Quadrivalent (ACWY) meningococcal vaccine is recommended for travelers to Africa’s sub-Saharan “meningitis belt” (Figure 2) during the dry season from December through June, especially if prolonged contact with the local population is likely. Health care workers to the meningitis belt might consider vaccination year-round. Out-of-season epidemics have occurred in Ethiopia, Somalia, and Tanzania. Muslims undertaking Hajj and Umrah pilgrimages in Saudi Arabia are at a higher risk of meningococcal disease, and proof of current vaccination with quadrivalent vaccine within the previous 5 years is required to obtain pilgrimage visas. Immunity to some serotypes in the tropics may wane in as little as 3 years, a consideration for most travelers to the developing world not included in US recommendations.65,66 Many travel advisors recommend revaccination after 3 years for very high-risk travelers. Meningococcal B vaccine is not indicated for travel unless the traveler has another routine indication such as asplenia or complement deficiency. The incidence of meningococcal B infection is not increased in developing countries when compared with the United States.101 Sporadic outbreaks may occur, as in the United States, so if a traveler was going to a closed setting such as a school outbreak, vaccination could be considered.

**Polio**

Because of eradication efforts, poliomyelitis remains endemic in only Afghanistan, Pakistan, and Nigeria, but complete control remains elusive. A handful of other countries periodically have outbreaks of human polio cases due to circulating vaccine-derived polio viruses. Adults who have previously completed a primary vaccine series and plan to travel to countries that are polio-endemic or have had cases of vaccine-derived polio in the previous year (updated information is available from the Global Polio Eradication Initiative30) should receive a one-time single dose of inactivated polio vaccine as a booster. Completely unvaccinated adults traveling to risk countries may need to receive an entire primary series prior to the trip. However, even a single dose is beneficial. Revaccination with an inactivated polio vaccine primary series may be needed for a child who had been vaccinated with a routine oral polio vaccine series outside the United States. Vaccination is occasionally required for travelers going to certain polio-free countries that have a mandatory entry requirement for travelers (residents or long-stay visitors) coming from countries on a defined list of suspected polio-endemic countries.13

**TRAVEL-ONLY VACCINES FOR ADULTS**

Hepatitis A and typhoid vaccines are considerations for most travelers to developing countries. The remaining vaccines in this section are indicated for specific risk areas (Figure 2) and for specific risk activities within the specified countries, with the exception of YF.

**Hepatitis A**

Unless routine or catch-up vaccination has been administered since 2005, young adults in the United States generally have little to no immunity to HA. Hepatitis A vaccine is indicated for every nonimmune traveler to countries or areas with moderate to high risk of infection, which includes essentially every destination other than the United States, Canada, Japan, Australia, New Zealand, Scandinavian countries, and developed countries in Europe. A single dose of HA vaccine given any time before travel, even on the way to the airport, provides adequate protection to the healthy adult. The Centers for Disease Control and Prevention (CDC) recommends ancillary concomitant
immunoglobulin for travelers older than 40 years who are planning to depart in 2 weeks or less, but this recommendation has not been widely adopted in practice. Individuals born in the developing world may already be immune to HA. Persons with a history of hepatitis or who previously lived in an endemic country for a prolonged period may benefit from prevaccination serum antibody testing. Nevertheless, they merit HA vaccine unless immunity can be confirmed. When considering the combination HA/HB vaccine, the accelerated schedule should not be used unless at least 2 doses can be given prior to departure because the combination vaccine contains half of the HA antigen compared with that in a dose of monovalent adult HA vaccine. In this circumstance, monovalent HA and HB vaccines should be administered separately. Infants aged 6 to 11 months should be given one dose (noncountable) prior to travel. Following this dose, routine vaccination with HA vaccine (2 additional age-appropriate doses) should be administered. When pretravel vaccination cannot be given, intramuscular immunoglobulin dosing is (1) 0.1 mL/kg for trips of less than 1 month’s duration, (2) 0.2 mL/kg for trips of less than 2 months, and (3) 0.2 mL/kg every 2 months for trips of 2 months or longer.

For unvaccinated travelers who have had a specific HA exposure while traveling, a single dose of HA vaccine for postexposure prophylaxis is now recommended for all persons aged 12 months or older, preferably within 2 weeks of exposure; additionally, immunoglobulin (if available) may be administered to immunocompromised adults of all ages as well as to those older than 40 years, depending on the physician’s risk assessment (eg, chronic liver disease, risk level of the exposure).

Typhoid

Typhoid vaccine is indicated for all travelers to the Indian subcontinent and considered for those traveling to other endemic areas (Figure 2) under all but the most deluxe and protected conditions. Risk increases with trip duration, lodging and/or eating with local residents, and extent of travel off the usual tourist itineraries. In risk areas, food and water precautions should still be followed rigorously because typhoid vaccines are only 53% to 72% protective, and a large oral inoculum may overwhelm even an optimal antibody response. The recent increase in quinolone-resistant Salmonella enterica serotype Typhi in Asia and extremely resistant typhoid in Pakistan has decreased the threshold for typhoid vaccination because infection, once acquired, may require inpatient parenteral therapy with sophisticated antibiotics. Current typhoid vaccines do not protect against S enterica serotype Paratyphi, which is emerging in many areas. Adherence to the oral vaccine regimen may be as low as 70%. Although revaccination with the injectable Vi polysaccharide vaccine is recommended by the US Food and Drug Administration every 2 years, revaccination every 3 years is recommended in Canada, Australia, the United Kingdom, and other countries if continued or repeated exposure exists.

Yellow Fever

The main indication for YF vaccination is to prevent infection in individuals at risk. However, YF is currently the only vaccine that falls under the International Health Regulations (IHR) that may necessitate vaccination purely for regulatory reasons. Neither YF vaccine nor any other vaccine is currently required on return to the United States. In general, all healthy adult travelers to areas with a risk of YF transmission (Figure 2) should be vaccinated. This endemic area may be restricted to only a portion of a country. Because of rare but serious vaccine-associated adverse effects, persons who are not at any risk of exposure should not be vaccinated. Only first doses of YF vaccine, but not booster doses, are associated with rare but severe or fatal adverse events. The overall rate is 1 event per 334,000 doses, but severe events occur most frequently in persons older than 60 years (increasing with advancing age) and in any person with a thymus disorder.
Urban YF rarely occurs in South America, but the situation is currently evolving in Brazil and up-to-date maps should be checked. Persons who have anything less than a definite, fixed itinerary and who will travel anywhere close to regions with risk of transmission should be vaccinated. Decisions about YF vaccination depend on risk-benefit for the person, the itinerary, and the destination country entry requirements.

A number of African countries and one in South America (French Guiana) require proof of YF vaccination from all arriving travelers. Other countries, both within and outside the risk zone, have submitted more complex requirements to the World Health Organization (WHO). They may require an official vaccination certificate only for individuals arriving directly from or via a country in the YF endemic zone but not from travelers arriving from other countries. Such transits may include even an airplane connection in an affected country. These YF-free countries usually have the conditions and vectors to initiate a YF transmission cycle, and the purpose of the vaccine requirement is to prevent entry of viremic travelers. Current country-by-country YF entry requirements are available from the WHO. The requirement often applies even if the arriving traveler has not visited an area within a country of departure that is endemic for YF.

A special permit, obtainable in the United States from state health departments, is required to legally stamp an international certificate of vaccination as being from an authorized YF vaccine center. The IHR specify that clinicians who decide that YF vaccine is contraindicated on medical grounds can provide a letter stating the reasons for an exemption, which is shown on arrival at the destination. Acceptance of a “waiver letter” depends on the discretion of the authorities at the port of entry. On arrival, the destination country may also quarantine the traveler for up to 6 days or request that the traveler be placed under surveillance. The variable risk within the endemic regions of the world must be considered (in consultation with an expert, if necessary), and cancellation of travel should be recommended strongly if the risk is more than negligible and YF vaccine cannot be given or is declined by the traveler. A YF certificate becomes valid for entry 10 days after it is stamped and dated.

The YF vaccine has until several years ago been thought to provide protection for 10 years. Currently, the CDC recommends that 10-year boosters should be restricted to healthy travelers planning a long stay in any country with any risk of YF transmission, to all travelers spending any amount of time in high-risk areas (notably West Africa), and to all persons going to locations with a current outbreak. A CDC analysis found that 92% of vaccine recipients have virus-neutralizing antibody at 10 years and 80% have the antibody at 20 years. Thus, almost all healthy persons appear to have long-term immunity. For the purposes of the IHR, documentation of a single dose of YF vaccine at any time during the person’s life suffices for entry to any country.

Rabies
A preexposure rabies series is indicated for long-stay travel to endemic areas of Latin America, Asia, or Africa, where the rabies threat is constant and access to adequate postexposure rabies immunoglobulin and vaccine is likely to be limited. Preexposure vaccination does not eliminate the need for vaccination after an exposure. However, it dramatically simplifies the postexposure vaccine schedule to 2 injections and eliminates the need for rabies immunoglobulin, which is often very difficult to access abroad. Countries with the highest risk of rabies include the Indian subcontinent, Thailand, Vietnam, and most sub-Saharan African countries. For short-term travel, risk groups for whom immunization should be considered include adventure travelers, bikers, hikers, cave explorers, or business travelers who travel for short but frequent trips and plan to go running outdoors on these trips. Regardless of vaccination status, travelers should be instructed to cleanse well with soapy water any bite or animal scratch involving broken skin immediately and to seek postexposure
treatment for rabies within a maximum of 48 hours. Seeking quality biologicals and additional postexposure vaccine doses is critical to prevent rabies. In 2018, the WHO recommended that preexposure prophylaxis rabies regimens can be shortened to intradermal rabies vaccine at 2 separate sites on 2 visits (days 0 and 7). Recent evaluations add support to the reduced-dose preexposure prophylaxis. Changes to existing national guidelines (0, 7, 28 days, intramuscular dosing) in major countries (United States, Canada, Australia, France) have yet to be considered; the United Kingdom has formally considered the WHO advice and has elected to stay with the status quo.

**Japanese Encephalitis**

Japanese encephalitis is endemic to many rural farming areas of Southeast Asia and the Indian subcontinent (Figure 2). Sporadic cases with severe sequelae continue to occur in travelers. Overall risk is very low for short-stay travelers and for those who confine their travel to urbanized areas or brief daytime rural exposures during typical tourist excursions. However, cases may be sporadic and have occurred in short-stay visitors traveling out of season whose only rural travel had been to beach resorts. In temperate regions, the transmission season is from April through November. In tropical or subtropical regions of Oceania and Southeast Asia, transmission may occur year-round. Vaccination is recommended for (1) long-stay travel to an endemic rural area, (2) expatriation to anywhere in an endemic country, (3) short-term travel to endemic rural areas with potential unprotected outdoor exposure, such as with adventure travel, or (4) short-term travel during a current local epidemic.

**Cholera**

Cholera vaccination is no longer required by any country, and the risk to typical travelers is insignificant. However, aid, refugee, and health care workers in areas where cholera is endemic or epidemic may consider cholera vaccine. A live attenuated oral cholera vaccine was approved in 2016 by US Food and Drug Administration for use only in immunocompetent adults in the United States; duration of immunity is unknown at present. A highly effective oral, killed, whole-cell–B subunit cholera vaccine is available widely outside the United States. This vaccine also has about 50% efficacy against enterotoxigenic Escherichia coli and a 7% to 23% efficacy against all traveler’s diarrhea, but this indication is not generally recommended by authoritative sources.

**Tick-Borne Encephalitis**

Tick-borne encephalitis is an emerging, important, and serious flavivirus central nervous system infection in endemic areas. Distribution is highly focal in a range that extends in a swath from Germany through Scandinavia and the Baltic states to Siberia and Vladivostok in the east. Risk to travelers is low unless extensive outdoor activities are planned in forested regions in endemic areas. Immunization against tick-borne encephalitis is recommended for adventure travel, extensive outdoor exposure, or camping in the forests of the endemic countries between April and October. Tick precautions are also recommended. The vaccine is available in most endemic countries but not in the United States or Canada. Three to 4 weeks are required for accelerated vaccination and development of immunity, making vaccination on arrival impractical for short-stay travelers.

**TRAVEL VACCINES FOR SPECIAL POPULATIONS**

Immunocompromised travelers and travelers living with HIV comprise up to 4% of travelers seen in some US travel clinics and pursue itineraries largely similar to those of immunocompetent travelers. Different conditions and medications produce widely varying degrees of immunocompromise, and there are many unknowns in this field. Guidance regarding vaccination of immunocompromised travelers is less evidence-based than with other categories of travelers. Health hazards at the destination that would exacerbate the underlying condition can be
more severe in an immunocompromised traveler.

Advice from a specialized travel clinic is of benefit for persons who are severely immunocompromised (transplants, active malignancy, congenital immunodeficiency) or have underlying chronic disease, especially those who are planning to live abroad for a long time or who have complicated itineraries.

Travelers with autoimmune diseases (eg, systemic lupus erythematosus, inflammatory bowel disease, rheumatoid arthritis, multiple sclerosis) who are not being treated with immunosuppressive or immunomodulatory drugs are not considered significantly immunocompromised, but definitive data are lacking.

Immunocompromised persons including those taking immunosuppressive drugs and most biological response–modifying drugs should not receive live vaccines. In the context of specific travel vaccines, this includes YF, MMR, oral cholera, and oral typhoid. Asplenia is not a contraindication for live viral vaccines. Nonlive vaccines, although safe, may have suboptimal efficacy in immunocompromised hosts, and the implications of this issue should be discussed with the traveler. In general, such vaccines are indicated because of specific risk of potentially serious infection at the destination.

Unvaccinated travelers with severe immune compromise should be strongly discouraged from travel to destinations that present a true risk for YF. If travel is unavoidable to an area where YF vaccine is recommended for personal protection and the vaccine has not been given, these travelers should be informed of the risk of YF and carefully instructed in methods to avoid mosquito bites.

Significant immunosuppression is a contraindication to YF vaccination. Recent data suggest that YF vaccination before solid organ transplant, even long before transplant, generally provides protective antibody levels after transplant. Patients with asymptomatic HIV or CD4 cell counts greater than 200/mL may be offered YF vaccine if travel to YF-endemic areas is unavoidable; recipients should be monitored closely for possible adverse effects. Patients with undetectable viral loads respond well to YF vaccination regardless of CD4 cell count. Because vaccine response may be suboptimal, such vaccinees are candidates for serologic testing 1 month after vaccination. If international travel requirements, and not true exposure risk, are the only reasons to vaccinate a traveler with asymptomatic HIV infection or a limited immune deficit, the physician should provide a waiver letter.

The period of time clinicians should wait after discontinuation of immunosuppressive therapies before administering a live vaccine such as YF is not consistent across all live vaccines. No specific data exist for the safety or efficacy of YF vaccine in this regard. For cancer chemotherapy, radiation therapy, and highly immunosuppressive medications (exclusive of lymphocyte-depleting agents and organ transplant immunosuppression), the waiting period is 3 months. For lymphocyte-depleting agents (alemtuzumab and rituximab), the waiting period is 6 months or more, although some experts believe the waiting period should be 1 year or more. For corticosteroid regimens considered immunosuppressive, the waiting period is 1 month. Restarting immunosuppression after live vaccination has not been studied, but some experts would recommend waiting at least 1 month.

Immunocompromised travelers may require additional nontravel vaccines compared with healthy travelers. All travelers are at increased risk of respiratory illness. Unvaccinated persons who have the accepted routine indications for the pneumococcal vaccines, which includes most individuals with chronic disease and immunocompromising conditions, should receive this vaccine during the pretravel consultation if not already done. Adult asplenic or functionally asplenic individuals often arrive at the clinic incompletely vaccinated against meningococcal disease (ACWY and B), Haemophilus influenzae type B, and pneumococcal infection. Asymptomatic adults with HIV and reconstituted CD4 cell
counts of more than 200/mL are considered to have limited immune deficits and should receive additional vaccines according to the usual guidelines found elsewhere in this Mayo Clinic Proceedings vaccine thematic series.94

The HB vaccine high-dose regimen is recommended for all immunocompromised persons and adult hemodialysis patients.98 Titers should be determined for HB surface antibody response after vaccination; patients should be revaccinated if response is absent. Immunocompromised travelers may have inadequate seroconversion after a single dose of HA vaccine.83 Efforts should be made to administer 2 doses over a 6-month period prior to their trip. Instead of concomitant immunoglobulin with the first dose, the approach of giving a second dose of vaccine at least 4 weeks after the first dose for time-constrained travelers who can get both doses before travel has been effective in selected studies.90

CONCLUSION
Vaccine-preventable diseases occur during travel, including in developed countries, and impact the need for otherwise routinely recommended immunizations as well as for specific travel immunizations based on destinations or activities. The pretravel evaluation is an ideal setting to update all age-appropriate immunizations and provide protection against travel-associated diseases. Malaria chemoprophylaxis and education is an additional critical component of the pretravel health encounter. Prevention of other potential risks such as traveler’s diarrhea, altitude illness, and blood-borne and sexually transmitted pathogens should be addressed, and travelers should be prepared to recognize or self-manage certain illnesses should they arise.

Abbreviations and Acronyms: CDC = Centers for Disease Control and Prevention; HA = hepatitis A; HB = hepatitis B; IHR = International Health Regulations; MMR = measles, mumps, and rubella; VPA = vaccine-preventable disease; WHO = World Health Organization; YF = yellow fever

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The Thematic Review on Vaccines will continue in an upcoming issue.

REFERENCES


