



Individualizing immunization for international travelers

Take into account routine childhood vaccinations, those that are mandatory for specific destinations, and these highly recommended immunizations.

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PRACTICE RECOMMENDATIONS

➤ *Recommend immunizations and safety precautions to international travelers based on their destinations, previous immunizations, health status and anticipated activities, and time available before departure.* (C)

➤ *Consider accelerating routine immunizations for children who may be traveling abroad.* (C)

➤ *Refer immunocompromised or pregnant patients to a travel medicine clinic for consultation before departure.* (C)

Strength of recommendation (SOR)

- (A) Good-quality patient-oriented evidence
- (B) Inconsistent or limited-quality patient-oriented evidence
- (C) Consensus, usual practice, opinion, disease-oriented evidence, case series

International travel, whether for business, pleasure, child adoption, medical tourism, or adventure, continues to grow. In 2015, more than 70 million US citizens traveled internationally.¹ Many individuals contact family physicians first about their plans for travel and questions about travel-related health advice. This article provides an overview of the vaccines recommended for travelers headed to international destinations. Because country-specific vaccination recommendations and requirements for entry and departure change over time, check the Centers for Disease Control and Prevention (CDC) Web site for up-to-date requirements and recommendations (www.cdc.gov/travel).

Vaccine schedules vary according to destination and individual risks

There is no single vaccination schedule that applies to all travelers. Each schedule should be individualized based on the traveler's destination, risk assessment, previous immunizations, health status, and time available before departure.^{2,3} Pregnant or immunocompromised travelers should seek advice from an experienced travel medicine consultant on the immunization recommendations specifically meant for them.^{4,5}

Travel vaccines (TABLE⁶) are generally categorized as routine, required, or recommended.

1. Routine vaccines are the standard child and adult immunizations recommended by the Advisory Committee on Immunization Practices (ACIP). These include such vaccines as diphtheria-tetanus toxoids-acellular pertussis (DTaP), inactivated polio vaccine (IPV), *Haemophilus influenzae* type b (Hib), hepatitis B, rotavirus and pneumococcal vaccines, and human papillomavirus (HPV).
2. Required vaccines—eg, yellow fever and meningococcal vaccines—must be documented on the International Certificate of Vaccination before entry into certain countries.

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Flu vaccine is recommended for all travelers ≥6 months of age, as flu season varies internationally.

3. Recommended vaccines are advised based on the travel destination and anticipated activities. These would include vaccines for typhoid, rabies, Japanese encephalitis, and polio (adult booster).

Routine vaccinations may need to be accelerated

Pre-travel patient encounters are an opportunity to update routine vaccinations.^{7,8} Immunization against childhood diseases remains suboptimal in developing countries, where vaccine-preventable illnesses occur more frequently.⁹

Routine vaccines may be administered on an accelerated basis depending on geographic destination, seasonal disease variations, anticipated exposures, and known outbreaks at the time of travel.

■ **MMR vaccine.** Measles is still common in many parts of the world, and unvaccinated or incompletely vaccinated travelers are at risk of acquiring the disease and importing it to the United States (see “Measles: Why it’s still a threat,” 2017;66:446-449.) In 2015, a large, widespread measles outbreak occurred in the United States, linked to an amusement park in California, likely originating with an infected traveler who visited the park.¹⁰

All children older than 12 months should receive 2 doses of measles-mumps-rubella (MMR) vaccine separated by at least 28 days before departure (regardless of their destination). Infants between 6 and 11 months are at risk for high morbidity and may therefore receive a single dose of MMR earlier than the routinely recommended age of 12 to 15 months. Adolescents and adults without evidence of immunity against measles should get 2 doses of MMR separated by at least 28 days.¹¹ Acceptable presumptive evidence of immunity against measles includes written documentation of adequate vaccination, laboratory evidence of immunity, laboratory confirmation of measles, or birth before 1957.

■ **Varicella vaccine.** Children, adolescents, and young adults who have received only one dose of varicella should get a second dose prior to departure. For children 7 to

12 years, the recommended minimum interval between doses is 3 months. For individuals 13 years or older, the minimum interval is 4 weeks.^{7,8}

■ **Influenza vaccine** is routinely recommended for all travelers 6 months of age or older, as flu season varies geographically. Flu season in the Northern Hemisphere may begin as early as October and can extend until May. In the Southern Hemisphere, it may begin in April and last through September. Travelers should be vaccinated at least 2 weeks before travel in order to develop adequate immunity.^{12,13}

Required vaccinations: Proof is needed before traveling

Yellow fever (YF) is a mosquito-borne viral illness characterized by fever, chills, headache, myalgia, and vomiting. The disease can progress to coagulopathy, shock, and multi-system organ failure.¹⁴ YF vaccine is recommended for individuals 9 months or older who are traveling to or living in areas of South America or Africa where YF virus transmission is common (map: <http://www.cdc.gov/yellowfever/maps/>).

YF vaccine is a live-attenuated virus formulation and, therefore, should not be given to individuals with primary immunodeficiencies, transplant recipients or patients on immunosuppressive and immunomodulatory therapies, or patients with human immunodeficiency virus (HIV) whose CD4 count is below 200/mL. Other contraindications to YF vaccine are age younger than 6 months, allergy to a vaccine component, and thymic disorders. Serious adverse reactions to the vaccine are rare, but include 2 syndromes: YF-associated neurotropic disease and YF vaccine-associated viscerotropic disease.¹⁵

In many YF-endemic countries, vaccination is legally required for entry, and proof of vaccination must be documented on an International Certificate of Vaccination or Prophylaxis (ICVP). Additionally, some countries may require proof of vaccination before allowing travel through an endemic region, to prevent introduction of the disease elsewhere. Travelers with a specific contrain-

TABLE
Common vaccines for international travel⁶

Vaccine	Brand	Dose	Route	Age	Schedule	Booster
Hepatitis A (adult)	Havrix	1 mL	IM	≥19 y	0 and 6-12 mo	None
	Vaqta	1 mL	IM	≥19 y	0 and 6-18 mo	None
Hepatitis A (pediatric)	Havrix	0.5 mL	IM	1-18 y	0 and 6-12 mo	None
	Vaqta	0.5 mL	IM	1-18 y	0 and 6-18 mo	None
Combined hepatitis A and hepatitis B	Twinrix	1 mL	IM	≥18 y	0, 1, 6 mo; accelerated schedule: 0, 7, 21-30 d, 12 mo	None
Hepatitis B (adult)	Engerix-B	1 mL	IM	≥20 y	0, 1, 6 mo; accelerated schedule: 0, 1, 2, 12 mo	None
	Recombivax HB	1 mL	IM	≥20 y	>0, 1, 6 mo	None
Hepatitis B (pediatric)	Engerix-B	0.5 mL	IM	≤19 y	0, 1, 6 mo; accelerated schedule: 0, 1, 2, 12 mo	None
	Recombivax HB (primary)	0.5 mL	IM	≤19 y	0, 1, 6 mo	None
	Recombivax HB (adolescent accelerated)	1 mL	IM	11-15 y	0, 4-6 mo	None
Inactivated polio (adult)	Ipol	0.5 mL	SC or IM	≥18 y	1 dose at ≥18 y, if patient has received polio vaccine series	None
Japanese encephalitis	Ixiaro	0.5 mL	IM	≥17 y	0 and 28 d	≥1 y after primary series
		0.5 mL	IM	3-16 y	0 and 28 d	Data unavailable
		0.25 mL	IM	2 mo-2 y	0 and 28 d	Data unavailable
Meningococcal conjugate (MenACWY)	Menactra (MenACWY-D)	0.5 mL	IM	9-23 mo	2-dose primary series separated by 3 mo	If last dose at <7 y of age, give an additional dose 3 y after the last dose If last dose at ≥7 y of age, give a booster dose 5 y after the last dose
		0.5 mL	IM	2-55 y	1 dose	
	Menveo (MenACWY-CRM)	0.5 mL	IM	2-12 mo	2, 4, 6, 12 mo	
		0.5 mL	IM	7-23 mo	2-dose series separated by 3 mo	
		0.5 mL	IM	2-55 y	1 dose	
Meningococcal polysaccharide (MPSV4)	Menomune	0.5 mL	SC	≥2 y	1 dose	If multiple doses are anticipated at ≥56 y, MenACWY should be used instead
Rabies	Imovax	1 mL	IM	All ages	Preexposure series: 0, 7, 21 or 28 d	None
	RabAvert	1 mL	IM	All ages	Preexposure series: 0, 7, 21 or 28 d	None
Typhoid capsular polysaccharide	Typhim Vi	0.5 mL	IM	≥2 y	1 dose	Every 2 y
Typhoid oral, live, attenuated	Vivotif	1 pill	Oral	≥6 y	1 pill every other day for 4 doses	Every 5 y
Yellow fever	YF-Vax	0.5 mL	SC	≥9 mo	1 dose	See text

IM, intramuscular; SC, subcutaneous.

➤ **Many countries in which yellow fever is endemic don't allow entry without proof of vaccination on an International Certificate of Vaccination or Prophylaxis.**

dication to YF vaccine should obtain a waiver from a physician before traveling to a country requiring vaccination.¹⁶

The vaccination certificate is valid beginning 10 days after administration of YF vaccine. Immunity after a single dose is long lasting and may provide lifetime protection. Previously, re-vaccination was required every 10 years; however, in February 2015, ACIP approved a new recommendation stating a single dose of YF vaccine is adequate for most travelers.¹⁷

Although ACIP no longer recommends booster doses of YF vaccine for most travelers, clinicians and travelers should review the entry requirements for destination countries because changes to the International Health Regulations have not yet been fully implemented. Once this change is instituted, a completed ICVP will be valid for the lifetime of the vaccine.^{18,19} Country-specific requirements for YF can be found at <http://www.cdc.gov/yellowfever/maps/>. (Click on the link below the appropriate map.) In the United States, the YF vaccine is distributed only through approved vaccination centers. These designated clinics are listed in a registry on the CDC travel Web site at <https://wwwnc.cdc.gov/travel/yellow-fever-vaccination-clinics/search>.

■ **Meningococcal disease.** ACIP recommends routine vaccination against meningococcal disease for people 11 to 18 years of age and for individuals with persistent complement component deficiency, functional or anatomic asplenia, and HIV. Vaccination is recommended for travelers who visit or reside in areas where meningococcal disease is hyperendemic or epidemic, such as the meningitis belt of sub-Saharan Africa during the dry season of December to June (map: <http://wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/meningococcal-disease>). Travelers to Saudi Arabia during the annual Hajj and Umrah pilgrimages are required to have a certificate of vaccination with quadrivalent (serogroups A, C, Y, W-135) meningococcal vaccine issued within 3 years (and not less than 10 days) before entry.

Several meningococcal vaccines are available in the United States. The quadriva-

lent vaccines are Menactra (MenACWY-D, Sanofi Pasteur) and Menveo (MenACWY-CRM, GSK). A bivalent (serogroups C and Y) conjugate vaccine MenHibrix (Hib-MenCY-TT, GSK) is also licensed for use in the United States, but infants traveling to areas with high endemic rates of meningococcal disease who received this vaccine are not protected against serogroups A and W and should receive quadrivalent meningococcal conjugate vaccine. Serogroup B vaccination is not routinely recommended for travelers. Approximately 7 to 10 days are required after vaccination for the development of protective antibody levels.^{7,8,20,21}

■ **Polio.** Although polio has been nearly eradicated, as of the time this article was written, the disease has not been eliminated in Afghanistan, Guinea, Laos, Nigeria, or Pakistan. Other countries, such as Cameroon, Chad, and Ukraine remain vulnerable to international transmission.²² The CDC recommends that adults who are traveling to areas where wild polio virus (WPV) has circulated in the last 12 months and who are unvaccinated, incompletely vaccinated, or whose vaccination status is unknown should receive a series of 3 doses of IPV to prevent ongoing spread.²³ Adults who completed the polio vaccine series as children and are traveling to areas where WPV has circulated in the last 12 months should receive a one-time booster dose of IPV.²³

Infants and children in the United States should be vaccinated against polio as part of a routine age-appropriate series. If a child cannot complete the routine series before departure and is traveling to an area where WPV has circulated in the last 12 months, an accelerated schedule is recommended. Vaccination should be documented on the ICVP, as countries with active spread of poliovirus may require proof of polio vaccination upon exit. A list of the countries where the polio virus is currently circulating is available at <http://polioeradication.org/polio-today/polio-now/wild-poliovirus-list/>.

Both routine and accelerated vaccination schedules for children and adults are published annually by the CDC and are available at <http://www.cdc.gov/vaccines/schedules/hcp/index.html>.

Recommended vaccines

Japanese encephalitis (JE) is endemic throughout most of Asia and parts of the Western Pacific region (map: <http://www.cdc.gov/japaneseencephalitis/maps/>). JE vaccine is recommended for travelers who plan to spend more than a month in endemic areas during the JE virus transmission season. (In temperate areas of Asia, JE virus transmission is seasonal and usually peaks in the summer and fall. In the subtropics and tropics, transmission can occur year-round, often with a peak during the rainy season.)

This recommendation includes recurrent travelers or expatriates who are likely to visit endemic rural or agricultural areas during a high-risk period of JE virus transmission. Risk is low for travelers who spend less than a month in endemic areas and for those who confine their travel to urban centers. Nevertheless, vaccination should be considered if travel is planned for outside an urban area and includes such activities as camping, hiking, trekking, biking, fishing, hunting, or farming. Inactivated Vero cell culture-derived vaccine (Ixiaro) is the only JE vaccine licensed and available in the United States. Ixiaro is given as a 2-dose series, with the doses spaced 28 days apart. The last dose should be given at least one week before travel.²⁴

■ **Typhoid fever.** Vaccination against typhoid fever is recommended for travelers to highly endemic areas such as the Indian subcontinent, Africa, and Central and South America. Two typhoid vaccines are available: Vi capsular polysaccharide vaccine (ViCPS) administered intramuscularly (IM), and oral live attenuated vaccine (Ty21a). Ty21a is a live vaccine and should not be given to immunocompromised people or those taking antibiotics, as it may reduce immunogenicity. Ty21a must be kept refrigerated at 35.6° F to 46.4° F (2° C–8° C) and administered with cool liquid no warmer than 98.6° F (37° C). Both vaccines are only 50% to 80% efficacious, making access to clean food and water essential.^{3,5,25}

■ **Hepatitis A vaccine** should be given to all children older than one year traveling to areas where there is an intermediate or high risk of the disease. Children younger than

one year who are traveling to high-risk areas can receive a single dose of immunoglobulin (IG) 0.02 mL/kg IM, which provides protection for up to 3 months. One 0.06 mL/kg-dose IM provides protection for 3 to 5 months.

If travel continues, children should receive a second dose after 5 months. IG does not interfere with the response to YF vaccine, but can interfere with the response to other live injected vaccines (such as MMR and varicella).²⁶

■ **Hepatitis B vaccination** should be administered to all unvaccinated travelers who plan to visit an area with intermediate to high prevalence of chronic hepatitis B (HBV surface antigen prevalence $\geq 2\%$). Unvaccinated travelers who may engage in high-risk sexual activity or injection drug use should receive hepatitis B vaccine regardless of destination. Additionally, travelers who access medical care for injury or illness while abroad may also be at risk of acquiring hepatitis B via contaminated blood products or medical equipment.²⁷

Serologic testing and booster vaccination are not recommended before travel for immunocompetent adults who have been previously vaccinated. The combined hepatitis A and B vaccine provides effective and convenient dual protection for travelers and can be administered with an accelerated 0-, 7-, and 21-day schedule for last-minute travelers.^{7,8}

■ **Rabies** remains endemic in developing countries of Africa and Asia, where appropriate post-exposure prophylaxis is limited or non-existent.²⁸ Consider pre-exposure rabies prophylaxis for traveling patients based on the availability of rabies vaccine and immunoglobulin in their destination area, planned duration of stay, and the likelihood of animal exposure (eg, veterinarians, animal handlers, cavers, missionaries). Advise travelers who decline vaccination to avoid or minimize animal contact during travel. In the event the traveler sustains an animal bite or scratch, immediate cleansing of the wound substantially reduces the risk of infection, especially when followed by timely administration of post-exposure prophylaxis.

Post-exposure prophylaxis for unvaccinated individuals consists of local infiltration



Adults who completed the polio vaccine series as children and are traveling where wild polio virus has circulated in the last 12 months should receive a one-time booster dose of IPV.

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of rabies immunoglobulin at the site of the bite and a series of 4 injections of rabies vaccine over 14 days, or 5 doses over one month for immunosuppressed patients. The first dose of the 4-dose course should be administered as soon as possible after exposure. Two vaccines are licensed for use in the United States: human diploid cell vaccine (HDCV, Imovax Rabies, Sanofi Pasteur) and purified chick embryo cell vaccine (PCECV, RabAvert, Novartis Vaccines and Diagnostics). The vaccine should never be administered in the gluteal area, as this may result in lower antibody titers.²⁹

Additionally, promising new vaccines against malaria and dengue fever are under clinical development and may be available in the near future. **JFP**

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