

Travel Vaccination Update

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Abstract

As international travel increases, an update on the current guidance regarding travel vaccinations is important for healthcare providers. There have been recent changes to availability of certain vaccines that providers should familiarize themselves with. This article provides adult and pediatric-specific guidance for the most commonly required and requested travel vaccines, particularly the Japanese encephalitis vaccine, typhoid vaccines, and the yellow fever vaccine.

In addition to routine adult and childhood vaccination, travel vaccination is a key component to traveler's health when going abroad. Consultation with a primary care physician and/or travel medicine specialist can be helpful to review guidance at least six weeks prior to travel. The need for travel vaccinations is based on the individual's previous vaccination status, underlying health conditions, and expected exposures when traveling. Endemic pathogens and need for vaccination based on country of travel can be found on the Centers for Disease Control (CDC) website under Traveler's Health and Destination.¹ In the United States, the available travel vaccines include cholera, hepatitis A, hepatitis B, Japanese encephalitis, meningococcal vaccine, polio, rabies, typhoid, and yellow fever. The cholera and typhoid vaccines paused manufacturing in December 2020 as the COVID-19 pandemic decreased travel and the need for vaccination. The manufacturers plan on restarting production in the future, but no timeline has been given. This article discusses the current guidance regarding some of the most common adult and childhood travel-specific vaccines (see Table 1).

Table 1. Travel-Specific Vaccines Given in the United States^{2,3}

| Disease | Vaccine | Adult Dose | Pediatric Dose | Booster Dose |
|------------------------------|-----------------|---|--|---|
| Japanese Encephalitis | Ixiaro | <u>Dose:</u> 0.5 ml IM/dose for two total doses <u>18 to 65 years:</u> 1 st dose: day 0 2 nd dose: between days 7 to 28 <u>>65 years:</u> 1 st dose: day 0 2 nd dose: day 28 | <u>2 months to <3 years:</u> 0.25 mL IM/dose for two doses 1 st dose: day 0 2 nd dose: day 28 <u>≥3 years:</u> 0.5 ml IM/dose for two doses 1 st dose: day 0 2 nd dose: day 28 | Single booster dose given >1 year after completion of primary series if identified to have ongoing risk |
| Typhoid Fever | Ty21a (Vivotif) | <u>Dose for all adults:</u> 1 capsule by mouth every other day x 4 doses | <u>≥6 years:</u> 1 capsule by mouth every other day x 4 doses | Repeat full four dose regimen every 5 years if identified to have ongoing risk |

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|---------------------|---------------------------|---|---|--|
| | Vi polysaccharide vaccine | <u>Dose for all adults:</u> 0.5 mL IM for one dose | <u>≥2 years:</u> 0.5 mL IM for one dose | Repeat single injection every 2 years if identified to have ongoing risk |
| Yellow Fever | YF-VAX | <u>Dose for all adults:</u> 0.5 mL SQ for one dose | <u>≥9 months:</u> 0.5 mL SQ for one dose | Single dose considered to provide lifelong protection High risk travelers with ongoing risk can consider a single booster dose every 10 years |

Japanese Encephalitis (JE) Vaccine

Japanese encephalitis virus is an RNA virus that belongs to the genus *Flavivirus* and is transmitted via the bite of an infected *Culex* mosquito. Most infections are asymptomatic; however, approximately one percent of infected persons will go on to develop acute encephalitis.² The virus is endemic in most of Asia and parts of the western Pacific. JE primarily affects children. Most adults in endemic countries have natural immunity after childhood infection, but individuals of any age may be affected. The virus is transmitted mostly in areas of rice cultivation and flood irrigation as well as during the monsoon rains where mosquitos are drawn to water. Each individual country has specific JE virus seasons that can be referenced on the CDC website.¹ The incidence in endemic areas is 6-11 cases per 100k children; however, the incidence in travelers from non-endemic countries is less than one case per one million travelers. Since the likelihood of developing disease is low, the vaccine is recommended only in those persons that are considered to be at higher risk for developing infection.^{2,3}

There is only one JE virus vaccine licensed and available in the US. Ixiaro is an inactivated Vero cell culture-derived vaccine that protects against five JE virus genotypes. It was FDA approved in March 2009 for use in persons ages 17 years and over, and in May 2013 for use in children ages two months through 16 years. There are other JE virus vaccines available outside of the US, which includes the childhood vaccine given in endemic areas around 12 months of age.

JE vaccine is recommended for those individuals moving to a JE endemic area to take up residence, longer term travelers (one month or longer) to a JE endemic area, frequent travelers to JE endemic areas, and laboratory workers with potential exposure to JE viruses other than vaccine virus. JE vaccine can be considered for those who are unclear of the duration of travel and for those shorter-term travelers (less than one month) with an increased risk for development of disease based on travel duration, season, location, activities, and accommodations. JE vaccine is not recommended for those with short travel times in urban areas outside of JE virus transmission season.

JE vaccine is a two-dose primary series given at days 0 and 28, and should be completed at least one week prior to travel. For those 18 years of age or older, the second dose can be given between days 7 and 28. A booster dose can be given one year or more after the primary series. Some individuals with frequent travel and ongoing risk can consider a booster dose every 10

years for prolonged protection. A single dose in the prefilled adult syringe is 0.5 ml, but children two months to two years of age should only be given 0.25 ml. There have not been any safety concerns after approval of this vaccine.

Typhoid vaccine

Salmonella enterica serotype typhi is a Gram-negative bacteria that invades the blood stream and causes a severe, febrile illness termed typhoid fever. Transmission is via the ingestion of contaminated food or water and within 6 to 30 days, travelers develop fever, headache, myalgias, abdominal pain, and/or diarrhea. Most cases occur in southern Asia (India, Pakistan, Bangladesh), but other areas that are considered a risk include Africa, Southeast Asia, South America, and the Caribbean. Each year, there are 26 million cases of typhoid fever worldwide and 215,000 deaths. In the US, 85% of typhoid cases are from international travel. There are currently three typhoid vaccines being manufactured. Two are available in the US and one available outside of the US.^{2,3}

Ty21a (Vivotif) is an oral, live-attenuated vaccine that is indicated for children and adults six years of age and older. It is administered as one capsule given every other day for four doses. The capsules must be kept refrigerated, taken with a cool liquid lower than body temperature, and given one hour before a meal and two or more hours after a previous meal. All doses should be completed more than one week before travel. A booster dose is recommended every five years for those travelers that remain at risk. Since this is a live vaccine, it is contraindicated in immunocompromised patients, pregnant women, and those with acute gastroenteritis.

The Vi capsular polysaccharide vaccine (ViCPS) is a single dose, injectable vaccine indicated for children and adults two years of age and older. It should be administered more than two weeks before travel. A booster dose is recommended every two years for those travelers that remain at risk.

The third type of vaccine is the protein-conjugate Vi vaccines that are indicated for children six months of age and older, and have been shown to have greater efficacy in children greater than two years old as well as longer duration of protection compared to the polysaccharide vaccine. Two of these vaccines have been licensed in India and are currently in use. They are not available in the US.^{2,3}

Yellow Fever Vaccine

Yellow fever virus is an RNA virus that belongs to the genus *Flavivirus*. Transmission is via the bite of the *Aedes* or *Haemogogus* mosquito in tropical areas of Africa and South America. Worldwide cases approach 200,000 annually and deaths as high as 30,000 per year. Most individuals will be asymptomatic or have mild symptoms including fever, chills, body aches, and fatigue. There will be a small proportion of travelers that develop severe disease characterized by high fever, jaundice, organ failure, bleeding, and shock.^{2,3}

YF-VAX is a single dose Yellow fever vaccine available in the US and is a live, attenuated injectable vaccine given to adults and children nine months of age and older. Proof of Yellow fever vaccination is valid ten days after injection. It is required for all travelers arriving from an area where Yellow fever is endemic. A single dose is now considered to provide life-long protection, but a booster dose ten years later can be considered for those living or traveling to

areas where there are outbreaks. The vaccine was not readily available for many years due to manufacturing issues, but in April 2021 it is now available and ready for administration.

Yellow fever vaccine should not be given to immunocompromised persons or pregnant women. Since it is a live vaccine, it should be given either with other live vaccines or separated by 30 days. There are three well-described vaccine adverse reactions (1) hypersensitivity or anaphylaxis, (2) vaccine-associated neurologic disease, and (3) vaccine-associated viscerotropic disease. Children 6-8 months of age and adults over 60 years of age have a higher risk of a vaccine adverse event and immunization in these age groups should be considered carefully.

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