

INFORMATION PAPER

DHA-IHD
26 April 2019

SUBJECT: Japanese Encephalitis and Japanese Encephalitis Vaccine

1. Purpose. To describe Japanese Encephalitis (JE) and the vaccine to prevent it.
2. Facts.
 - a. Microbiology. Japanese encephalitis (JE) virus is a single-stranded RNA virus that belongs to the *Flavivirus* genus, and is closely related to West Nile and St. Louis encephalitis viruses.
 - b. Disease. Incubation is on average 5-15 days. Most human infections with JE virus are associated with mild flu-like symptoms or asymptomatic. Less than 1% of those infected with JE virus develop severe clinical disease. JE virus infection of the brain, spinal cord, and meninges may be associated with fever, headache, mental status changes, focal neurologic deficits, generalized weakness, and movement disorders. When encephalitis occurs, the case-fatality rate is 20%–30%, and 30%–50% of survivors experience serious neurologic, cognitive, or psychiatric sequelae.
 - c. Epidemiology. JE disease occurs throughout south-central, southeastern, and eastern Asia, and parts of the western Pacific. JE is the leading cause of mosquito-borne encephalitis in these areas. JE virus is transmitted through the bite of infected mosquitoes, primarily *Culex* species. Pigs and birds are intermediate hosts. Infected humans are incidental or dead-end hosts because they usually do not develop a level or duration of viremia sufficient to infect mosquitoes. Transmission primarily occurs in rural agricultural areas, often associated with rice cultivation and flood irrigation. In temperate areas of Asia, transmission is seasonal, and human disease usually peaks in summer and fall. In the tropics and subtropics, seasonal transmission varies with monsoon rains and irrigation practices and may occur year-round. For most travelers to Asia, risk for JE is low but varies based on destination, duration, season, and activities. Groups at high risk include:
 - (1) Persons moving to a JE-endemic country to take up residence, longer-term (e.g., > 1 month) travelers to JE-endemic areas, and frequent travelers to JE endemic areas.

- (2) Shorter-term (e.g., < 1 month) travelers with an increased risk of JE based on planned travel duration, season, location, activities, and accommodations.
 - (3) Travelers visiting endemic areas who are uncertain of specific duration of travel, destinations, or activities.
- d. Vaccine. Japanese Encephalitis Vero Cell vaccine (JE-VC) is an inactivated vaccine product, trade named IXIARO®, manufactured by Valneva Scotland Ltd. and distributed in the United States by Valneva USA, Inc. Currently, this is the only FDA-approved vaccine for JE prevention available in the United States. IXIARO® is a sterile purified vero cell-culture-derived vaccine, available in single-dose, pre-filled syringes. It does not contain thimerosal or other preservatives, and it is latex-free. IXIARO® is a clear liquid with white precipitate; when shaken before use, a white/cloudy suspension forms.
- e. Immunization. IXIARO® is licensed for persons older than 2 months traveling to areas at risk for JE. It is administered as a two-dose primary series.
- (1) For children ages 2 months through 3 years, administer a 0.25 mL dose intramuscularly in the anterolateral thigh. Carefully follow the steps outlined in the package insert to prepare the 0.25 mL pediatric dose.
 - (2) For children ages 3 years or older, and adults, administer a 0.5 mL dose intramuscularly in the deltoid region.
 - (3) In children >2 months to 18 years, the primary vaccination schedule is two doses administered on days 0 and 28.
 - (4) In adults aged 18-65 years, the primary vaccination schedule is two doses administered on days 0 and 7-28.
 - (5) In adults aged >65 years, the primary vaccination schedule is two doses administered on days 0 and 28.
 - (6) Booster. For adults and children, a one-time booster dose (i.e., third dose) should be given >1 year after completion of the primary JE-VC series if ongoing exposure or re-exposure to JE virus is expected. Children who get the booster dose before age 3, should get 0.25 mL dose.

- (7) JE-VC vaccination should be completed at least one week prior to potential exposure to JE virus, whenever possible.
 - (8) Individuals who previously received JE-MB (also called JEVax®), the mouse brain-derived vaccine formerly used in the United States, and who continue to require protection against JE virus, should receive a 2-dose primary series of JE-VC (IXIARO®).
- f. **Contraindications and Precautions.** A severe allergic reaction after a previous dose of JE-VC (IXIARO®) or any other JE vaccine or to any component of IXIARO® is a contraindication to administration of IXIARO®. IXIARO® contains protamine sulfate, a compound known to cause hypersensitivity reactions in some people. Individuals who show hypersensitivity reactions after receiving the first dose of the vaccine should not be given the second dose. Defer vaccination in people with moderate to severe acute illness until illness has resolved. Safety and effectiveness of JE vaccines have not been established in pregnant women; use in pregnancy should be considered with clinical consultation of potential risk and benefit.
 - g. **Adverse Events.** The most common adverse events following JE-VC (IXIARO®) administration are injection site reactions, fever, headache, myalgia, and influenza-like illness. Fever, irritability, and diarrhea are most common in infants aged 2-12 months.
 - h. **DoD Policy.** Administer JE-VC vaccine to military personnel deploying to or traveling within INDOPACOM including USFK in accordance with Force Health Protection guidance. In addition, vaccination is highly recommended for service members, DoD civilians, family members, and other beneficiaries moving to a JE-endemic country to take up residence, longer-term (e.g., >1 month) travelers to JE-endemic areas, and frequent travelers to JE-endemic areas. JE vaccine should also be considered for shorter-term (e.g., <1 month) travelers with an increased risk of JE based on planned travel duration, season, location, activities, and accommodations. Vaccination also should be considered for travelers to endemic areas who are uncertain of specific duration of travel, destinations, or activities. JE vaccine is not recommended for travelers with very low risk itineraries, such as shorter-term travel limited to urban areas or travel that occurs outside of a well-defined JE virus transmission season.
 - i. **Special Considerations.** Laboratory workers with a potential for exposure to infectious JE virus should be vaccinated against JE virus in accordance with recommendations of the Advisory Committee on Immunization Practices (ACIP).

3. References.

- a. Centers for Disease Control and Prevention. Japanese Encephalitis Vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2010;59(No. RR-1):1-27
- b. Centers for Disease Control and Prevention. Recommendations for Use of a Booster Dose of Inactivated Vero Cell Culture-Derived Japanese Encephalitis Vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2011;60(20):661-663.
- c. Centers for Disease Control and Prevention. Use of Japanese Encephalitis Vaccine in Children: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2013;62(45):898-900.
- d. Center for Disease Control and Prevention Yellow Book: <https://wwwnc.cdc.gov/travel/yellowbook/2018/infectious-diseases-related-to-travel/japanese-encephalitis>.
- e. Multiple resources (e.g., package inserts, Vaccine Information Statements) assembled by DHA-IHD: www.health.mil/JEV.

Pacific Region Vaccine Safety Hub
Approved: Deputy Chief, Immunization Healthcare Division
877-438-8222 (DSN 761-4245)