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) Travelers staying for prolonged periods in rural areas where JE is endemic or epidemic.

   (2) Travelers with extensive unprotected outdoor, evening/nighttime exposure in rural areas.
(3) Travelers visiting an area with an ongoing JE outbreak.

(4) Travelers visiting endemic areas who are unsure of their travel itineraries and destinations.

d. Vaccine. Japanese Encephalitis Vero Cell vaccine (JE-VC) is an inactivated vaccine product, trade named IXIARO®, manufactured by Valneva, and distributed in the United States by VaxServe, a Sanofi Pasteur company. 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, with doses administered at least 28 days apart.

(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) Accelerated schedule. For adults 18 through 65 years of age, an accelerated two-dose primary series with IXIARO® is administered at least 7 days apart.

(4) Booster. A one-time only booster dose (third dose) may be given at least 11 months after completion of the two-dose primary immunization series if ongoing exposure or re-exposure to JEV is expected. Children who get the booster dose before age 3, should get 0.25 mL dose.

(5) JE-VC vaccination should be completed at least one week prior to potential exposure to JE virus, whenever possible.

(6) 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 PACOM in accordance with PACOM Force Health Protection guidance. In addition, vaccination is highly recommended for service members, DoD civilians, family members, and other beneficiaries who will be stationed or visiting for more than 30 days in JE endemic areas. Vaccination is recommended for short-term (<1 month) travelers to endemic areas if they plan to travel outside of urban areas; travelers to areas with ongoing outbreaks; and travelers to endemic areas who are unsure of travel itineraries/destinations.

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.


e. Multiple resources, including vaccine package inserts and Vaccine Information Statements, available on: www.health.mil/JEV.