Japanese encephalitis

Japanese encephalitis is transmitted to humans in predominantly rural parts of Asia and the Western Pacific especially where rice growing and pig farming are common

Key messages

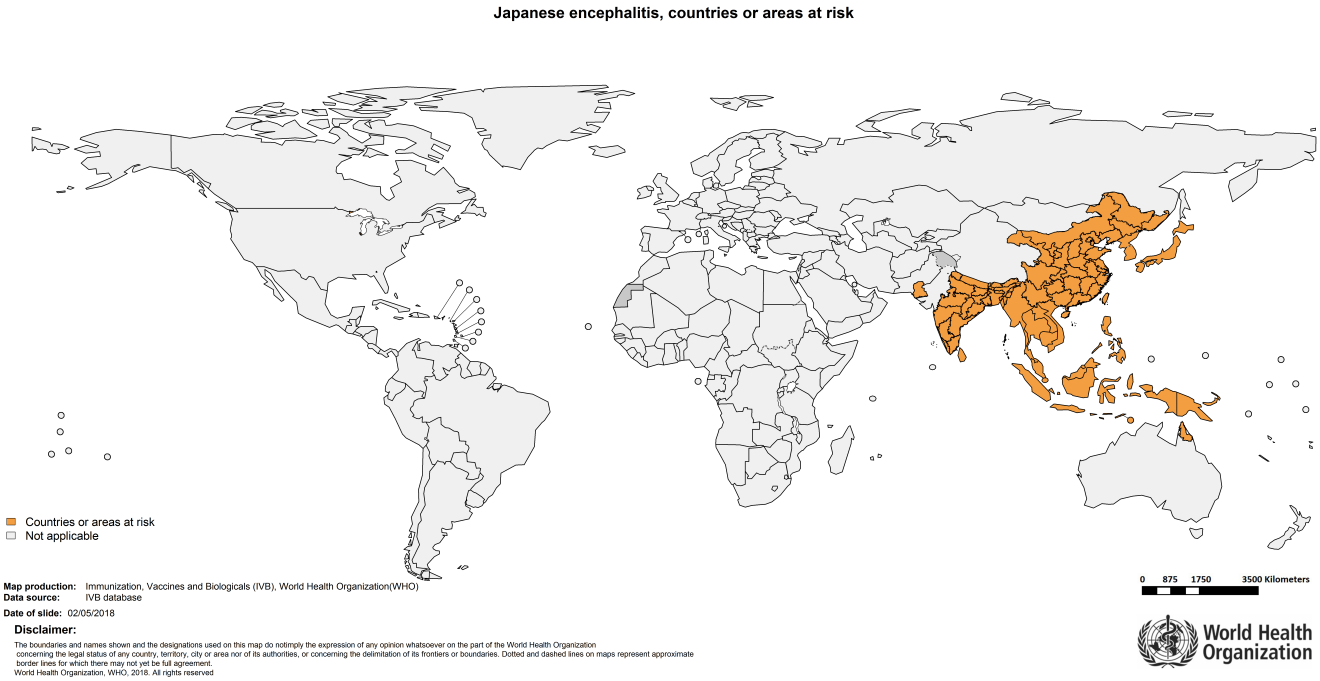
- **Japanese encephalitis (JE) is a viral infection that can cause encephalitis (inflammation of the brain).**
- **It is transmitted (spread) through the bite of an infected *Culex* spp. mosquito.**
- **The disease occurs in large parts of Asia and the Western Pacific, usually in rural areas where rice growing and pig farming are common.**
- **Most human JE infections with JE virus do not cause symptoms. If symptoms are severe and require hospitalisation, death rates are high and neurological complications are common.**
- **Risk of contracting JE for most travellers is very low, especially for short term travellers visiting urban areas. Long stay visits to risk areas and spending time near rice fields or pig farms increases the risk.**
- **All travellers should avoid mosquito bites particularly if outside at night and during twilight periods at dusk and dawn [1].**
- **An effective vaccination is available for travellers at increased risk.**

Overview

JE is a viral encephalitis caused by a flavivirus. Other flaviviruses include dengue, West Nile virus and yellow fever [2]. JE infection is transmitted to humans by *Culex* spp. mosquitoes in predominantly rural parts of Asia and the Western Pacific where rice cultivation and pig farming are common [2].

Risk areas

Figure 1: Countries or areas at risk



Source: World Health Organization

Please check our Country Information pages for individual country vaccine recommendations.

JE was first recognised in Japan in the late 1800s, but the first major outbreak (involving 6,000 cases) was described in 1924 [3]. Since then, JE has increasingly been recognised throughout most countries in East and Southeast Asia (see figure 1) where it is the main cause of viral encephalitis [2].

The global incidence of JE is unknown. It is estimated that 68,000 clinical cases of JE occur every year in 24 JE endemic countries in South-East Asia and the Western Pacific [2]. In 2022, the first reported JE outbreak in mainland Australia was declared [4]. In endemic countries JE is primarily a disease of children [5].

Most JE infections are mild or have no apparent symptoms and it is likely many cases are not reported [6]. Approximately one in 250 infections results in severe infection with encephalitis (inflammation of the brain), of these many will die or be left with long term significant neurological problems [2].

The incidence of JE in humans varies by country, higher incidence usually coincides with the rainy season. However, seasonal patterns can vary within individual countries and from year to year.

Cases may be reported outside of the normal seasonal period of high transmission [7].

Risk for travellers

The overall incidence of JE in travellers from non-JE risk countries visiting Asia is estimated to be less than one case per one million travellers [8]. However, cases of JE have been reported in travellers. Between 1973 and 2020, a total of 88 confirmed cases of JE were reported in travellers from non-endemic countries [8].

There have been eight documented cases of JE in UK citizens [9-13]. The three cases diagnosed in 2014/2015 resulted in severe neurological illnesses and long-term sequelae. None of these three travellers had received the JE vaccine, despite having indications for it [12].

The risk for most travellers visiting risk areas is very low, especially for short-term travellers visiting urban areas. There is an increased risk for people who intend to live or travel for long periods of time in JE risk areas or during outbreaks and have rural trips [3, 14]. Certain activities, even during short trips where there is significant rural, outdoor or night-time exposure e.g., fieldwork or camping can increase the traveller's risk [8].

Transmission

JE virus is transmitted to humans from animals and birds through the bite of an infected *Culex* spp. mosquito. These mosquitoes feed mostly at night, between dusk and dawn; pigs and wading birds are the principal hosts.

Culex spp. mosquitoes become infected when they bite animals (particularly pigs) or birds already infected with JE. JE is mostly found in rural and peri-urban settings. Flooded rice fields and marshes provide ideal breeding grounds for *Culex* spp. mosquitoes. In temperate regions of Asia, most cases occur in the warm season, when large outbreaks can occur [2].

Cases of JE can also occur outside the normal high transmission season [15]. In the tropics and subtropics, JE can occur year-round, but transmission often intensifies during the rainy season and pre-harvest period in rice-cultivating regions [2].

Signs and symptoms

The incubation period for JE is between four to 14 days; most JE infections are mild or have no symptoms [2]. Approximately one in 250 infections will result in severe illness, including a rapid onset fever, headache, neck stiffness, disorientation, seizures and coma [16, 17]. Approximately 30 percent of those who develop a severe illness will die. In those who survive, it is estimated that 20-30 percent will develop permanent neurological, behavioural or intellectual problems [2].

Diagnosis and treatment

JE should be suspected in individuals with symptoms, who live in or have recently visited an area where JE is known to occur. Clinical advice should be sought in the first instance from a local microbiology, virology, or infectious disease consultant. Health professionals who suspect JE should send appropriate samples for testing (with full clinical and travel history) to the Rare and Imported Pathogens Laboratory, UK Health Security Agency (UKHSA) [7].

There is no specific treatment for JE and treatment focuses on relieving symptoms often in intensive care. Long-term care for neurological complications may be needed.

Preventing Japanese encephalitis

The risk of acquiring JE can be reduced by insect bite avoidance methods, particularly at night (between dusk and dawn), when the *Culex* spp. mosquito is most active.

Travellers are at increased risk of infection when visiting rural areas. Short trips (usually less than a month) especially if only travelling to urban areas, are considered lower risk.

A JE vaccine is available and is recommended for those intending to stay for long periods in regions where JE is known to occur or whose planned activities will increase their risk (see vaccine recommendations below).

Vaccine information

All travellers should undergo a careful risk assessment which considers the itinerary, duration of stay, season of travel and planned activities. Country-specific recommendations can be found in the Country Information pages.

JE vaccine is recommended for individuals at increased risk of exposure during travel or through their occupation [7] including:

- Travellers who are going to live in an area where JE is known to occur.
- Travellers staying for a month or more in a JE risk area, particularly during transmission season.
- Those who are frequently travelling to JE risk areas.
- Those with potential exposure to JE in a laboratory.

The JE vaccine may also be considered for

- Travellers staying for less than one month in a risk area but where there may be an increased risk of exposure to JE infection, e.g. visiting rice fields or pig farms or where travel plans are uncertain.

The UKHSA 'Green Book' JE chapter, has a flowchart to help when deciding who might be suitable for JE vaccination.

Availability

There is currently one licensed vaccine recommended for use in the UK, IXIARO® [18]. The Green Cross (GC) vaccine and Biken vaccine (JE Vax) are no longer available in the UK.

IXIARO® is licensed for immunisation against JE in adults and children from two months of age [18]. This vaccine is distributed in the UK by Valneva. IXIARO® may be used as a booster for travellers who have received a course of GC or Biken vaccine previously [7].

IXIARO® vaccine schedule

Age range	Dose	Primary course	Reinforcing immunisation
Under 2 months of age	Not usually recommended (no safety or efficacy data)	–	–
Children aged 2 months to under 36 months of age	0.25ml (discard half of the vaccine)*	2 doses: Day 0 and 28 See also accelerated schedule***	For those at ongoing risk** a single first booster dose of IXIARO® 12 months after primary immunisation is recommended. Others should be offered a first booster dose at 12-24 months following the primary course, prior to re-exposure to JE virus. Duration of protection, beyond three years after

Children aged 3 to 17 years	0.5ml	2 doses: Day 0 and 28 See also accelerated schedule***	the first booster is uncertain.
Adults 18 to 64 years	0.5ml	2 doses: Day 0 and 28 See also accelerated schedule***	For those at ongoing risk** a single dose of IXIARO® booster 12 months after primary immunisation is recommended. Others should be offered the first booster dose at 12-24 months following the primary course prior to re-exposure to JE virus. A 2nd booster (4th dose) should be offered at 10 years for those who remain at risk.
Adults aged 65 years and older	0.5ml	2 doses: Day 0 and 28 See also accelerated schedule***	For those at continued/further risk a single dose of IXIARO® booster at 12 months should be considered. The duration of

			protection is uncertain for the primary course. The length of protection following a booster dose (3rd dose) is not known. Response to the vaccine may be reduced in this age group and immunity may wane before 10 years.

***See IXIARO® Summary of Product Characteristics for details on preparing the 0.25 ml dose for children aged 2 months to less than 3 years.**

****Long-term travellers who expect to reside in endemic areas for appreciable periods of time.**

*****See also accelerated schedule below.**

Accelerated schedule

Adults aged 18-65 years can be vaccinated using a licensed accelerated schedule as follows: first dose at day 0, second dose: 7 days after first dose. With both schedules, the primary immunisation schedule (first and second dose) should be completed at least one week prior to potential exposure to JE [7, 18]. Use of this accelerated schedule can also be considered off-license for travellers 2 months - 17 years of age and those over 65 years of age when time is short [7].

In situations where the primary course (days 0 and 28 or days 0 and 7) plus the first booster has been interrupted, the schedule should be resumed, and not restarted.

IXIARO® is available in a small number of Asian countries currently. Therefore, travellers may not be able to complete their vaccination course overseas with this vaccine. It is recommended that vaccinees who received the first dose of IXIARO® complete the primary two-dose vaccination course with IXIARO®.

Contraindications for IXIARO® vaccine

- Serious illness or acute febrile illness.
- Hypersensitivity to any components of the vaccine.
- Serious reaction to a previous dose of vaccine.

Post vaccination adverse reactions

In clinical studies, approximately 40 percent of vaccinated individuals experienced systemic adverse reactions, and approximately 54 percent experienced injection site reactions, such as pain, tenderness and muscle ache. These reactions usually occur within the first three days after vaccination, are usually mild and resolve within a few days [3].

Pregnancy and breastfeeding

As a precautionary measure, the use of IXIARO® in pregnant and breastfeeding women should be avoided [7, 18]. However, travellers and their medical advisers must make a risk assessment on the theoretical risks of JE vaccine in pregnancy against the potential risk of acquiring JE disease [7].

Resources

- UK Health Security Agency: Immunisation against infectious disease, Japanese encephalitis
- World Health Organization: Japanese encephalitis fact sheet
- World Health Organization: Japanese encephalitis vaccines position paper

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