Japanese Encephalitis

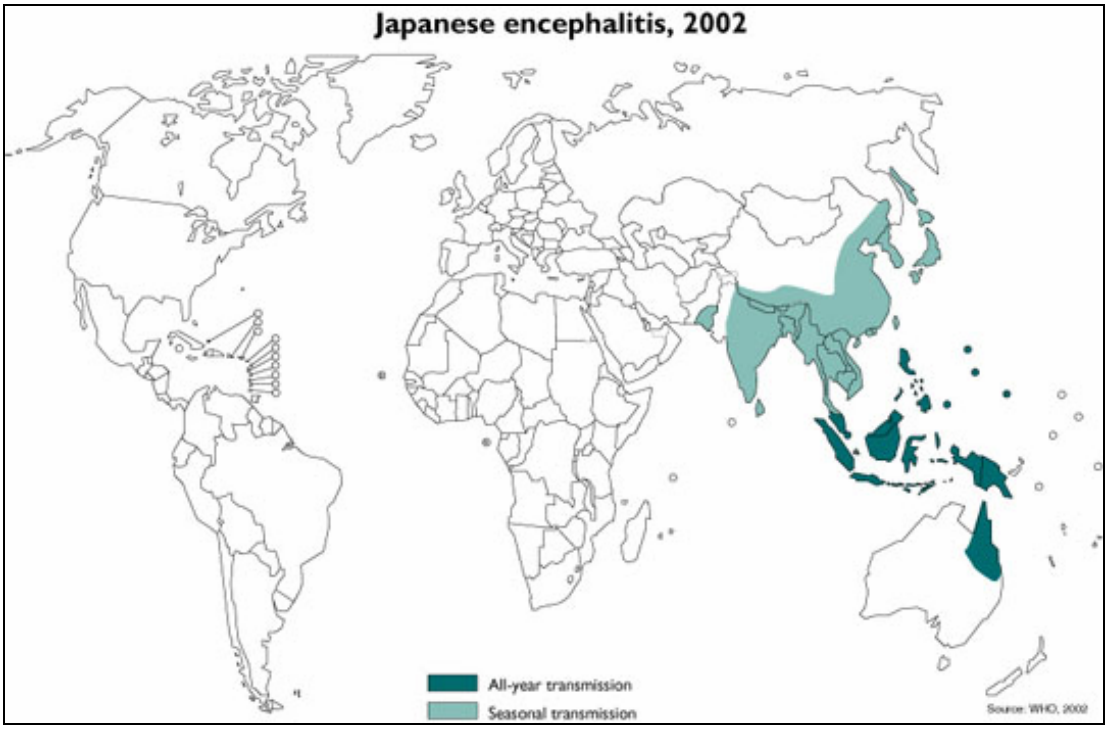
Introduction

Japanese encephalitis (JE) is a flavivirus found in Asia, transmitted to humans by *Culex* mosquitoes. The virus is closely related to West Nile virus; dengue and yellow fever are other examples of diseases caused by flaviviruses.

Epidemiology

Data from the Travel Health Surveillance Section of the Health Protection Agency Communicable Disease Surveillance Centre

Global Epidemiology



Japanese encephalitis (JE) was first recognised in Japan in the late 1800s, but the first major epidemic (involving 6000 cases) was described in 1924[1]. Since then, JE has increasingly been recognised throughout most countries of South East Asia, where it is now the leading cause of viral encephalitis and where approximately 30,000 to 50,000 cases are reported each year[2]. Factors favouring the prevalence of the disease in this area include: the vector (*Culex spp.* mosquitoes), the mosquito habitats (such as, rice-growing fields, swamps, and marshes) and the viremic amplifying hosts (pigs and birds). In endemic countries, the disease primarily

affects children under 15 years of age. The World Health Organization reported 15,000 deaths from JE in 2001 with a fatality rate in symptomatic cases of between 5 and 35%; however the disease is under-reported[3].

The incidence of JE in humans is seasonal and varies by country. May to September is the peak transmission season for the temperate climates of Korea and Japan, and April to October for the more tropical countries of South East Asia such as Thailand, Cambodia and Vietnam. For Nepal and Northern India, the season is between September and December[1]. The reason for the difference in seasonality may be because of differing irrigation practices and migratory patterns of the susceptible bird hosts in affected countries.

The virus first appeared in the Torres Strait Islands of Australia in 1995, where an outbreak of three cases occurred[4]; it is likely that it was introduced by migratory birds from South East Asia (although this is not proven). The virus has continued to be found in pigs in the Torres Strait and the transmission season in this area is probably year round.

For more country-specific details on transmission seasons for Japanese encephalitis, see the CDC website www.cdc.gov/travel/diseases/jenceph.htm#table_3_2

Japanese Encephalitis in UK Travellers

There have been two documented cases of JE in UK travellers. The first was a British woman who had been living and working in Hong Kong and was diagnosed with JE in 1982; she died as a result of cardiac and respiratory complications[5]. The second was a woman who had been to Thailand in 1994; she recovered fully after 4 months[6]. There have also been American and Australian military cases reported following the Korean and Vietnamese wars and postings to South East Asia[7].

Risk for Travellers

The risk to short term travellers to Asia is very low, particularly if they are only visiting urban areas, with overall estimates of 1 case per million travellers[8]. The risk becomes greater for those persons who intend to live or travel for long periods of time, and have extensive trips into rural areas during transmission seasons. Certain activities may increase this risk, such as fieldwork, camping or cycling in rural areas. If engaging in these activities, shorter trips may then pose a higher risk. The risk amongst these rural travellers has been calculated to be in the region of 1 per 5000 to 1 per 20,000 per week[8].

The transmission season in the northern, temperate part of the endemic area is during the hotter, wetter seasons, usually May to October. The season tends to be year round in Malaysia, Indonesia and the Philippines

Transmission

JE virus is transmitted to humans from animals and birds via the bite of an infected *Culex* mosquito. These mosquitoes feed mainly during the dusk to dawn hours; pigs and wading birds are the principle hosts. *Culex* mosquitoes are prolific in rural areas where flooded rice fields and marshes provide breeding grounds, however, they have also been found to be present in urban locations.

Signs and symptoms

The majority of cases of JE are asymptomatic or non-specific. Children and the elderly most commonly suffer a clinical illness, which can be severe. Encephalitis is estimated to occur in 1 in 300 patients[9]. The incubation period is 6-16 days, and presenting symptoms include fever, headache, altered mental state and convulsions. Some patients will make a full, but slow, recovery from this acute stage. However, 25-30% will be left with residual neurological deficits, including paralysis, ataxia and speech difficulties. Approximately one third of patients with clinically manifested JE die[10].

Treatment

There is no specific anti-viral treatment, but rather supportive intervention.

Prevention

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

A JE vaccine is available which should be considered for those intending to stay for long periods in rural endemic regions during the main transmission season, or whose planned activities will increase their risk.

Japanese Encephalitis Vaccine Information

Indications for use of vaccine

Japanese encephalitis (JE) vaccine should be considered for

- Travellers spending a month or longer in rural epidemic or endemic areas during the transmission season
- Travellers spending less than a month in epidemic or endemic areas whose planned activities place them at particularly high risk.

Availability

Two inactivated vaccines are available in the UK, although neither vaccine is licensed in this country at the present time. The Biken vaccine (JE Vax) is manufactured in Japan and is the most widely used. Most published research refers to this vaccine. JE Vax was granted a licence in the USA in December 1992 [11].
The Green Cross vaccine is not widely available in Europe, but is manufactured in Korea and is licensed in several south-east Asian countries.
The use of both vaccines in the UK is on a named patient basis.
Details of available vaccines and manufacturers can be found in the summary table below.

Vaccine Schedules

Vaccine	Manufacturer	Distributor	Schedule	Length of Protection	Age Range
JE-Vax (Biken)	The Research Foundation for Microbial Diseases of Osaka University, Japan	Aventis Pasteur MSD	3 doses. Day 0, 7 and 30.	Boost every 2-3 years following 3rd dose, if at continued risk.	From 1 year
			2 doses given 1 week apart will induce antibodies in approximately 80% of vaccinees.	Studies suggest a booster 3 months following 2- dose rapid schedule.[2]	
Japanese encephalitis Green Cross vaccine	Green Cross Vaccine Corp.	MASTA	3 doses. Day 0, 7 and 28.	Boost at 12 months following primary course, then every 3 years unless at particular risk in which case annual boosters are recommended.	From 1 year

We strongly advise that the vaccine SPC is consulted prior to the administration of any vaccine

In non-immune travellers three doses of vaccine are advised prior to travel for optimum protection.

The vaccine schedule for both vaccines should be completed at least 10 days prior to departure to observe for delayed allergic reactions (see below), and ideally a month before travel to allow immunity to develop.

Contraindications

- Serious illness or acute febrile illness
- Hypersensitivity to components of the vaccine, including thiomersal and neural or rodent protein.
- Serious reaction to a previous dose of vaccine
- Unstable neurological conditions, particularly convulsions in the previous year.
- The vaccine should be used with caution in persons with a past history of urticaria following envenomation, drugs, or other cause.

Adverse Reactions

Japanese encephalitis vaccine is associated with a moderate frequency of local and mild systemic side effects. They occur in 10-20% of vaccinees.
Serious systemic reactions may include urticaria, angioedema and cardiovascular collapse, and occur in about 0.6% of vaccine recipients. These reported reactions may have an onset as long as 2 weeks after vaccination, but most will occur within the first few minutes to one week following vaccination.
Rare neurological events including encephalitis have also been reported in Japan between 1965 and 1973 and occurred at a rate of 1-2.3 per million vaccinees[12].
Detailed studies of adverse events associated with JE vaccine have concluded that severe adverse events are rare, and although milder events are more common, they remain within acceptable rates compared with other vaccines.
Nevertheless, all vaccinees should be observed for 30 minutes, and be advised of possible delayed side effects. Full resuscitation facilities should be present.

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Reading List

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