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Japanese Encephalitis

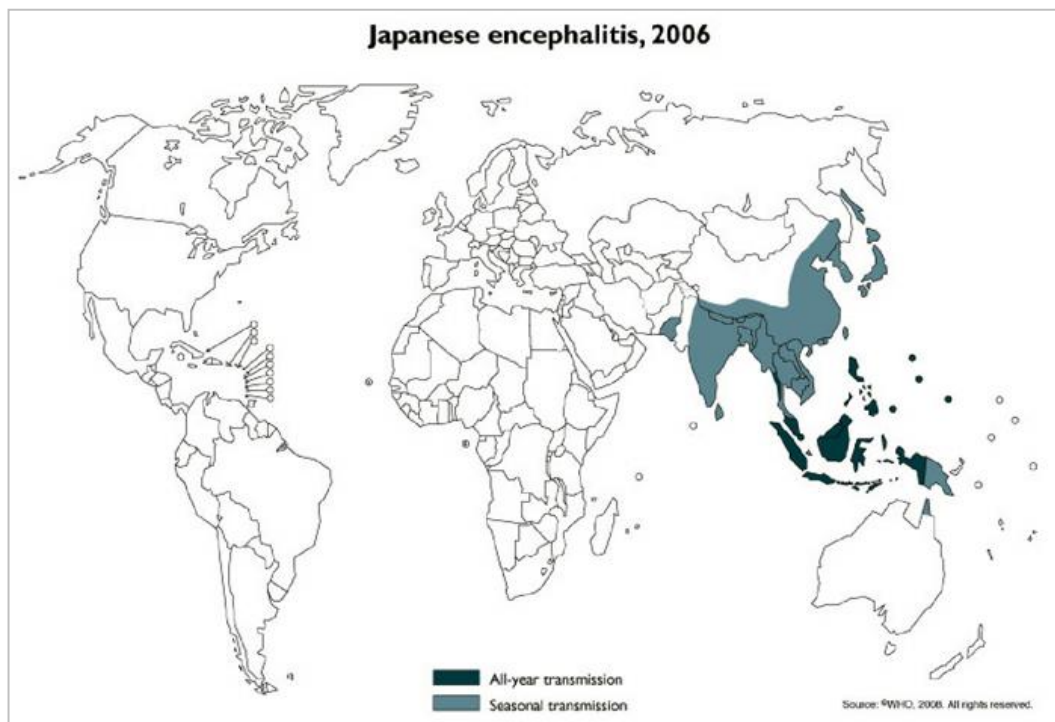
Introduction

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

Global Epidemiology

Japanese Encephalitis, 2006



Map

courtesy of the World Health Organization. (*International Travel and Health 2008*).

Japanese encephalitis (JE) was first recognised in Japan in the late 1800s, but the first major epidemic (involving 6,000 cases) was described in 1924 [1]. Since then, JE has increasingly been recognised throughout most countries of east and South East Asia (see map above), where it is the leading cause of viral encephalitis and approximately 30,000 to 50,000 cases are reported each year [2]. Factors favouring disease in this area include: the vector (*Culex spp.* mosquitoes), environmental conditions necessary for the mosquito breeding cycle (rainfall, humidity, tropical temperatures), mosquito habitats (such as rice-growing fields, swamps, and marshes) and presence of the amplifying hosts (pigs and birds). In endemic countries, the disease primarily affects children; seroprevalence studies show almost universal exposure by the age of 15 years [3]. Most cases of JE are asymptomatic, and there is widespread under reporting. [4].

The incidence of JE in humans varies by country and is usually seasonal, coinciding with the rains. 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 transmission season tends to be year round in Malaysia, Indonesia, and the Philippines, where rain may fall throughout the year. Seasonal variations may be due to differing irrigation practices and migratory patterns of the susceptible bird hosts in endemic countries.

The Torres Strait Islands of Australia had their first cases of JE in 1995 [5]. It is possible that it was introduced by migratory birds from South East Asia. The virus continues to be found in pigs on the Islands of the Torres Strait, and the transmission season in this area is probably year round.

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 [6]. The second was a woman who had been to Thailand in 1994; she recovered fully after 4 months [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 one case per million travellers [8]. The risk becomes greater for persons who intend to live or travel in risk areas for long periods of time, and have rural trips during transmission seasons. Certain activities, even during short trips, may increase the risk such as fieldwork, camping, or cycling in rural areas. The risk amongst rural travellers has been estimated to be in the range of 1 case per 5,000 travellers to 1 per 20,000 per week [8].

Transmission

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

A JE vaccine is available which should be given to 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 given to:

- Travellers to epidemic or endemic areas whose itineraries take them through areas of rice fields and marshland during the transmission season. Risk activities may include fieldwork, camping, or cycling.
- Long stay travellers may also be at higher risk.

Availability

Japanese encephalitis Green Cross (GC vaccine) is unlicensed in this country at the present time and is supplied on a named patient basis. It is distributed in the UK by [MASTA](#). The Green Cross vaccine is not widely available in Europe, but is manufactured in Korea and is licensed in several South East Asian countries.

In May 2009 a new, licensed Japanese encephalitis vaccine, Ixiaro®, became available. Ixiaro® is distributed in the UK by Novartis Vaccines and can be used in adults aged 18 years and older.

Manufacture of the previously available Biken vaccine (JE Vax) has now ceased and [distribution of JE Vax in the UK has been discontinued](#).

Vaccine Schedule

Vaccine	Manufacturer	Distributor	Schedule	Length of Protection	Age Range
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
Ixiaro	Intercell AG	Novartis Vaccines	2 doses. Day 0 and 28.	Data is limited and length of protection is not currently known.	Adults aged 18 years and older.

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

In non-immune travellers, three doses of GC Vaccine are advised prior to travel for optimum protection. Where travellers do not have sufficient time before travel to complete a recognised

pre-exposure course, an accelerated or abbreviated schedule of vaccine may be indicated. Such schedules may result in lower antibody titres and a shorter duration of protection [11,12]. Expert opinion should be sought.

Contraindications

- Serious illness or acute febrile illness.
- Hypersensitivity to components of the vaccine.

Specific contraindications for Green Cross vaccine

- 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.

Adverse Reactions

JE vaccine is associated with a moderate frequency of local and mild systemic side effects. They occur in 10% to 20% of vaccinees.

Most published research refers to the Biken vaccine (JE VAX), which is no longer available in the UK. However, similarities exist between the Biken and Green Cross vaccines, and a similar side effect profile cannot be discounted. For the Biken vaccine serious systemic reactions include urticaria, angioedema and cardiovascular collapse, and occur in about 0.6% of vaccine recipients. These reported reactions can have an onset as long as two weeks after vaccination, but most occur within minutes to one week following vaccination. These systemic reactions are more likely to occur in persons with a history of urticaria or allergies [13]

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 vaccine doses administered [14].

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 rates compared with other vaccines. All vaccinees should be observed for 30 minutes, and be advised of possible delayed side effects. Full resuscitation facilities should be present.

The most commonly reported adverse events following Ixiaro® vaccine were headache and myalgia affecting 20% and 13% of subjects respectively [15].

References

1. Endy TP, Nisalak A. Japanese encephalitis virus: ecology and epidemiology. *Curr Top Microbiol Immunol.* 2002;267:11-48.
2. Centers for Disease Control and Prevention. Japanese encephalitis fact sheet [online] [cited 31.10.2006]. Atlanta, USA: CDC, 2003. Available at: <http://www.cdc.gov/ncidod/dvbid/jencephalitis/facts.htm>
3. World Health Organization. Position paper on Japanese Encephalitis. *Wkly Epidemiol Rec.* 1998;44:337-344 . Available at: http://www.who.int/immunization_delivery/new_vaccines/je/en/index2.html
4. World Health Organization. State of the art of new vaccines: research & development. January 2006. WHO/IVB/06.01 WHO: Geneva Accessed 31.10.2006 Available online at <http://www.who.int/vaccines-documents/DocsPDF06/814.pdf>
5. Hanna JN, Ritchie SA, Phillips DA et al. An outbreak of Japanese encephalitis in the Torres Strait, Australia, 1995. *Med J Aust.* 1996;165:256-260.
6. Rose MR, Hughes SM, Gatus BJ. A case of Japanese B encephalitis imported into the United Kingdom. *J Infect.* 1983;6:261-5.

7. Burdon JT, Stanley PJ, Lloyd G, Jones NC. A case of Japanese encephalitis. *J Infect* 1994;28:175-9.
8. Centers for Disease Control and Prevention. Inactivated Japanese encephalitis virus vaccine. Recommendations of the advisory committee on immunization practices (ACIP). *Morbidity and Mortality Weekly Report* 1993;42(No. RR-1):1-15. Available at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/00020599.htm>
9. Broom AK, Smith DW, Hall RA, Johansen CA, Mackenzie JS. Arbovirus Infections in *Manson's Tropical Diseases* 21st ed Elsevier Science Ltd, 2003
10. Shlim D, Solomon T. Japanese encephalitis vaccine for travellers: Exploring the limits of risk. *Clin Infect Dis* 2002;35:183-8.
11. Poland JD, Cropp CB, Craven RB, Monath TP. Evaluation of the potency and safety of inactivated Japanese encephalitis vaccine in US inhabitants. *J Infect Dis* 1990;161:878-82.
12. Defraites RF, Gambel JM, Hoke CH Jr., et al. Japanese encephalitis vaccine (inactivated, BIKEN) in U.S soldiers: immunogenicity and safety of vaccine administered in two dosing regimens. *Am J Trop Med Hyg* 1999;61:288-93.
13. Plesner A, Ronne T, Wachmann H. Case-control study of allergic reactions to Japanese encephalitis vaccine. *Vaccine* 2000;18:1830-6.
14. Biken Product Information Sheet for Japanese encephalitis. Feb 1997 Osaka, Japan
15. Novartis Vaccines. Summary of Product Characteristics for Ixiaro. April 2009. [Accessed 21 May 2009]. Available at [http://emc.medicines.org.uk/medicine/21683/SPC/IXIARO+suspension+for+injection+-+Japanese+encephalitis+vaccine+\(inactivated%2c+adsorbed\)/](http://emc.medicines.org.uk/medicine/21683/SPC/IXIARO+suspension+for+injection+-+Japanese+encephalitis+vaccine+(inactivated%2c+adsorbed)/)

Links

Centers for Disease Control and Prevention. Division of Vector-Borne Infectious Diseases: Japanese encephalitis available at: <http://www.cdc.gov/ncidod/dvbid/jencephalitis/index.htm>