Japanese encephalitis (JE) is a mosquito-borne viral encephalitis caused by a flavivirus. It is the leading cause of childhood encephalitis in Asia, with 20,000 to 50,000 cases per annum (Halstead et al., 2008; World Health Organization, 1998).

It is endemic in rural areas, especially where rice growing and pig farming coexist, and epidemics occur in rural and occasionally in urban areas. Highest transmission rates occur during and just after wet seasons, when mosquitoes are most active, but seasonal patterns vary both within individual countries and from year to year. This disease is not transmitted from person to person.

The incubation period is from five to 15 days. Illness ranges from asymptomatic infection (about one in 250 infections is estimated to become clinically apparent) to severe encephalitis with a high mortality and a high rate of permanent neurological sequelae (approximately 30%) in survivors (Halstead et al., 2008).

**History and epidemiology of the disease**

Outbreaks were recorded in Japan as early as 1871; the first major epidemic in Japan was described in 1924 and involved 6000 cases. JE spread throughout Asia but national immunisation campaigns and urban development in the 1960s led to the near-elimination of JE in Japan, Korea, Singapore and Taiwan. However, JE remains endemic in much of the rest of Asia. The virus was isolated in the 1930s, and the first inactivated mouse-brain derived vaccines were produced in the same decade.
Japanese encephalitis

The Japanese encephalitis vaccination

There is currently one licensed vaccine recommended for use in the UK – IXIARO®. IXIARO® is licensed in the UK for individuals aged two months and older.

IXIARO® is an inactivated vaccine produced in Vero cells and adsorbed onto an adjuvant of aluminium hydroxide to improve its immunogenicity.

IXIARO® does not contain thiomersal.

The vaccine is inactivated and does not contain live organisms so cannot cause the disease against which it protects.

Storage

Vaccines should be stored in the original packaging at +2°C to +8°C and protected from light. All vaccines are sensitive to some extent to heat and cold. Heat speeds up the decline in potency of most vaccines, thus reducing their shelf life. Effectiveness cannot be guaranteed for vaccines unless they have been stored at the correct temperature. Freezing may cause increased reactogenicity and loss of potency for some vaccines. It can also cause hairline cracks in the container, leading to contamination of the contents.

Presentation

IXIARO® is available as a 0.5ml suspension in a pre-filled syringe (Type 1 glass) with a plunger stopper (chlorobutyl elastomer).

Dosage and schedule

<table>
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<th>IXIARO®</th>
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<tr>
<td>Children aged two months to under 36 months</td>
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<tr>
<td>First dose of 0.25 ml at day 0</td>
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<td>Second dose of 0.25 ml 28 days after first dose</td>
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<tr>
<td>Children aged 3 years and over and adults</td>
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Administration

IXIARO® should be given by intramuscular injection. However, for individuals who have a bleeding disorder, IXIARO® should be given by deep subcutaneous injection to reduce the risk of bleeding.
IXIARO® can be given at the same time as other travel or routine vaccines. The vaccines should be given at a separate site, preferably in a different limb. If given in the same limb, they should be given at least 2.5cm apart (American Academy of Pediatrics, 2003).

**Disposal**

Equipment used for vaccination, including used vials, ampoules, or partially discharged vaccines should be disposed of at the end of a session by sealing in a proper, puncture-resistant ‘sharps’ box according to local authority regulations and guidance in the technical memorandum 07-01 (Department of Health, 2006).

**Recommendations for the use of the vaccine**

The objective of JE vaccination is to protect individuals at high risk of exposure during travel or in the course of their occupation. Guidance on the employer’s responsibility under Control of Substances Hazardous to Health (COSHH) Regulations is described in Chapter 12.

**Primary immunisation**

Two JE vaccines are available in the UK, IXIARO® and Green Cross. Only IXIARO® is licensed and recommended for the following age groups. It is not known whether the two vaccines are interchangeable during a course of vaccination, although IXIARO® may be used as a booster for those that received Green Cross vaccine previously.

**Infants under two months of age**

There are no safety or efficacy data on the use of IXIARO® in children under two months of age. IXIARO® is not usually recommended in children under two months of age in the UK.

**Children aged two months to under 36 months of age**

The recommended vaccine schedule is two doses of IXIARO®: 0.25 ml on days 0 and 28. Full immunity takes up to one week to develop after the second dose.

Green Cross vaccine is no longer recommended for immunization against Japanese encephalitis in the UK as a licensed vaccine (IXIARO®) is available.
Japanese encephalitis

Children aged three years and over and adults

The recommended vaccine schedule is two doses of IXIARO®: 0.5ml on days 0 and 28. Full immunity takes up to one week to develop after the second dose.

Green Cross vaccine is not recommended in this age group as a licensed vaccine (IXIARO®) is available.

Under exceptional circumstances, when time constraints preclude giving the second dose of IXIARO® at 28 days and based on a risk assessment, IXIARO® can be given up to four days earlier, although this is not a licensed use. There are insufficient data to support a recommendation for any further acceleration of the schedule.

Reinforcing immunisation

Adults at continuous risk of acquiring JE, e.g. laboratory personnel and long-term travellers who expect to reside in JE endemic areas for appreciable periods of time, should receive a booster dose at 12-24 months after primary immunisation. Adults who have had a previous course of any Japanese encephalitis vaccine can receive a single dose of IXIARO® as a booster. There are no data to permit recommendations for boosting in infants and children below 18 years or for longer term boosting in adults. However, should sustained protection be needed in infants or children a booster may need to be considered. Recommendations will be made by the JCVI relating to any further boosters needed for IXIARO® as soon as the necessary data becomes available.

Travellers and those going to reside abroad

All travellers should undergo a careful risk assessment that takes into consideration their itinerary, season of travel, duration of stay and planned activities. The risk of JE should then be balanced against the risk of adverse events from vaccination. JE vaccine is recommended for those who are going to reside in an area where JE is endemic or epidemic.

There is geographical variation in transmission periods – from all year round to seasonal. In temperate regions of Asia, transmission is generally from May to September. It extends from March through to October in areas further south, and can be year round in tropical areas. Travellers to South and South-East Asia and the Far East should be immunised if staying for a month or longer in endemic areas during the transmission season, especially if travel will include rural areas. Other travellers with shorter exposure periods should be immunised if the risk is considered sufficient. For
example, those spending a short period of time in rice fields (where the mosquito vector breeds) or close to pig farming (a reservoir host for the virus) should be considered for vaccination.

Country-specific recommendations and information on the global epidemiology of JE can be found in the following websites www.nathnac.org and www.travax.nhs.uk.

**Laboratory workers**

Immunisation is recommended for all research laboratory staff who have potential exposure to the virus. Worldwide there have been more than 20 cases of laboratory-acquired JE virus infection (Halstead *et al.*, 2008).

**Contraindications**

There are very few individuals who cannot receive either IXIARO® or Green Cross vaccine. When there is doubt, appropriate advice should be sought from a travel health specialist.

IXIARO® should not be given to those who have had:

- a confirmed anaphylactic or serious systemic reaction to a previous dose of IXIARO® vaccine, or
- a confirmed anaphylactic reaction to any component of the vaccine.

**Precautions**

**Individuals with pre-existing allergies**

There is no known extra risk of hypersensitivity reactions to the IXIARO® vaccine.

**Pregnancy and breast-feeding**

**IXIARO®**

As a precautionary measure, administration of IXIARO® during pregnancy or lactation should be avoided. However, travellers and their medical advisers must make a risk assessment of the theoretical risks of JE vaccine in pregnancy against the potential risk of acquiring JE. Miscarriage has been associated with JE virus infection when acquired in the first two trimesters of pregnancy (Canadian Medical Association, 2002).
Japanese encephalitis

Adverse reactions

IXIARO®

The most common adverse reactions observed after administration of IXIARO® are pain and tenderness at the injection site, headache, and myalgia. Other reactions commonly reported are erythema, hardening, swelling and itching at the injection site, influenza-like illness, pyrexia and fatigue.

Management of cases

No specific therapy is available for JE. Supportive treatment can significantly reduce morbidity and mortality. Diagnostic testing is available through Public Health England (PHE).

Supplies

- IXIARO® is manufactured by Intercell Biomedical Ltd and available from Novartis Vaccines (Tel: 08457 451500)
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References


