5 Tick-borne encephalitis

NOT NOTIFIABLE

The disease

Tick-borne encephalitis (TBE) is caused by members of the flavivirus family that can affect the central nervous system. Although TBE is most commonly recognised as a meningo-encephalitis, mild febrile illnesses can also occur.

There are three forms of the disease related to the virus subtypes, namely European, Far Eastern and Siberian (Hayasaka, 2001).

The incubation period is from two to 28 days (Dumpis *et al.*, 1999). The European form of the disease is biphasic with an initial viraemic phase of fever and influenza-like symptoms followed in some cases (after an afebrile period of one to 20 days) by central nervous system involvement. The case fatality rate of the European form is 1%. Long-lasting or permanent neuropsychiatric sequelae are observed in 10–20% of affected patients. The Far Eastern version is more gradual in onset and normally takes a more severe and longer course with a reported mortality of 5–20%.

TBE is transmitted to humans by the bite of an infected tick or, less commonly, by ingestion of unpasteurised milk from infected animals, especially goats. The virus is maintained in nature by small mammals, domestic livestock and certain species of birds.

More men tend to be infected than women and most of these infections are caused by leisure activity such as hiking (Kaiser, 1995). The incidence peaks in spring and early summer, but can occur throughout the year (Lindgren and Gustafson, 2001).

TBE occurs in most or parts of Austria, Germany, southern and central Sweden, France (Alsace region), Switzerland, Norway, Denmark, Poland, Croatia, Albania, the Baltic states (Estonia, Latvia and Lithuania), the Czech and Slovak Republics, Hungary, Russia (including Siberia), Ukraine, some other countries of the former Soviet Union, and northern and eastern regions of China (Hayasaka, 2001).

History and epidemiology of the disease

The TBE virus is almost exclusively restricted to areas of Europe and Asia. The disease has never been endemic in the UK. Since the 1930s, TBE has been a major public health problem in central Russia.

Austria has had a universal, annual, national vaccination campaign since 1980. There is widespread use of TBE vaccine in other central European countries.

The TBE vaccination

One licensed vaccine (Tico-Vac) is available currently. It is produced from virus grown in chick fibroblasts and then inactivated by formaldehyde; it is supplied as a suspension of 0.5ml for injection in a pre-filled syringe.

The vaccine contains the Neudörfl virus strain, has been shown to be effective against the European subtype of TBE, and is probably effective against the more aggressive Far Eastern subtype.

The vaccine contains aluminium hydroxide and trace quantities of neomycin and gentamicin, and is thiomersal-free. It is inactivated, does not contain live organisms and cannot cause the disease against which it protects.

Dosage and schedule

- First dose of 0.5ml (0.25ml Tico-Vac Junior for children aged one year and below 16 years of age) at day 0.
- Second dose of 0.5ml (0.25ml of Tico-Vac Junior for children aged one year and below 16 years of age) one to three months after the first dose.
- Third dose of 0.5ml (0.25ml Tico-Vac Junior for children aged one year and below 16 years of age) five to 12 months after the second dose.

For rapid short-term protection of children and adults the second dose may be given two weeks after the first dose and gives at least 90% protection (Plotkin and Orenstein, 2004)

Storage

Vaccines should be stored in the original packaging at $+2^{\circ}$ C to $+8^{\circ}$ 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.

Administration

Vaccines are routinely given intramuscularly into the upper arm or anterolateral thigh. However, for individuals with a bleeding disorder, vaccines should be given by deep subcutaneous injection to reduce the risk of bleeding.

TBE vaccine can be given at the same time as other travel and routine vaccines. The vaccines should be given at separate sites, preferably in different limbs. 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 or ampoules, should be disposed of at the end of a session by sealing in a proper, puncture-resistant 'sharps' box (UN-approved, BS 7320).

Recommendations for the use of the vaccine

TBE vaccine is used for the protection of individuals at high risk of exposure to the virus through travel or employment.

Awareness of risk areas is essential. The following measures are advised whether or not vaccine is given. Some protection against TBE is provided by covering arms, legs and ankles, and using insect repellents on socks and outer clothes (Dumpis *et al.*, 1999). Any ticks attaching to the skin should be removed completely as soon as possible. Evidence suggests that the best method is slow, straight removal with tweezers (Teece and Crawford, 2002). Unvaccinated individuals bitten by ticks in endemic areas should seek local medical advice.

Unpasteurised milk should not be drunk.

The vaccine is recommended particularly for spring and summer travel in warm, forested parts of the endemic areas, where ticks are most prevalent. Individuals who hike, camp, hunt and undertake fieldwork in endemic forested areas should be vaccinated.

TBE vaccine is recommended for those who will be going to reside in an area where TBE is endemic or epidemic, and particularly for those working in forestry, woodcutting, farming and the military (WHO, 1995).

More detailed country-by-country information is contained in *Health information for overseas travel* (Department of Health, 2001).

Laboratory workers who may be exposed to TBE should be vaccinated.

Reinforcing immunisation

A booster dose is recommended every three years (Dumpis *et al.*,1999) after an initial three-dose schedule, if the individual continues to be at risk.

Contraindications

There are few individuals who cannot receive TBE vaccine.

The vaccine should not be given to those who have had:

- a confirmed anaphylactic reaction to a previous dose of TBE vaccine
- a confirmed anaphylactic reaction to one of the vaccine components
- a confirmed anaphylactic reaction to egg ingestion.

Precautions

Pregnancy and breast-feeding

TBE vaccine has not been associated directly with adverse outcomes of pregnancy. There is no evidence of risk from vaccinating pregnant women, or those who are breast-feeding, with inactivated virus or bacterial vaccines or toxoids (Hayasaka *et al.*, 2001).

Adverse reactions

Reported reactions to TBE vaccine are rare. Local reactions such as swelling, pain and redness at the injection site may occur.

Pyrexia, particularly after the first dose, can occur in children and adults, usually occurring within 12 hours of immunisation and settling within 24–48 hours (Dumpis *et al.*, 1999; Kunz *et al.*, 1980). Febrile convulsions have rarely occurred, and antipyretic treatment and cooling should be initiated in good time.

All suspected adverse reactions to vaccines occurring in children, or in individuals of any age after vaccines labelled with a black triangle ($\mathbf{\nabla}$), should be reported to the Commission on Human Medicines using the Yellow Card scheme. Serious suspected adverse reactions to all vaccines in adults should also be reported through the Yellow Card scheme.

Management of cases

No specific therapy is available for TBE. FSME Bulin (TBE immunoglobulin) has been discontinued (Kluger, 1995) and is no longer available either in the UK or in Europe.

Supportive treatment can significantly reduce morbidity and mortality.

Supplies

Tico-Vac[®] and Tico-Vac Junior are both currently available from Pfizer Ltd (Tel: 0800 089 4033) and MASTA (Tel: 0113 238 7500).

References

American Academy of Pediatrics (2003). Active immunization. In: Pickering LK (ed.) *Red Book: 2003 Report of the Committee on Infectious Diseases*, 26th edition. Elk Grove Village, IL: American Academy of Pediatrics, p 33.

Department of Health (2001) *Health information for overseas travel*, 2nd edition. London: TSO.

Dumpis U, Crook D and Oksi J (1999) Tick-borne encephalitis. *Clinical Infect Dis* 28: 882–90.

Hayasaka D, Goto A, Yoshii K *et al.* (2001) Evaluation of European tick-borne encephalitis virus vaccine against recent Siberian and far-eastern subtype strains. *Vaccine* **19**(32): 4774–9.

Kaiser R (1995) Tick-borne encephalitis in southern Germany. Lancet 345(8947): 463.

Kluger G, Schottler A, Waldvogel K *et al.* (1995) Tick-borne encephalitis despite specific immunoglobulin prophylaxis. *Lancet* **346**: 1502.

Kunz C, Heinz FX and Hofmann H (1980) Immunogenicity and reactogenicity of a highly purified vaccine against tick-borne encephalitis. *J Med Virol* **6**: 103–9.

Lindgren E and Gustafson R (2001) Tick-borne encephalitis in Sweden and climate change. *Lancet* **358**: 16–18.

Plotkin SA and Orenstein WA (eds) (2004) Vaccines, 4th edition, Philadelphia: WB Saunders Company, p 1039–57.

Tick-borne encephalitis

Teece S and Crawford I (2002) Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary. How to remove a tick. *Emerg Med J* **19**(4): 323–4.

WHO (1995) Tick-borne encephalitis. WHO Wkly Epidemiol Rec 70: 120-2.