

Tick Borne Encephalitis

Introduction

Tick borne encephalitis (TBE) virus is one of the major human pathogenic flaviviruses and causes disease that can impact on public health in endemic countries. The TBE virus belongs to a closely related group of flaviviruses that includes yellow fever, dengue and Japanese encephalitis.

There are three subtypes of TBE:

- Western subtype, (or Central European encephalitis) transmitted by *Ixodes ricinus* ticks. This subtype occurs in the forested areas of Central, Eastern and Northern Europe.
- Far Eastern subtype, (or Russian Spring/Summer encephalitis) transmitted by *Ixodes persulcatus* ticks. This subtype occurs in the former USSR, east of the Ural Mountains, and also in areas of China and Japan.
- Siberian subtype, transmitted by *Ixodus persulcatus* ticks, which occurs in Siberia.

Global Epidemiology

Tick-borne encephalitis (TBE) is caused by three different subtypes of tick borne encephalitis virus: Western European TBE virus, Far Eastern TBE virus and Siberian TBE virus.

Western European TBE (also known as Central European encephalitis) is endemic in western and central European countries, and is particularly common in forest and mountainous regions of Austria, Estonia, Latvia, Lithuania, the Czech Republic, Slovakia, Germany, Hungary, Poland, Switzerland, western Russia, Ukraine, Belarus, Croatia and Slovenia. It occurs at a lower frequency in Denmark, France, Liechtenstein, Italy, Norway, the Åland archipelago and neighbouring Finnish coastline, and along the coastline of southern Sweden, from Uppsala to Karlshamn. It is possible TBE also occurs in Albania, Bosnia and Herzegovina, Bulgaria, Greece, Kazakhstan, Serbia and Montenegro, Moldova and Romania, although little data are available on the incidence of disease within these countries.

Thousands of cases of TBE occur each year from late spring to early autumn; the total number of annual cases in Western European countries has averaged 3000 over the last five years [1]. This type of TBE is transmitted by the tick *I. ricinus* and outbreaks often follow periods when voles (the principle reservoir) and ticks are numerous (between May and June and between September and October).

Far Eastern TBE (also known as Russian Spring/Summer encephalitis) is transmitted by the tick *I. persulcatus*, and occurs in the spring and summer months in eastern Russia and some countries in East Asia, particularly in forested regions of China and Japan.

Siberian TBE (also known as west-Siberian encephalitis) is, as its names suggests, endemic in Siberia and is also transmitted by the tick *I. persulcatus*.

Data on TBE in Europe is collected by the International Scientific Working Group on Tick-Borne Encephalitis. This data is based on local reports of disease, screening of TBE antibodies in healthy unvaccinated populations and screening for TBE virus in ticks and hosts. This information, which includes a map of endemic areas, is published on-line at www.tbe-info.com.

NB. Although the map represents the most up to date information available on endemic areas for TBE, it should be interpreted with caution as data may be incomplete, and the extent of epidemiological information available from different countries varies.

TBE in UK travellers

(Data from the Travel and Migrant Health Section of the Health Protection Agency Centre for Infections)

Tick borne encephalitis is not a notifiable disease in England, Wales and Northern Ireland. As of mid 2006, no cases of TBE have ever been reported to the Health Protection Agency (HPA) (although it is possible that there may have been cases imported into England, Wales or Northern Ireland which have not been diagnosed or reported to the HPA).

Risk for travellers

The risk of acquiring TBE infection is dependent on a number of factors including:

- destination
- duration of travel in risk area
- season of travel
- activities undertaken
- tick activity in the endemic country
- vaccination status of traveller

Travellers to endemic areas may be at risk when walking, camping or working in woodland terrain where they will be exposed to the tick vector. Infection may also be acquired by consuming un-pasteurised dairy products from infected animals.

The risk period for infection ranges from April to November, with infection with the Eastern subtype more common in the spring and with the Western subtype more common in the autumn.

Transmission

Ticks are the main vectors of TBE virus. The virus is maintained in nature by small mammals (such as mice and voles), domestic livestock (including sheep, goats and cattle) and certain species of birds. Humans are incidental hosts for the TBE virus.

Transmission in humans occurs mainly through the bite of an infected tick with introduction of the virus via the tick saliva. As saliva contains an anaesthetic, the bite itself usually goes unnoticed. This emphasises the importance of checking the body for attached ticks. Unusually, humans may become infected after consumption of infected unpasteurised dairy produce (2, 3).

Infected ticks are found on forest fringes with adjacent grassland, forest glades, riverside meadows and marshland, forest plantations with brushwood, and shrubbery. They reside most commonly on ground level vegetation, on the underside of foliage, from where they can be brushed onto clothing or drop onto passing humans. Ticks are capable of transmitting the TBE virus throughout the multiple stages of their life (larvae, nymphs or adults), and once infected, carry the virus for life.

Tick activity and lifecycle development relate to climatic factors such as temperature, soil moisture and relative humidity. Wet summers and mild winters tend to increase tick population density. In central Europe two peaks of activity have been observed: in May / June and again in September / October. In colder regions in northern Europe and in mountain regions these two peaks converge into a single peak in the summer (4).

The tick vectors are rarely found at altitudes of more than 1000 metres, although some reports suggest ticks may be found up to 1400m (5).

The risk for infection of humans after a single tick bite varies between 1 in 200 and 1 in 1,000 in the different endemic areas (6).

Signs and symptoms

The typical course of TBE is biphasic. The incubation period is 7-14 days, with a range of 2 to 28 days. The first clinical stage of the disease (which corresponds to the viraemic phase) may last from 1 – 8 days and affects two-thirds of infected patients. It is characterised by a non-specific flu-like illness with fatigue, headache, myalgia, nausea, general malaise and fever. An interval of 1 – 20 days follows, during which time patients are usually asymptomatic.

Approximately a third of those who were symptomatic during the first phase proceed to a second phase of disease heralded by a sudden rise in temperature and central nervous system involvement with meningitis. About a third of these cases progress to encephalitis, which may include paralysis.

The second phase of illness in children is usually limited to meningitis whereas adults older than 40 years are at increased risk of developing encephalitis, with higher mortality in those over the age of 60.

The clinical course of TBE disease is largely determined by the virus subtype. The Far Eastern subtype is generally more virulent,, tending to lead to paresis, and is associated with a higher mortality (approximately a 5 - 20% case fatality compared to 1 – 2% for the European subtype). There is currently little information on the virulence of the more recently described Siberian subtype.

Treatment

Treatment relies on supportive management; there is no specific anti viral treatment for TBE.

Prevention

The risk of acquiring TBE can be reduced by insect bite avoidance methods. Travellers should be advised to:

- Wear clothing with long sleeves and long trousers (tucked into socks), which can be treated with insecticide sprays such as permethrin.
- Apply insect repellent to exposed skin.
- Check the body for ticks regularly. After a tick has attached itself to the host it may not start feeding for 12 hours (6). The larval form of *Ixodes* ticks are tiny and difficult to see. Adult ticks, once they have fed and become engorged, may be the size of a coffee bean. Common areas for ticks to attach are at the hair-line, behind the ears, elbows, backs of knees, groin and armpits.
- Remove ticks as soon as possible by using a pair of tweezers or tick remover. The tweezers should be placed as close as possible to the skin and then the tick pulled slowly, ensuring the mouth parts are removed completely. Evidence suggests that slow, straight method is best for removal without leaving the mouthparts (7, 8). Care needs to be taken not to squeeze the stomach contents into the site of the bite.

Travellers should also avoid consumption of un-pasteurised dairy products in areas of risk.

TBE vaccination ([link](#)) is available for those travellers intending to visit rural endemic areas, or whose occupation may put them at higher risk.

Advice if bitten by a tick in a TBE risk country

TBE immunoglobulin (TBE IG) was at one time used as post exposure prophylaxis after a tick bite in TBE endemic countries. However, there are concerns that it may have a negative effect on the course of the disease. TBE IG is therefore no longer recommended in England or other European countries for post exposure prophylaxis for travellers in the event of a tick bite in a TBE endemic country.

If a traveller is bitten by a tick in an area of risk for TBE, they should remove the tick with tweezers as soon as possible (see above). If any signs of illness occur within 28 days of a tick bite, advice should be sought from a medical practitioner immediately.

Tick Borne Encephalitis Vaccine

Vaccination against TBE is considered to be the most effective means of preventing TBE for those living in endemic countries (9). The vaccine has been used in national vaccination campaigns in Austria since 1982 and has continued on an annual basis since. There is also widespread use of TBE vaccine in many other central European countries.

Vaccine should be considered for travellers to endemic areas (see indications below).

Vaccine Availability

The vaccines FSME-IMMUN and FSME-IMMUN Junior were re-named TicoVac and TicoVac Junior in December 2007. The vaccine itself is unchanged. Both these vaccines are licensed in the UK..

Details of these vaccines can be found in the summary table below.

Indications for use of TBE vaccine

Tick borne encephalitis vaccine should be considered for:

- All persons living in TBE-endemic areas
- Those at occupational risk in endemic areas, e.g. farmers, forestry workers, soldiers
- Travellers to rural endemic areas during late spring and summer e.g. campers, hikers, Scout / Guide groups

The optimum time to begin the course of vaccination against TBE is during the winter months in order to ensure protection prior to the start of the tick season in spring.

TicoVac is effective against the Far Eastern and Siberian subtypes as well as the European subtype of TBE (10).

Vaccine Schedules

The Summary of Product Characteristics (SmPC) for the individual vaccines should be consulted prior to the administration of any vaccine (available at www.emc.medicines.org.uk), together with the appropriate chapter in the Department of Health publication Immunisation against Infectious disease (link)

Table has been changed on the site BUT pdf needs changing to match please

Vaccine	Manufacturer	Schedule	Rapid Schedule	Length of protection	Age range
TicoVac 0.5ml	Baxter Currently distributed by MASTA	3 doses on days 0, between 1 and 3 months later and then between 5 and 12 months after the second dose	2 nd dose can be given 2 weeks after the 1 st dose	*First booster no more than 3 years after 3 rd dose. After this, boosters may be given at 3 – 5 year intervals if at risk	Persons at least 16 years of age
TicoVac 0.25ml Junior	Baxter Currently distributed by MASTA	3 doses on days 0, between 1 and 3 months later and then between 5 and 12 months after the second dose	2 nd dose can be given 2 weeks after the 1 st dose	First booster no more than 3 years after 3 rd dose. After this, boosters may be given at 3 – 5 year intervals if at risk	Children above 1 year of age and below 16 years of age

*In those aged > 60 years, booster intervals should not exceed three years (see below).

Primary vaccination schedule

The primary course of TBE vaccine consists of three doses on days 0, between 1 and 3 months later, and then between 5 and 12 months after the second dose. If more rapid protection is required, two doses of vaccine can be administered a minimum of two weeks apart (11). In this case the 3rd dose should be administered 5 – 12 months after the second vaccination.

Booster doses of TBE vaccine

In those under the age of 60 years, the first booster dose of TBE vaccine should be given three years after the primary course. Further boosters should be administered at intervals of between 3 and 5 years.

Serologic studies indicate that the persistence of TBE immunity is compromised in the elderly and there is a more rapid decline of antibodies in those who received only three immunisations. The immune response following booster doses of vaccine is

also of lower magnitude in the elderly compared to that in younger adults (12). Because of these findings, booster doses continue to be recommended every three years in adults > 60 years.

Immunogenicity

A seroconversion rate of 97% has been observed in adults between 21 and 35 days after the second dose of FSME-IMMUN. 100% of vaccinees seroconverted after the 3rd dose (13). Data for those having had the rapid schedule (i.e. two doses of TBE vaccine two weeks apart) indicate that 92% of subjects showed seropositive antibody levels by day 14 after the second dose of vaccine (14).

Children have also been shown to have a high seroconversion rate (96%) between 21 and 35 days after the second dose of vaccine and 100% seroconversion following the third dose of vaccine (11).

Contraindications

- Current febrile illness
- Allergies to constituents of the vaccine, including severe reactions to egg

Precautions

- Persons with known or suspected auto immune disease
- Persons with pre-existing cerebral disorders
- Pregnancy
- Lactation

Adverse Events

Adverse reactions following TBE vaccine are most commonly mild and transient. In adults they include local reactions such as swelling, redness and pain at the injection site. Generalised reactions such as fatigue, malaise, headache, muscle pain and nausea have been reported but were transient and mainly mild.

Studies in children reported mild local and systemic reactions. The most common local reactions reported were pain and tenderness at the injection site. The most frequently reported systemic reactions were fever and restlessness in young children, as well as headache in all children. Fever, particularly after the first dose, has been reported.

In rare cases there are more serious reactions, for example meningitis and neuritis.

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Reading list

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Links

CDC <http://www2.ncid.cdc.gov/travel/yb/utls/ybGet.asp?section=dis&obj=tickenceph.htm&cssNav=browseyb>

International Scientific Working Group on TBE www.tbe-info.com