Tick-borne encephalitis

Tick-borne encephalitis is a viral infection which can cause a range of symptoms from a mild and short-lived febrile illness to a severe infection of the central nervous system

Key messages

- Tick-borne encephalitis (TBE) is a viral infection that rarely causes a serious neurological illness. Although it is usually spread through the bite of an infected tick, consumption of unpasteurised dairy products from infected animals can also pose a risk.
- Areas with a known TBE risk extend from central, eastern and northern Europe across Russia to parts of eastern Asia and the Far East.
- Generally, TBE infections are asymptomatic (symptom free).
 However, some cases follow a two-stage process with a mild flu-like illness followed by a potentially serious central nervous system (brain and spinal cord) infection. Some cases can be more severe from the start and/or cause prolonged symptoms.
- While TBE is rarely fatal in Europe, sub-types found in Asia can have a higher fatality rate and long-term neurological complications are more common.
- TBE is rare in United Kingdom (UK) travellers. However, individuals are at increased risk when visiting areas where TBE is known to occur, particularly woods, forests, glades, forest fringes, city parks and grasslands.
- Travellers may reduce their risk of infection by avoiding risk areas and taking tick bite prevention measures. A vaccine course is available for travellers whose planned activities increase their risk of acquiring TBE.

Overview

Tick-borne encephalitis (TBE) is a viral infection that usually causes a mild illness, or no symptoms, but in rare cases can affect the central nervous system. It is spread by a bite from an infected *Ixodes* tick or, more rarely, by eating and drinking unpasteurised "raw" dairy products from infected animals. TBE is caused by a ribonucleic acid (RNA) virus know as tick-borne encephalitis virus (TBEV) which belongs to a group of viruses called flaviviruses (which includes yellow fever, dengue and Japanese encephalitis). There are five main subtypes of TBEV, with different geographic locations:

- European or Western (TBEV-Eur)
- Siberian (TBEV-Sib)
- Far Eastern (TBEV-FE previously known as Russian Spring Summer encephalitis)
- Baikalian (TBEV-Bkl)
- Himalayan (Him-TBEV) [1]

TBE is rarely fatal in Europe. However, in Asia, it may be fatal in up to 20 percent of cases and long-term neurological problems are common [2].

Risk areas

TBE is reported from western and northern Europe through to northern and eastern Asia [3].

Climate change is thought to have resulted in ticks, and therefore TBE risk areas, moving northward and to higher altitudes [4, 5].

During the past 30 years, the range of TBEV transmission appears to have expanded to new geographic areas and to higher altitudes; TBEV has been found at \geq 5,000 ft (\approx 1,500 m). These trends are likely to be due to a complex combination of advances in diagnostics/surveillance, changes in human activities and other socioeconomic, ecologic, and climatic factors [3].

Approximately 10,000-12,000 clinical cases of tick-borne encephalitis are confirmed every year worldwide, but this figure is considered to be significantly lower than the actual total number of cases due to the mild or symptomatic nature of the majority of infections [6].

TBE is a seasonal infection, with cases usually reported from spring and summer through to autumn [7].

In 2019, the first TBE virus detection in UK ticks was reported from Thetford Forest, East Anglia in England. In 2019, TBE was confirmed in ticks in a different geographical location in England, the Hampshire/Dorset border [8].

In July 2019, a probable, autochthonous (locally acquired), human TBE case was reported in a visitor from mainland Europe who became ill after a tick bite in the New Forest, Hampshire, England [8, 9]. Diagnosis was made by serological (blood) testing. As TBEV can cross react with other flaviviruses found in the UK (such as Louping ill virus) a confirmed diagnosis was not possible [8]. In



July 2020, a second probable case of TBE was diagnosed, in Hampshire, England, also based on serological testing [10].

A third TBE case was reported in England in September 2022 and was likely to have acquired infection in Scotland in June 2022. A fourth case was reported in England in October 2022 and was likely due to an exposure in the North Yorkshire Moors. These third and fourth cases were both confirmed positive for TBEV by polymerase chain reaction (PCR) testing [11].

Current assessment of overall TBE risk in the UK is very low for the general population, and low for high-risk groups: those living, working or visiting affected areas, determined by duration of time spent outside [1].

<u>Vaccine recommendations</u> for TBE risk countries depend on areas visited, planned activities, season of travel and medical history of individual travellers.

Please see our <u>Country Information pages</u> for specific country risk areas, vaccine recommendations and guidance.

Risk for travellers

Risk of acquiring TBE infection is dependent on several factors including:

- Destination of travel.
- Duration of travel in risk area.
- Season of travel.
- Activities undertaken.
- Tick activity in country visited.
- Vaccination status of the traveller.

Risk of TBE infection for an individual traveller is affected by planned itinerary and activities [3]. In TBE endemic regions, travellers are at risk in rural areas, forests, grasslands, woods and urban parks; anywhere they can be exposed to infected ticks. Outdoor activities and working or spending long periods of time in endemic areas increase risk, but cases have also been reported after short trips [12]. TBE can also be acquired by eating or drinking unpasteurised dairy products from infected animals [1]. In Europe, the early spring through to late autumn are generally higher risk, but seasons vary according to location [13].

Between 2014 and 2018, a total of seven travel-related TBE cases were confirmed in UK residents who visited endemic areas [1].

Transmission

TBE is most commonly spread by the bite of an infected *Ixodes* tick. Certain *Ixodes* species of tick are both the source and reservoir of TBEV, spreading the virus between wild mammals and



occasionally to humans and domestic animals. The main type of ticks that spread TBE are:

- Ixodes ricinus (sheep tick) for TBEV-Eur.
- Ixodes persulcatus (Taiga tick) for TBEVm-FE, TBEV-Sib and the Baikalian subtype [1].

TBEV is maintained by a number of animal 'hosts' including small rodents like mice and voles, domestic animals such as sheep, goats or cattle and certain bird species. This interaction between tick and host creates a pool of TBEV in the environment. People get infected when they are in areas where TBEV is present and are bitten by infected ticks [5, 6].

Ticks are found on forest fringes next to or near grasslands, forest glades, riverside meadows and marshland, forest plantations with brushwood, and shrubbery. Ticks can also be found in parks and gardens. They tend to live on ground level vegetation, on the underside of foliage, from where they can be brushed onto clothing. Ticks can spread TBEV throughout their lifecycle stages: larvae, nymphs or adults and once infected, carry the virus for life. Tick activity and development are affected by local climate factors such as temperature, soil moisture and relative humidity.

The number of ticks infected in risk areas can vary. In some endemic countries in central Europe the prevalence of TBEV infected ticks varies from 0.1 to 5% [15].

Signs and symptoms

Most people infected with TBEV do not develop symptoms. However, a range of clinical manifestations can be observed following infection by any TBEV sub-types.

Two phases of symptoms are usually seen after infection with European/Western TBE sub-type. Approximately two to 30% of those infected with this sub-type develop a non-specific flu-like illness with fever, fatigue, headache and muscle pain after an incubation period of about eight days (range of two to 28 days) [16, 17].

An interval of one to 20 days follows, during which patients usually have no symptoms. After this, approximately one third of those with initial symptoms will progress to the second stage; with a sudden rise in temperature, clinical features of meningitis (inflammation of brain lining), meningoencephalitis (affecting brain and lining) and meningoencephalomyelitis (the most severe form also affecting the spinal cord) [16-18]. According to a 10-year follow-up survey; 80% of patients with the primary meningoencephalomyelitic type developed long-term health complications [18].

TBE is rarely fatal in Europe (<2%). With milder disease and longer-term neurological problems in less than 30% of patients. Infection with Far Eastern TBE sub-type is generally more severe, with a higher-fatality rate [3].

Diagnosis and treatment

Diagnosis of TBE is made when antibodies to TBEV are detected in samples of blood or, less commonly, in cerebrospinal fluid. During the first phase of the illness, TBEV can sometimes be detected in blood or urine samples by PCR. Treatment relies on supportive management; there is no specific drug or antiviral treatment for TBE. Severely affected individuals may need admission to hospital intensive care, with some requiring assisted ventilation [18]. Long-term support for neurological complications may be required.

Preventing tick-borne encephalitis

All travellers to TBE endemic areas during spring, summer and autumn should be advised to take risk avoidance measures including:

- <u>Practising bite avoidance methods: for example, wear appropriate clothing and use effective insect repellents</u> [19].
- Wearing light coloured clothes makes ticks easier to spot.
- Checking clothes and the whole body for ticks regularly and remove any as soon as possible using the correct technique. Larval forms of *Ixodes* ticks are tiny and difficult to see (they can be the size of a freckle or speck of dirt). After feeding, adult ticks become engorged and can be the size of a coffee bean. Common areas for ticks are armpits, back of knees, elbows, groin and hairline. However, ticks can attach anywhere, so a full body check is recommended [19].
- Removing ticks correctly and as soon as possible with a pair of fine tipped tweezers or tick remover [20].
- Avoiding consumption of unpasteurised "raw" dairy products.
- TBE vaccine is available for those visiting risk areas or individuals whose occupation puts them at higher risk (see below).

If any signs of illness occur within 28 days of a tick bite, individuals should seek prompt advice from a medical practitioner, mentioning any relevant exposures and travel history.

TBE immunoglobulin (antibodies) was previously used as post-exposure prophylaxis after a tick bite in TBE endemic countries. However, there were concerns that it had a negative effect on the disease course. TBE immunoglobulin is no longer recommended in the UK or other European countries for treatment.

Vaccine information

Indications for use of TBE vaccine

TBE vaccine is recommended for:

- Anyone living in TBE risk areas.
- Those at occupational risk in endemic areas, e.g. farmers, forestry workers, woodcutters, soldiers.

- Travellers visiting TBE affected areas including forests, grassland and city parks whose activities put them at increased risk: camping, fieldwork, hiking and hunting.
- Laboratory workers who may be exposed to TBE [21].

Vaccines

TicoVac and TicoVac Junior vaccines (known in some countries as FSME IMMUN and FSME IMMUN Junior) are licensed in the UK [22-24].

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

Vaccine schedules

The Summary of Product Characteristics (SPC) for the individual vaccines should be checked before the administration of any vaccine [22, 23].

Vaccine	Schedule	Accelerated schedule	Length of protection	Age range
TicoVac 0.5ml	3 doses on days 0, between 1 and 3 months, and 5 to 12 months after the second dose*	be given 2 weeks after the	**First booster no more than 3 years after 3rd dose. After this, boosters may be given at 5-year intervals if at risk	least 16 years of age and
TicoVac 0.25ml Junior	days 0, between 1 and	be given 2 weeks after the	First booster no more than 3 years after 3rd dose. After this, boosters may be given at 5-year intervals if at risk	1 year of age and below 16

^{*}After the first two doses, sufficient protection can be expected for the on-going tick season (protection rate over 90 percent after the second dose)

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

The best time to start a course of TBE vaccination, if at risk and travelling to areas where vaccination is recommended, is during the winter to ensure protection before the tick season starts in spring. TicoVac is probably effective against the Far Eastern subtype as well as the European subtype of TBE [23, 24]. In general, for individuals over 60 years of age, booster dose intervals should not exceed three years [23].

Contraindications

• Confirmed anaphylactic reaction to a previous dose of the vaccine or to any component of the vaccine or to egg [24].

Precautions

- · current febrile illness
- known or suspected auto-immune disease
- pre-existing cerebral disorders
- pregnancy
- breastfeeding

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 brief and usually 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, more serious reactions of meningitis and neuritis have occurred.

Resources

- <u>European Centre for Disease Control and Prevention: Surveillance and disease data for tick-borne encephalitis</u>
- NHS: Tick-borne encephalitis
- UK Health Security Agency: Tips and tricks to stay safe from ticks
- World Health Organization: Tick-borne encephalitis
- Getting to grips with tick-borne encephalitis

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