Tick-borne encephalitis

TBE is a viral infection that affects the central nervous system and may cause a spectrum of disease, from a mild short-lived illness to a more severe life-threatening illness.

Key Messages

| Tick-borne encephalitis (TBE) is a viral infection usually transmitted through the bite of an infected tick. |
| Areas with known TBE exist within a band that extends from central, eastern and northern Europe across Russia to parts of eastern Asia. |
| Typically the disease occurs in two stages: The first is a mild-flu like illness. The second is a potentially serious infection of the central nervous system (brain and spinal cord). |
| TBE is rarely fatal in Europe, however in Asia TBE may be fatal in up to 20 percent of cases. Long-term neurological complications are common. |
| TBE is a rare disease in UK travellers, however individuals are at increased risk if they visit areas where TBE is known to occur particularly in woodland or grassland e.g. when camping or hiking. |
| Travellers may reduce the risk of infection by avoiding risk areas and taking bite prevention measures. A vaccine is also available for travellers whose planned activities put them at increased risk. |

Overview

Tick-borne encephalitis (TBE) is a viral infection that is transmitted predominantly through the bite of an infected Ixodes tick. The TBE virus belongs to a closely related group of viruses called flaviviruses. These include yellow fever, dengue and Japanese encephalitis. There are three different subtypes of TBE virus: European TBE virus, Siberian TBE virus and Far Eastern TBE virus.

TBE affects the central nervous system and may cause a spectrum of disease, from a mild short-lived illness to a more severe life-threatening illness with the potential for severe neurological complications. The disease occurs in parts of central, northern and Eastern Europe, Siberia and parts of Asia [1]. TBE is rarely fatal in Europe however in Asia may be fatal in up to 20 percent of cases. Long-term neurological problems are common [2].

Risk areas

Areas where TBE occurs exist within a band that extends from central, eastern and northern Europe across Russia to parts of eastern Asia, predominantly within the non-tropical regions of the Eurasian forest steppe. These areas are generally at altitudes lower than 1500m, however they have been noted at higher altitudes [3, 4]. Climate change is thought to have resulted in TBE risk areas moving northward and to higher altitudes. Social, political, ecological and demographic factors are also considered to be important [5]. Within this band TBE occurs in highly focal areas and from year to year.
to year the incidence (number of cases) may vary significantly according to local environmental conditions [6]. In Europe and Asia, approximately 10,000-12,000 TBE cases are reported annually [4]. Of these, approximately 2000 cases are reported in Europe each year [6-9].

The general geographical distribution of the three virus subtypes is as follows:

- **European TBE virus** – prevalent in Europe and western Russia. Transmitted by *Ixodes ricinus*
- **Siberian TBE virus** – prevalent in parts of Eastern Europe, all parts of Russia and parts of northern Asia. Transmitted by *Ixodes persulcatus*
- **Far Eastern TBE virus** – prevalent in eastern Russia, China and Japan. Also transmitted by *Ixodes persulcatus*

Vaccination recommendations for countries highlighted in Figure 1 will depend on regions visited within a country, a traveller’s planned activities, the season of travel, and the medical history of the individual traveller. The Country Information pages should be consulted for specific guidance.

Fig 1: NaTHNaC Tick-borne encephalitis country risk map April 2017. This map should be interpreted with caution, as epidemiological information available from different countries may be limited and the risk may be different within a country.

Further information on TBE Risk Class as detailed in this map is available in the rationale for country specific disease recommendations.

**Risk for travellers**

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

- Destination of travel
- Duration of travel in risk area
- Season of travel
Activities undertaken
- Tick activity in the country visited
- Vaccination status of the traveller
- Travellers to areas where TBE occurs 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 unpasteurised dairy products from infected animals [6]. In Europe the early spring through to late autumn are generally higher risk, but seasons vary according to location [8, 9].

As of December 2016, six confirmed cases of TBE have been reported in the UK since 2011. All the cases had history of travel to the TBE endemic areas of Czech Republic (one case), Latvia (one case), Sweden (three cases) and one case travelled to multiple destinations of (Latvia, Lithuania and Estonia) [10].

Transmission

TBE is usually transmitted through the bite of an infected Ixodes tick, the main vectors of TBE virus. The virus is maintained in nature by a number of animal ‘hosts’ including; small mammals (such as mice and voles), domestic livestock (including sheep, goats and cattle) and certain species of birds. This interaction between vector and host creates a reservoir of disease in the surrounding environment. Human infection occurs incidentally when individuals encroach on the area where the virus is present and are inadvertently bitten by infected ticks [5, 6].

Ticks are found on forest fringes within adjacent grassland, forest glades, riverside meadows and marshland, forest plantations with brushwood, and shrubbery. Ticks can also be found in parks and gardens. They tend to reside on ground level vegetation, on the underside of foliage, from where they can be brushed onto clothing. Ticks are capable of transmitting the TBE virus throughout their lifecycle stages (larvae, nymphs or adults), and once infected, carry the virus for life. Tick activity and development are affected by local climatic factors such as temperature, soil moisture and relative humidity.

The number of ticks infected within risk areas may vary markedly. The number of infected Ixodes ricinus ticks is often low. In some endemic countries in Central Europe the prevalence of the virus in ticks varies from 0.1 to 5% [11]. Unusually, humans may become infected after consumption of unpasteurised dairy produce [9].

Signs and symptoms

Most people who are infected with TBE virus do not develop symptoms with approximately 2- 30% developing a temperature after an incubation period of around eight days, with a range of two to 28 days [12, 13]. Typically TBE follows two stages with the first stage of the disease lasting from up to a week characterised by a non-specific flu-like illness with fever, fatigue, headache and muscle pains [12, 13]. An interval of 1 to 20 days follows, during which time patients usually have no symptoms [2]. Approximately one third of those with the initial symptoms progress to the second stage of disease [14].
The second stage of TBE is heralded by a sudden rise in temperature with clinical features of: meningitis (inflammation affecting brain lining only), meningoencephalitis (affecting the brain and its lining), and meningoencephalomyelitis (the most severe form also affecting the spinal cord) in about 10 percent of symptomatic cases [12,13]. Cases that progress to the second stage develop long-term neurological complications. According to a 10-year follow-up survey, 80% of patients with the primary meningoencephalomyelitic form developed long term sequelae [14].

The second phase of illness in children is usually limited to meningitis whereas adults older than 40 years are at increased risk of developing meningoencephalitis or meningoencephalomyelitis, with higher mortality in those over the age of 60. The Far Eastern subtype appears to be more severe. TBE is rarely fatal in Europe (0.5 to 2%) however more deaths occur with the Siberian and Far East types [4].

Diagnosis and treatment

Diagnosis of TBE is made when antibodies to the TBE virus are detected in the blood or cerebrospinal fluid. During the first phase of the illness, TBE virus or viral RNA can sometimes be detected in blood samples by virus isolation or PCR. Treatment relies on supportive management; there is no specific anti-viral treatment for TBE. More severely affected individuals may need admission to intensive care with some requiring assisted ventilation [14]. Long-term support for neurological complications may be needed.

Preventing tick-borne encephalitis

Travellers should be advised to:

- Avoid known heavily tick-infested areas of forest and woodland during the spring, summer and autumn where possible.
- **Practise bite avoidance methods:** for example wear appropriate clothing and use effective insect repellents [13].
- Check the body for ticks regularly. The larval forms of *Ixodes* ticks are tiny and difficult to see (they can be the size of a freckle or speck of dirt). 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 fine tipped tweezers or tick remover.** After a tick has attached itself to the host it may not start feeding for approximately 12 hours [14, 15].
- Travellers should also avoid consumption of unpasteurised dairy products in areas of risk.
- If any signs of illness occur within 28 days of a tick bite, advice should be promptly sought from a medical practitioner.
- TBE vaccination is available for those travellers intending to visit risk areas, or those whose occupation may put them at higher risk (see below).

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 course
of disease. TBE immunoglobulin is no longer recommended in the UK or other European countries for treatment.

Vaccine information

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 at risk of disease. See ‘Risk for travellers’ section above
- Laboratory workers who may be exposed to TBE

Vaccines

TicoVac and TicoVac Junior vaccines (known in some countries as FSME IMMUN and FSME IMMUN Junior) are licensed in the UK.

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 consulted prior to the administration of any vaccine [18, 19].

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Schedule</th>
<th>Accelerated schedule</th>
<th>Length of protection</th>
<th>Age range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TicoVac 0.5ml</strong></td>
<td>3 doses on days 0, between 1 and 3 months, and 5 to 12 months after the second dose*</td>
<td>2nd dose can be given 2 weeks after the 1st dose</td>
<td><strong>First booster no more than 3 years after 3rd dose. After this, boosters may be given at 5 year intervals if at risk</strong></td>
<td>Persons at least 16 years of age and older</td>
</tr>
<tr>
<td><strong>TicoVac 0.25ml Junior</strong></td>
<td>3 doses on days 0, between 1 and 3 months and 5 to 12 months after the second dose*</td>
<td>2nd dose can be given 2 weeks after the 1st dose</td>
<td>First booster no more than 3 years after 3rd dose. After this, boosters may be given at 5 year intervals if at risk</td>
<td>Children above 1 year of age and below 16 years of age</td>
</tr>
</tbody>
</table>

* 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 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 probably effective against the Far Eastern subtype as well as the European subtype of TBE [18,19]. Booster doses continue to be recommended every three years in adults > 60 years [20].

**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 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**

- European Centre for Disease Control and Prevention: Tick-borne diseases
- U.S. Centres for Disease Control and Prevention: Tick borne diseases abroad
- NHS Choices: Tick-borne encephalitis

**REFERENCES**

9. Steffen R. Epidemiology of tick-borne encephalitis (TBE) in international travellers to Western/Central Europe and conclusions on vaccination recommendations Journal of Travel Medicine, 2016, 1-10.

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