Human Animal Infections and Risk Surveillance (HAIRS) group

Qualitative assessment of the risk that tick-borne encephalitis presents to the UK population
Qualitative assessment of the risk that TBE virus presents to the UK population

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About the Human Animal Infections and Risk Surveillance group

This document was prepared by Public Health England (PHE) on behalf of the joint Human Animal Infections and Risk Surveillance (HAIRS) group.

HAIRS is a multi-agency agency cross-government horizon scanning group, which acts as a forum to identify and discuss infections with potential for interspecies transfer (particularly zoonotic infections).

Qualitative risk assessment for tick-borne encephalitis (TBE) virus in the UK population

<table>
<thead>
<tr>
<th>Date of this assessment</th>
<th>16 July 2019</th>
</tr>
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<tbody>
<tr>
<td>Version</td>
<td>3.0</td>
</tr>
<tr>
<td>Reason for update</td>
<td>Update on research and epidemiological data</td>
</tr>
<tr>
<td>Completed by</td>
<td>HAIRS secretariat and members</td>
</tr>
<tr>
<td>Date of previous risk assessment</td>
<td>12 March 2006</td>
</tr>
<tr>
<td>Date of initial risk assessment</td>
<td>12 March 2006</td>
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Information on the risk assessment processes used by the HAIRS group can be found at [www.gov.uk/government/publications/hairs-risk-assessment-process](http://www.gov.uk/government/publications/hairs-risk-assessment-process)
<table>
<thead>
<tr>
<th><strong>SUMMARY OF RISK ASSESSMENT FOR TBE IN THE UK POPULATION</strong></th>
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<tbody>
<tr>
<td><strong>Overview</strong></td>
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</table>
| **Assessment of the risk of infection in the UK** | **Probability** | General population - VERY LOW  
High risk groups (ie those living, working or visiting the areas, as determined by duration of time spent outside) - LOW |
| | **Impact** | LOW |
| **Level of confidence in assessment of risk** | High, with some uncertainty regarding current geographic distribution of infected ticks |
| **Action(s)/Recommendation(s):** | • local awareness raising for the public and clinicians  
• seroprevalence amongst possibly exposed occupational groups  
• consideration of regionally appropriate follow-up to investigate evidence of historic and ongoing human TBEV exposure against a background of geographically varying presence of louping ill, to include evidence from veterinary surveillance and research activities focussed principally in sheep and grouse  
• further evidence from deer seroprevalence and tick testing, including from migratory birds  
• research into tick and virus ecology and tick transmission cycles |
Assessing the risk to the UK population from new and emerging infections

Step One: Assessment of the probability of infection in UK population
The likelihood of an infectious threat causing infection in the UK human population. Where a new agent is identified there may be insufficient information to carry out a risk assessment and this should be clearly documented. Please read in conjunction with the Probability Algorithm following the boxes shaded green.

<table>
<thead>
<tr>
<th>QUESTION</th>
<th>OUTCOME</th>
<th>QUALITY OF EVIDENCE</th>
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<tbody>
<tr>
<td>i) Is this a recognised human disease?</td>
<td>Yes</td>
<td>Good</td>
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</table>

Tick-borne encephalitis (TBE) is a viral infection involving the central nervous system (CNS). It is caused by tick-borne encephalitis virus (TBEV), an RNA virus belonging to the genus Flavivirus that was initially isolated in 1937 in Russia. Three main subtypes have been identified with differing geographic distributions: European or Western (TBEV-Eur), Siberian (TBEV-Sib), and Far Eastern (TBEV-FE) (formerly known as Russian Spring Summer encephalitis) (1). TBEV-Eur is endemic in rural and forested areas of central, eastern and northern Europe; TBEV-FE is endemic in far-eastern Russia and in forested regions of China and Japan; and TBEV-Sib is endemic in Urals region, Siberia and far-eastern Russia, and also in some areas in north-eastern Europe (2).

In 2017, 3,079 cases (2,550 confirmed) were reported in Europe, including 9 associated fatalities (3). The highest incidence rates were reported in the Czech Republic, Germany and Lithuania, while in previous years, Estonia, Latvia and Slovenia reported the highest rates. In the endemic regions of Europe, incidence varies considerably (4, 5). Annual peaks in incidence are correlated with seasonal periods of increased tick activity with the majority (92%) of cases reported between May and October (3, 5). Case numbers are increasing across the region (5), associated with a variety of factors including climate change, an extended active tick season and habitat range of tick vectors, reforestation and an increase outdoor leisure pursuits (4, 6). Improvements in case detection and reporting may also be partly responsible for the increase (4). Low endemicity countries are expected to experience an increase in TBEV burden. New foci of infections are also emerging with the Netherlands reporting TBEV for the first time in ticks, deer and a small number of human cases in 2016 and 2017 (7-10).

TBEV is transmitted mainly by Ixodes spp. ticks from a wild vertebrate host to humans and domesticated animals. The principal vectors are *Ixodes ricinus* (sheep tick) for TBEV-Eur. Human cases have been associated with consumption of unpasteurised milk or milk products from infected animals (11-13). TBEV is rarely transmitted from human to human via transplant (14) or blood transfusion and breastfeeding (15). Animal studies have shown the potential for vertical transmission from an infected mother to the foetus (16). Infection has also been acquired accidentally in laboratories (17).

The incubation period of tick transmitted TBE is on average 7 days (a maximum of 28 days) but is shorter following foodborne transmission (approximately 4 days). The majority (around two-thirds of cases) of human TBEV infections are asymptomatic. In
clinical cases, TBE often presents as a biphasic disease. The initial viraemic phase lasts approximately 5 days (range 2 to 10 days), and is associated with non-specific symptoms such as fever, fatigue, headache, myalgia and nausea. Following an asymptomatic interval of around 7 days, there is a second clinical phase involving the central nervous system (CNS) with presentations such as meningitis, meningoencephalitis, myelitis, paralysis and radiculitis (2).

Clinical presentation and outcomes differ across the three distinct subtypes of TBEV (2, 18). TBEV-Eur is associated with milder disease, with 20–30% of symptomatic individuals experiencing the second CNS phase, and a case fatality rate (CFR) of less than 2%. However, severe neurological sequelae are observed in up to 10% of patients. In children infected with TBEV-Eur, the second phase of illness is usually limited to meningitis, whereas adults older than 40 years are at increased risk of developing encephalitis, with higher mortality and long-lasting sequelae in those aged over 60 years. TBEV-FE subtype is associated with more severe but monophasic illness, has a CFR up to 35%, and higher rates of severe neurological sequelae. TBEV-Sib subtype is associated with a less severe disease (CFR <3%), and a tendency for chronic or extremely prolonged infections (2). Haemorrhagic forms of the disease have been reported in the Asian part of Russia, but are thought to be rare (18).

<table>
<thead>
<tr>
<th>ii) Is there zoonotic or vector borne spread?</th>
<th>Yes</th>
<th>Good</th>
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</thead>
</table>
| Ticks are the primary route of transmission. Several *Ixodes* species of tick are both reservoir and vector for TBEV, spreading the virus between wild vertebrate hosts and occasionally transmitting TBEV to humans and domesticated animals. The principal vectors are *Ixodes ricinus* (sheep tick) for TBEV-Eur and *I. persulcatus* (Taiga tick) for TBEV- FE and TBEV- Sib. All tick stages can be infected, acquiring the virus from viraemic hosts during co-feeding, trans-stadially, trans-ovarially or transexually (19). *Ixodes ricinus* is widespread in the UK, whereas *I. persulcatus* is considered absent. New foci of TBEV infections in ticks can appear intermittent, as suggested by a recent study in Denmark which reported the apparent absence of the virus from a previously known area (20). TBEV prevalence in ticks in endemic areas can often be less than 1%, so lack of detection in tick populations may be due to low prevalence (21). Other studies have detected the virus in ticks along with seropositive animals, without evidence of infection in humans (22). Virus prevalence in ticks does not correlate with increased risk for human infection. (23) Sustained TBEV transmission cycles are thought to require co-feeding of larvae and nymphs on small mammal hosts that experience viraemia for 2-3 days. This is considered the main reason why TBEV does not occur throughout the geographical range of its tick vectors. Foci are thought to be limited geographically, and the areas may be as small as 0.5km² (21). Larger hosts are also important for feeding and maintaining tick populations and, although not competent for the virus, can move infected ticks to new locations (24). Generally in the UK, peak larval activity occurs after peak nymphal activity, however there is some field evidence that larval and nymphal *I. ricinus* show coincident co-infestation on small rodents. In a woodland study in southern England, co-infestation rates of ticks on small mammals were lower than in TBEV endemic parts of Europe, but it does demonstrate that co-infestation is possible in the UK and therefore transmission could occur (25).
Recent evidence of TBEV transmission in the Netherlands highlights that climatic and other environmental factors may have an impact on changing viral distribution to parts of western Europe.

### iii) Is this disease endemic in the UK?

<table>
<thead>
<tr>
<th>Yes/No</th>
<th>Poor</th>
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<tbody>
<tr>
<td>No autochthonous human cases have been reported. Travel-related TBE cases are occasionally diagnosed in the UK - 5 confirmed cases were reported between 2012 and 2016 (5).</td>
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</tbody>
</table>

Louping ill virus (LIV), a related virus that displays a high degree of genetic homology to TBEV is present in areas of the UK and can complicate surveillance for TBEV in animals and humans due to serological cross-reactivity between the 2 viruses.

The TBEV vector *I. ricinus* is a common tick found throughout the British Isles in woodlands, grazed grasslands, moor- and heath-land and some urban parks (see [latest PHE map here](#)) (26). Across Europe, although both TBEV (27) and *I. ricinus* (see [latest ECDC map](#)) have a wide distribution, TBE incidence is variable and does not occur in all areas where the tick is found.

Recently, research conducted in England and Scotland detected evidence of TBEV for the first time through investigating deer seroprevalence, and by testing ticks (PHE data). During 2018, ~1,300 deer serum samples from England and Scotland were tested by TBEV IgG ELISA and LIV haemagglutination inhibition assay (HAI). Blood-fed ticks from deer in areas with seropositive deer were tested by RT-PCR using a LIV/TBEV RNA assay, and a secondary LIV specific assay. Five ticks from the Thetford Forest area were PCR positive and a full-length genome of TBEV was obtained by sequencing from 1 of these. Subsequent surveys of questing ticks in Thetford Forest were conducted, and collected ticks pooled. Two pools were positive.

This is the first evidence of TBEV in UK ticks, but it is not known if this is the result of a new incursion, or present previously but undetected.

### iv) Are there routes of introduction into the UK?

<table>
<thead>
<tr>
<th>Yes</th>
<th>Good</th>
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<tbody>
<tr>
<td>In 2019, TBEV was found for the first time in ticks (questing and on deer) in the East of England. (PHE data).</td>
<td></td>
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</tbody>
</table>

There is potential for migratory birds to introduce TBEV infected ticks into the UK from endemic areas, as *I. ricinus* ticks infected with TBEV have been detected on migratory birds in Europe (28). The virus has not been detected from samples taken from migratory birds in the UK (29) but surveys here are ongoing.

There is also a possibility of TBEV introduction through animal movement, including companion animals, inadvertently transporting infected ticks. Changes in the PETS travel scheme in 2012 which removed compulsory tick treatment of companion animals entering the UK from Europe increased this risk.
v) Are there effective control measures in place to mitigate against these?

| Prevention of the introduction of infected ticks through animal movement would be necessary to mitigate the risk of TBEV introduction. However, it is impossible to prevent introduction of ticks via migratory birds. The revised PETS travel scheme does not require the compulsory treatment of pets for ticks prior to return/entry to the UK. In recent years, public and animal health has focussed on education and awareness raising of this increased risk of importation of ticks with both veterinary professionals (via publications in veterinary journals and publications) and the general public (PHE tick poster). However, given the continued submissions of ticks from imported pets to the PHE Tick Surveillance Scheme (30), it can be presumed that imported ticks on pets, including those that have potentially travelled from/through TBEV endemic countries, will continue to present a risk of introduction of TBEV to the UK. |
|---|---|---|
| No | Good |

vi) Do environmental conditions in the UK support the natural reservoirs/vectors?

| I. ricinus, both a reservoir and the vector of TBEV, is present and abundant throughout the UK (26). Transmission of TBEV is highly reliant on co-feeding of nymphs and larvae. and a recent study has shown some evidence of co-infestation (25). Climate change models also suggested a northern spread of TBEV in Europe(31). |
|---|---|---|
| Yes | Good |

vii) Will there be human exposure?

| Since infected ticks have recently been found in a defined area in Thetford Forest, there is the potential for human contact. Although no locally acquired TBEV cases have yet been reported, further studies are now planned to assess whether exposure has taken place, particularly in the areas where the TBEV-infected ticks were found. With this new finding, at risk groups for potential human exposure to TBEV infected ticks may now include those visiting, living or working in areas where infected ticks are present in the UK, and certain occupational groups may be at increased risk. Risk areas elsewhere in Europe are usually geographically limited due to co-feeding transmission that occurs on a small scale, sometimes as small as 0.5km (21). Exposure to infected ticks in the UK will likely be limited to similarly small foci. There are farmed livestock of varied species on many premises within and around Thetford Forest (Defra data). The number of dairy holdings around the Thetford area is relatively low, twenty in total, and only 2 are registered for raw milk. (FSA data). There is a theoretical risk of TBE through the food chain. The Food Standards Agency (FSA) has assessed the overall risk of infection with TBEV to consumers as follows: |
|---|---|---|
| No/Yes | Good |

- From drinking unpasteurised milk from cattle affected by TBE to be **very low to low**
- From cheese made from unpasteurised milk to be **negligible to very low**
- From consuming meat from animals affected by TBE to be **negligible to very low**.
Comprehensive information on tick avoidance is on the GOV.uk website [https://www.gov.uk/government/publications/tick-bite-risks-and-prevention-of-lyme-disease](https://www.gov.uk/government/publications/tick-bite-risks-and-prevention-of-lyme-disease). (This is primarily for Lyme disease which is also transmitted by *I. ricinus*). Individuals can avoid exposure by using barrier methods when handling infested animals or entering tick infested environments. Protective measures include avoiding tick habitats, wearing long sleeves and trousers, using tick repellent or impregnated clothing, and checking frequently for ticks (32, 33).

### viii) Are humans highly susceptible?

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>Good</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humans are susceptible to TBEV but the majority (two-thirds) of infections result in asymptomatic infection. TBEV-Eur is associated with milder disease than the other subtypes, with 20–30% of patients experiencing the second CNS phase and severe neurological sequelae is observed in up to 10% of patients. All age groups are susceptible but individuals of older age or with existing chronic conditions may be at higher risk of mortality and longer-term sequelae (32), and morbidity in children can be significant (18). In TBEV endemic countries, a position paper by the World Health Organisation suggests that TBEV vaccine should be offered to all age groups in highly endemic areas; those with incidence rates above five per 100,000 (34). Due to the potential for high morbidity in children, many countries recommend vaccination of children in TBEV endemic areas (4). In the UK, a licenced TBE vaccine is available and is currently recommended only for those “at high risk of exposure to the virus”, through travel to endemic areas or employment (35-37). The Joint Committee on Vaccination and Immunisation is being asked to consider whether vaccination of high risk groups such as forestry workers is warranted at this stage, while further studies looking for evidence of human exposure/infection are undertaken.</td>
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</table>

### The PROBABILITY of human infection with TBEV in the UK population:

- General population - **VERY LOW**
- High risk groups (defined areas only) - **LOW**
Is this a recognised human disease? 

NO 

Is this a zoonosis or is there zoonotic potential? 

YES 

Is this disease endemic in the UK? 

NO 

Are there routes of introduction into the UK? 

NO 

Are effective control measures in place to mitigate against these? 

NO 

Do environmental conditions in the UK support the natural reservoirs/vectors of disease? 

NO 

Will there be human exposure? 

YES: general population 

YES: high risk groups 

Are humans highly susceptible? 

NO 

Is this disease highly infectious in humans? 

NO 

YES
Step two: Assessment of the impact on human health

The scale of harm caused by the infectious threat in terms of morbidity and mortality: this depends on spread, severity, availability of interventions and context. Please read in conjunction with the Impact Algorithm following the boxes shaded green.

<table>
<thead>
<tr>
<th>Question</th>
<th>Outcome</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>i) Is there human-to-human spread?</td>
<td>No</td>
<td>Good</td>
</tr>
<tr>
<td>TBEV is not directly transmitted from human to human, except in very rare cases via organ transplantation, blood transfusion or breastfeeding (14, 15). Human exposure to TBEV-Eur is primarily through the bite of an infected tick (<em>I. ricinus</em> in Europe) although foodborne transmission is occasionally reported (11-13). Accidental laboratory transmission has been reported (17).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ii) Is there zoonotic or vector borne spread?</td>
<td>Yes</td>
<td>Good</td>
</tr>
<tr>
<td><em>I. ricinus</em> is the primary vector for the TBEV-Eur transmission to humans, although foodborne transmission (mainly through contaminated unpasteurised milk) is occasionally reported (11-13).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>iii) For zoonosis/vector-borne disease, is the animal host/ vector present in the UK?</td>
<td>Yes</td>
<td>Good</td>
</tr>
<tr>
<td><em>I. ricinus</em> the tick vector for TBEV-Eur is present and abundant in the UK (26). Small mammals (eg rodents) that are able to support co-feeding transmission and large mammals (eg sheep, goat, roe deer) which serve as important hosts for maintaining tick population are also present in UK.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>iv) Is the population susceptible?</td>
<td>Yes</td>
<td>Good</td>
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<tr>
<td>Humans are susceptible to TBEV (36), but approximately two-thirds of infections are asymptomatic.</td>
<td></td>
<td></td>
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<tr>
<td>v) Does it cause severe disease in humans?</td>
<td>Yes</td>
<td>Good</td>
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</table>
Approximately two-thirds of human TBEV infections are subclinical, but the clinical spectrum ranges from mild disease (non-specific febrile illness) to CNS involvement (e.g., meningitis, severe meningoencephalitis with or without paralysis). Symptomatic infection can occur in all age groups, and is often more severe in adults, especially the elderly. The TBEV-EUR subtype is associated with milder disease compared to the other 2 virus subtypes.

TBE follows a typical biphasic course: a first viraemic phase with flu-like symptoms, followed by a period of quiescence, then the second phase with CNS involvement. Approximately a third of patients experience the second phase, and up to 20% of those with severe disease experience neurological sequelae. According to a 10-year follow-up survey, 80% of patients with primary myelitic disease will remain with sequelae (38). Overall the mortality rate is 0.5–2% (2).

### vi) Would a significant number of people be affected?

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<th>No</th>
<th>Good</th>
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The vast majority of TBEV infections are acquired by tick bite, thus only those who are exposed to and bitten by infected ticks will be affected. To date TBEV has only been found in a defined area of the eastern England, and exposure would be limited to those living working or visiting those areas. While the vector *I. ricinus* is a common tick found throughout the British Isles, even in endemic countries, the rate of infection is relatively low (e.g., Germany 0.4/100,000; Austria 1.1/100,000; Lithuania 21.9/100,000) (ECDC, 2016).

### vii) Are effective interventions available?

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<tr>
<th>Yes</th>
<th>Good</th>
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Individuals can avoid tick bites by keeping skin covered as much as possible when visiting a tick-infested areas and using insect repellents. Consumption of unpasteurised dairy products should also be avoided in endemic areas. An effective and well-tolerated vaccination is available for protection against TBE and has been introduced into childhood immunisation schedules in endemic areas.

In the UK, a licenced TBE vaccine is available and is currently recommended only for those “at high risk of exposure to the virus”, through travel to endemic areas or employment (35-37). The Joint Committee on Vaccination and Immunisation is being asked to consider whether vaccination of high-risk groups such as forestry workers is warranted at this stage, while further studies looking for evidence of human exposure/infection are undertaken.

There is no specific treatment for TBE. Supportive treatment can significantly reduce morbidity and mortality.

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The **IMPACT** of TBE on human health in the UK: **LOW**
'This question has been added to differentiate between those infections causing severe disease in a handful of people and those causing severe disease in larger numbers of people. 'Significant' is not quantified in the algorithm but has been left open for discussion and definition within the context of the risk being assessed.
References


37. Steffen R. Epidemiology of tick-borne encephalitis (TBE) in international travellers to Western/Central Europe and conclusions on vaccination recommendations. J Travel Med. 2016;23(4).