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INVITED SUBMISSION

Protection against tick-borne encephalitis (TBE) for people living in and travelling to TBE-endemic areas

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Summary Once considered a local health issue confined to certain regions in Russia and Central and Eastern Europe, tick-borne encephalitis (TBE) is now considered an international health concern, and the most important and widespread viral disease transmitted by ticks in Europe. The number of reported TBE cases continues to increase in many endemic regions, and new foci have been identified. Increases in travel, access to high-risk areas, and the pursuit of leisure activities within TBE-endemic areas are placing more people at risk of TBE. Travellers from non-endemic regions are often unaware of the risk of acquiring TBE and therefore many travellers are not protected against TBE. Active immunization is the most effective way to avoid TBE and its potentially life-threatening sequelae. After a tick bite, no post-exposure treatment including active/passive vaccination is available or recommended in the immunologically naive patient. Available vaccines have undergone a series of modifications and improvement in both composition (with special formulations for children) and schedules to further enhance the safety of immunization and to meet the needs of vaccinees. Efforts to develop internationally recognized recommendations for TBE vaccination for travellers are underway.
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Introduction

Tick-borne encephalitis (TBE) was previously considered a problem with limited global impact that was confined to a few well-defined areas in Russia and Central and Eastern Europe.[1] Over the past three decades, however, endemic areas have expanded, and new foci have been reported in Europe.[2,3] At the same time, increased international travel to endemic areas for business and leisure has placed more people at risk of TBE.[1,4] As a result, TBE is increasingly recognized as a major international health issue.[1,5]

The management of travel-related TBE faces many challenges. Immunization for TBE is not routinely recommended in travel medicine, and TBE vaccines are not available in many countries, such as the USA.[4] Travellers from non-endemic

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parts of Europe are often unaware of the risk of contracting a travel-related infection when travelling within Europe.[6] Clinical symptoms of TBE can manifest weeks after being bitten by an infected tick, which means that many travellers will return to their home country before being diagnosed.[4] Given the presently low levels of awareness of TBE in non-affected regions of the world, many cases are overlooked or incorrectly diagnosed.[1]

Curative treatment specifically for TBE is not available, but TBE remains a highly preventable disease. Recent improvements in the safety and efficacy of available vaccines have coincided with increased efforts to raise awareness of TBE, establish effective vaccination programmes in endemic areas, and develop internationally recognized guidelines for travellers.[1] These advances are part of an ongoing international collaboration that is making progress in the control of TBE on global level.

Epidemiology and disease characteristics

TBE is a serious acute viral infection of the central nervous system (CNS) that can lead to death or long-term neurological sequelae after recovery from infection.[7] The virus is transmitted to humans by a bite from an infected tick or, more rarely, from ingesting the unpasteurized milk and milk products of infected animals. In such cases, infections occur rapidly and often affect several people at the same time.[8] The main hosts and reservoir of the virus are small rodent species; ticks act as the vector, and humans are accidental hosts. Ticks carry the virus throughout their lifetime and pass the virus on to their progeny.[7]

The TBE virus is a member of the Flaviviridae family of viruses, which also includes the yellow fever virus and dengue fever virus. Among the flaviviruses, the TBE virus has one of the highest impacts as a human pathogen.[9] Three subtypes of the TBE virus have been identified based on comparative genomic sequencing.[10] The Western (European) subtype correlates with distribution of the tick species *Ixodes ricinus*. It is endemic to scattered areas within central, eastern, and northern Europe, ranging roughly between the Alsace-Lorraine region in the West, Scandinavia in the North, and parts of Italy, Greece, and Crimea in the South.[11] The Far Eastern subtype correlates with distribution of the tick species *Ixodes persulcatus*, which is found primarily in Russia, north-eastern China, and parts of northern Japan, but extends as far west as the Baltic States. A third subtype, known as the Siberian subtype, has also been identified.[12] This subtype spreads westwards and has recently been identified in Finland.[13] All three known subtypes co-circulate in Estonia.[14] Overall, the TBE virus circulates in a belt from Western Europe to Japan (Fig. 1).

Estimates of the global incidence of TBE range between 10,000 and 13,000 cases annually.[1,11,15] Approximately 3000–4000 cases are reported in Europe annually and roughly 6000–11,000 cases occur in Russia.[16] These estimates reflect the number of cases severe enough to require hospitalization only, and incomplete or incorrect diagnosis may contribute further to the underestimation of the actual incidence of the disease.[1]

The incidence of TBE follows a seasonal pattern that corresponds with periods of tick activity. Most cases occur between March and November, with two waves during June–July and September–October that correspond with peak feeding times for tick larvae and nymphs. During each stage of tick development (larva, nymph, adult), a tick feeds only once before proceeding to the next stage.

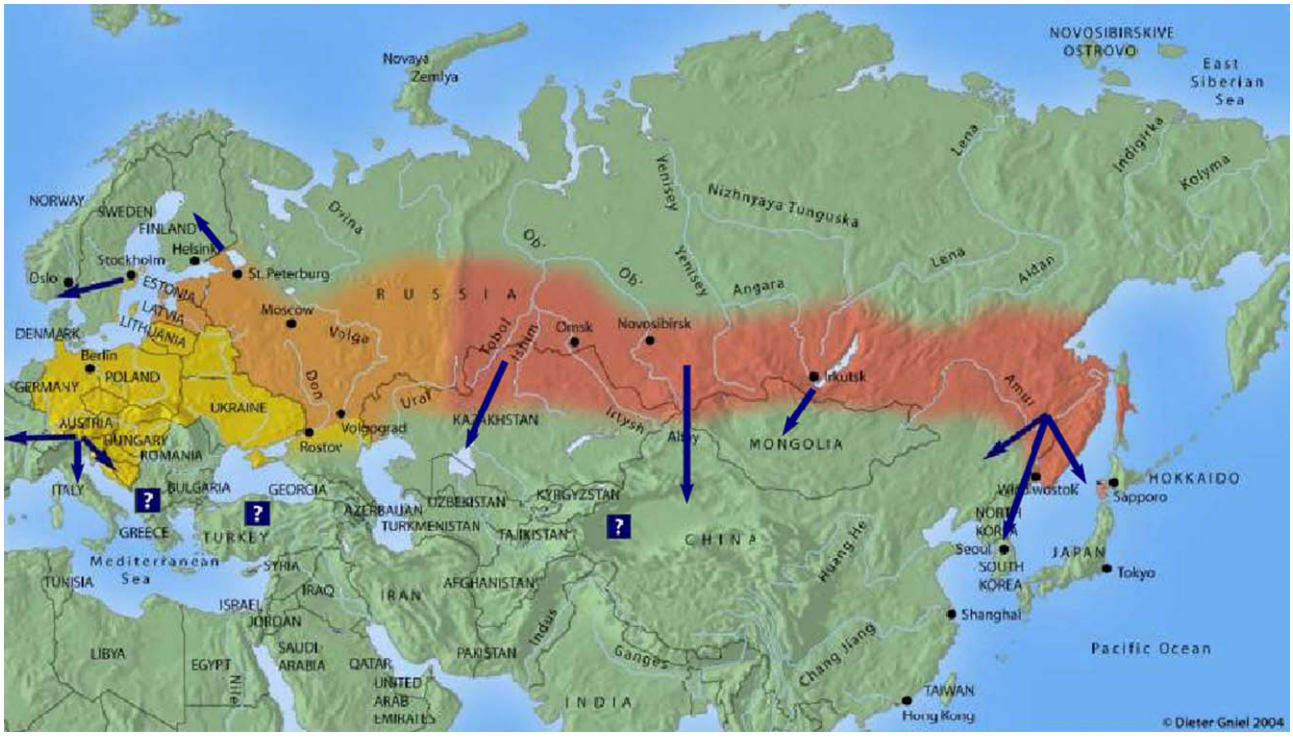

Figure 1 The TBE virus belt. Arrows indicate spread of virus.

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