Tick-borne encephalitis

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Summary

- Flavivirus, 3 subtypes
- Vector: Ticks, Ixodes species
- Main clinical presentation: Febrile disease, neurological syndrome (FD, NS)
- Effective vaccine is available

Virus

Tick-borne encephalitis (TBE) is caused by 3 closely related flaviviruses. These as known at present are European, Siberian, and Far Eastern strains.

Transmission

Tick-borne encephalitis (TBE) is also called Frühsommer Meningo-Enzephalitis (Early Summer Meningo-Encephalitis). This name is a misnomer, since transmission lasts well into autumn (April till October). TBE refers to both Central European encephalitis (CEE, syn. FSME) and Russian spring-summer encephalitis (RSSE). TBE is transmitted to humans usually by the bite of a tick (either Ixodes persulcatus or Ixodes ricinus). In contrast with Lyme disease, transmission of the TBE virus occurs immediately after the tick bite, hence tick removal will not prevent the disease. Occasionally, cases occur following consumption of infected unpasteurized milk.

All 3 subtypes co-circulate throughout most of the TBEV endemic areas. However, currently the Siberian subtype dominates in many endemic regions from Eastern Europe to Eastern Siberia. The geographical distribution of TBE is from eastern France, over South Germany, Switzerland, Austria, the previous East Block countries via Russia to northern Japan, and from Scandinavia (Sweden) and the Baltic states to Croatia and northern Italy. In Europe and Asia between 10000 and 15000 TBE cases are reported annually. The number is very likely underestimated because in many countries notification of the disease is not mandatory and only in a subset of the countries TBE case definition is in place. TBE is endemic in 27 European countries, and is a reportable disease in only 16 countries.

Vertical transmission in laboratory animals has been demonstrated to be widespread.

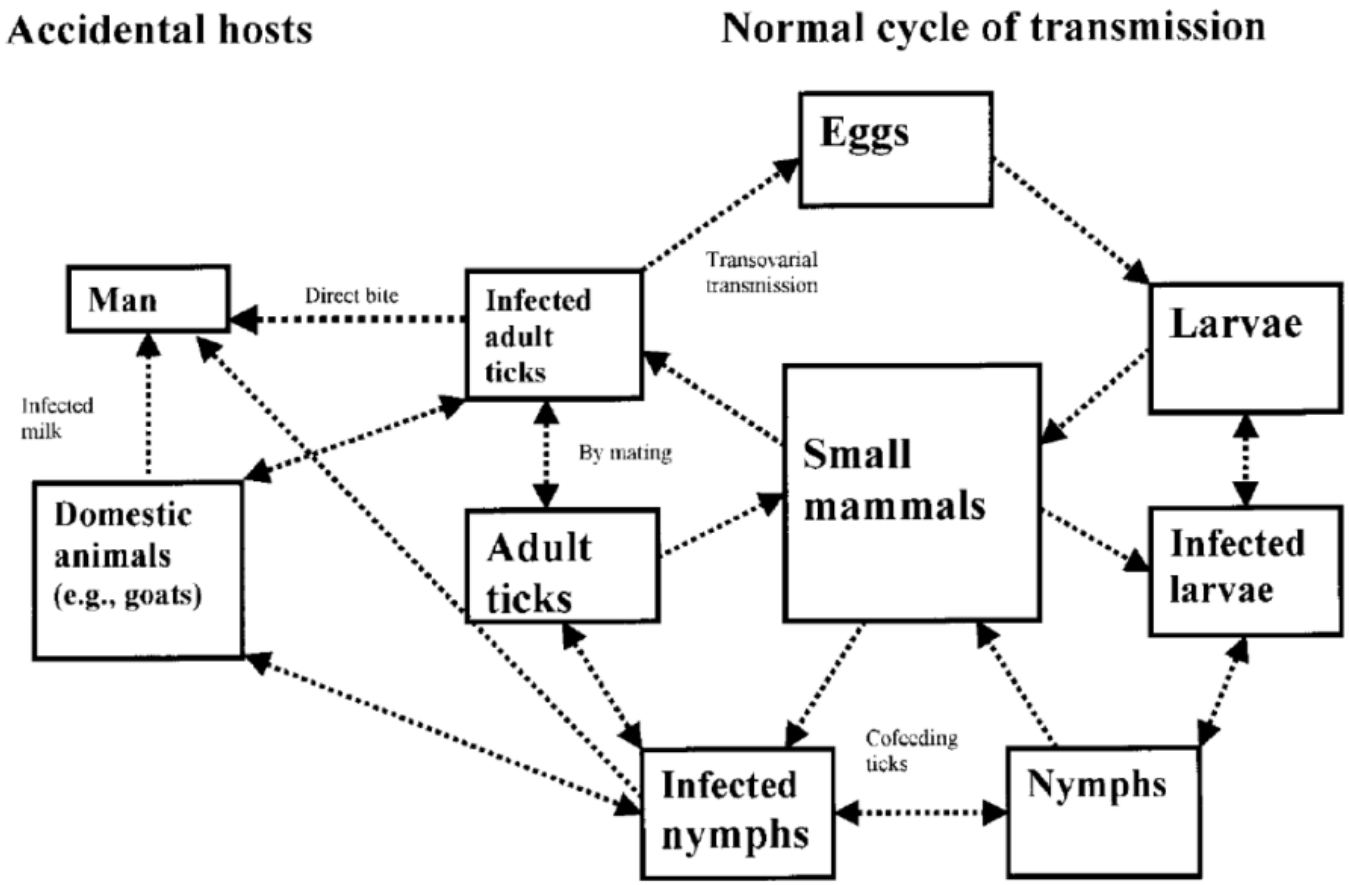

Figure: Transmission cycle of TBE (Dumpis et al, Clin Infect Dis)

Clinical aspects

The incubation period of TBE ranges from 2 to 28 days (7-14 days). After alimentary TBEV transmission the incubation period is generally 3 to 4 days. published data suggest that the ratio of asymptomatic infections is between 70% and 98%. However the proportion of asymptomatic cases is hard to ascertain because patients with mild clinical signs and symptoms may remain undiagnosed.

The initial phase correlates with viremia and like in other neurotropic flaviviruses, it presents with unspecific flulike symptoms (moderate fever, headache, body pain (myalgia and arthralgia), fatigue, general malaise, anorexia, nausea).

This phase lasts for 2 to 7 d and is followed by amelioration or even an asymptomatic interval that usually lasts for about 1 week (1-21 d). Then the second phase appears: in approximately 50% of adult patients it presents as meningitis, in about 40% as meningoencephalitis and in around 10% as

meningoencephalomyelitis

The severity of TBE increases with age; in children and adolescents, meningitis is the predominant form of the disease. The long-term prognosis is unfavorable in about 40% to 50% of patients who sustain sequelae (paresis, ataxia, and other gait disturbances) for months to years, and severity of TBE-related sequalae also seems age-related.

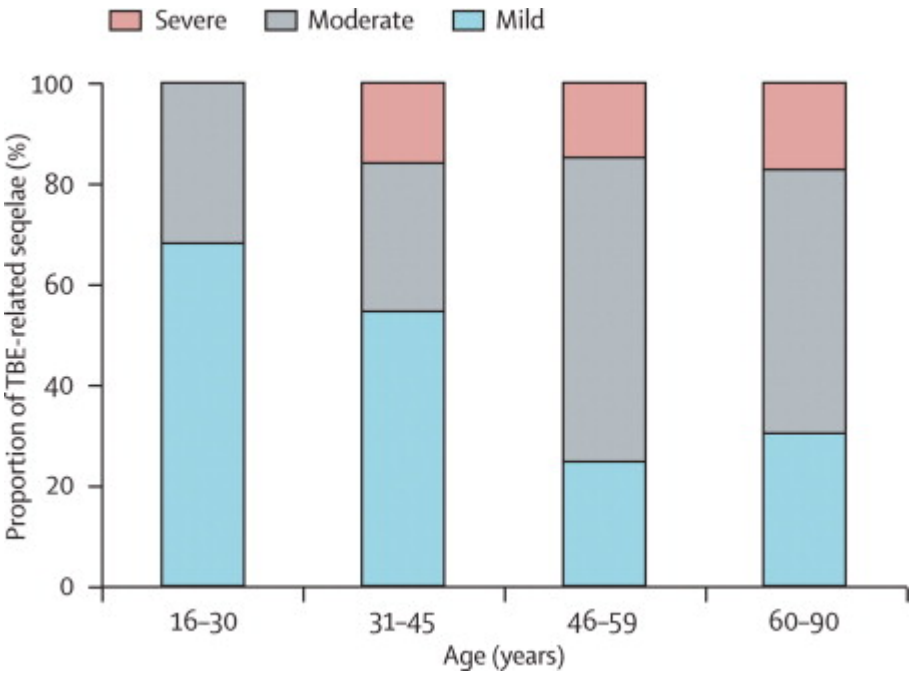

Figure: Relation TBE-related sequelae and age, (Lindquist et al, Lancet; after Mickiene et al, Clin infect Dis)

Classification of sequelae:

- Mild- without any real impact on quality of life.
- Moderate- residual symptoms or signs that affected quality of life but that did not require adjustments of daily activities.
- Severe- symptoms or signs that led to an inability to continue previous activities or that required adjustments of daily activities.

In general the case fatality rate is approximately 1–2% following European subtype infection but can be as high as 20–40% following infection with a far-eastern subtype. Infection with the Siberian subtype produces a mortality rate of 2–3%. However it is possible that the high mortality figures for

the far-eastern subtype may be due to the lack of detection of mild cases therefore skewing the mortality data.

Diagnosis

As a rule, anti-TBEV- IgM and usually TBEV-IgG antibodies are present in the first serum samples taken when CNS symptoms manifest in the second phase of the disease. In the first phase of illness, the virus can be isolated or detected by RT-PCR from blood, but only rarely is TBEV detected at the beginning of the second phase in CSF and occasionally in cases of progressive disease. Intrathecal IgM and IgG antibody response can be detectable in CSF, but several days later than in serum, and in all cases by day 10.

Enzyme immunoassays are usually used for specific serodiagnosis; these assays could be based on either purified virions or recombinant virus-like particles obtained by expression of prM and E proteins. ELISA for serum and/or CSF IgM antibodies to TBEV has been shown to be the most reliable serological test. Haemagglutination inhibition is also widely used but measures all antibody classes and needs a rise in antibody titre for definitive diagnosis. High cross-reactivity of the antigenic structure in the flavivirus may reduce specificity.

Treatment

There is no specific antiviral treatment for TBE. Patients as a rule need hospitalization and supportive care based on the severity of signs/symptoms, and usually encompasses administration of antipyretics, analgesics, antiemetics, maintenance of water and electrolyte balance and if necessary administration of anticonvulsive agents. In patients with neuromuscular paralysis leading to respiratory failure, intubation and ventilatory support are necessary.

Prevention

Personal protection

Personal protective measures help in prevention of tick bites (repellents like DEET being less effective than against mosquitoes) and protective clothing.

Vaccination

In Europe two vaccines are licensed: FSME immun® (from Baxter) and Encepur® (from Chiron

Behring). 14 days after the second dose of basic vaccination protective antibodies develop in about 85% of the subjects, while after three doses more than 98% of persons with normal immunity are protected.

In some countries, such as Austria, vaccination coverage is very high. Other areas where the cost of vaccination is prohibitive lag behind.

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