

WHO position paper on tick-borne encephalitis (TBE)

TBE is caused by 3 closely related subtypes of the TBE-virus, namely the Western-, the Siberian-, and the Far-Eastern subtypes. Blood-feeding ticks (*Ixodes* species) transmit the virus to a variety of animal species and occasionally also to humans. The vast majority of tick-bites do not cause TBE, however. Whereas most human cases of TBE are acquired through tick-bites during outdoor activities in forested areas, unpasteurized dairy products may sometimes transmit the virus from infected cows and goats.

TBE is endemic in most of the southern, non-tropical Eurasian forest belt. Approximately 10 000–12 000 cases are reported each year, but the disease may be significantly underreported. The highest incidences of TBE are reported from the Baltic States, Slovenia and the Russian Federation (annual national incidences of 2-10 per 100 000 inhabitants). Other countries have reduced incidence of TBE dramatically as a result of vaccination.

In about one third of TBE patients, the disease follows a biphasic clinical course: The uncharacteristic symptoms of the first phase are followed by a second phase characterized by variety of central nervous system manifestations, often including encephalitis. The case-fatality rates in TBE vary between 1% - 20%; permanent central nervous system sequelae occur in up to 40% of encephalitic cases. The disease tends to be more severe in older individuals.

Immunization offers the most effective protection against TBE. Currently, there are four widely used vaccines of assured quality, all based on cell-cultured, formalin-inactivated strains of the TBE virus: FSME-Immun and Encepur (including FSME-Immun Junior and Encepur-Children) are based on the Western viral subtype and manufactured in Austria and Germany, respectively. TBE-Moscow and EnceVir, based on the Far-Eastern subtype, are manufactured in the Russian Federation.

The Western vaccines are licensed for use in adults and children aged ≥ 1 years. Primary immunization consists of 3 doses; recommended intervals are 1-3 months between doses 1 and 2 and 5-12 (9-12) months between doses 2 and 3. For rapid protection, the former interval may be reduced to 1–2 weeks. The Russian vaccines are licensed for adults and children ≥ 3 years. Their 3-dose schedule requires the first 2 doses to be given 1-7 (or 5-7) months apart, and the third dose 12 months after the second.

Transient local reactions are commonly associated with TBE vaccines, but severe adverse reactions are rarely described*. There are no contraindications to TBE vaccination except allergy to vaccine components and severe acute infections. Pregnant women at risk can be vaccinated.

Although there are no randomized, controlled trials on vaccine efficacy against clinical TBE, numerous observational studies in Austria and other endemic countries provide evidence for the high effectiveness of these vaccines. Presence of minimum concentrations of specific antibodies (e.g. ≥ 10 by neutralization test) is often used as a surrogate marker of protection. The primary series induces serological responses suggesting protection in 90%-100% of the vaccinees. Interference between TBE vaccines and simultaneously administered vaccines has not been reported.

With the Western vaccines, healthy individuals aged < 50 years at continued risk of TBE are currently offered booster doses at intervals of 3–5 years, although in some endemic areas (Switzerland), intervals up to 10 years are now recommended. With Russian vaccines boosters are recommended every 3 years.

WHO recommends vaccination of people of all ages where TBE is highly endemic (average annual pre-vaccination incidence ≥ 5 cases/100 000 population). Where the pre-vaccination incidence of the disease is moderate or low, or is limited to particular locations or outdoor activities, immunization

should target the most severely affected groups. Travelers from non-endemic to endemic areas should be vaccinated if their visits will include extensive outdoor activities.

Since the incidence of TBE varies considerably between and within geographical regions, public immunization strategies should be based on careful assessments of the effectiveness and cost-effectiveness of current immunization regimens. Within the range of acceptable dose intervals, the most rational primary schedule should be selected for national, regional or district implementation.

Pending more information on the duration of protection, with Western vaccines booster intervals of 3 years should be maintained for individuals aged >50-60 years and with Russian vaccines for all vaccinees. For healthy individuals aged <50 years extended booster intervals (5-10 years) may be considered for those receiving Western vaccines.

Postexposure vaccination following a tick bite is not recommended. Administration of specific immunoglobulin for passive postexposure prophylaxis is not recommended in Western Europe, but is sometimes used in the Russian Federation

Improved TBE surveillance and reporting is critical. Standardization is required for clinical disease definitions as well as for laboratory reagents and methods.

*Recently, some lots of EnceVir have been associated with high fever and allergic reactions, in particular in children