Anti-TBE Virus ELISA 2.0 (IgM)

- **Semiquantitative determination of IgM antibodies against TBE virus to aid in the diagnosis of TBE virus infections**
- **Based on native, purified TBE virus antigens**
- **Fully automatable processing and evaluation**

Technical data

Antigen	The reagent wells are coated with native, purified TBEV antigens
Calibration	Semiquantitative; calculation of a ratio from the extinction of the sample and the extinction of the calibrator
Result interpretation	EUROIMMUN recommends interpretation of result as follows: Ratio < 0.8: negative Ratio ≥ 0.8 to < 1.1: borderline Ratio ≥ 1.1: positive
Sample dilution	Serum or plasma; 1 : 101 in sample buffer
Reagents	Ready for use, with the exception of the wash buffer (10x); colour-coded solutions, in most cases exchangeable with those in other EUROIMMUN ELISA kits
Test procedure	60 min (37 °C) / 30 min / 15 min, room temperature (sample / conjugate / substrate incubation), fully automatable
Measurement	450 nm, reference wavelength between 620 nm and 650 nm
Standard kit format	96 break-off wells; kit includes all necessary reagents
Order no.	**EI 2661-9601-2 M**

Clinical significance

Tick-borne encephalitis virus (TBEV) has three known subtypes: European (TBEV-Eu), Siberian (TBEV-Sib) and Far Eastern (TBEV-FE). TBEV is transmitted via tick bites or, less commonly, by consumption of raw milk and raw milk products of infected goats, sheep and cows. Most TBEV infections in humans are asymptomatic. Symptomatic courses are mono- or biphasic with varying severity depending on the subtype. Biphasic illness begins with unspecific flu-like symptoms. Viraemia occurs in this first phase lasting from day 1 to 8. After an asymptomatic interval of approximately one week, around a third of patients enter the second phase, in which the virus reaches the central nervous system. Typical symptoms include high fever and neurological manifestations such as meningitis, encephalitis and myelitis. The mortality rate is 1 % to 2 % (TBEV-Eu), 6 % to 8 % (TBEV-Sib) and 40 % (TBEV-FE).

Due to the mostly unspecific symptoms of TBE, differential diagnostics is particularly challenging. The diagnostic method of choice is the determination of TBEV-specific IgM and IgG antibodies in serum or CSF using ELISA. Specific antibodies in serum or CSF can usually be measured in the second phase of the disease. IgM is detectable for 6 to 7 weeks or longer. IgG persists lifelong and protects against reinfection with TBEV. TBEV infection is diagnosed based on simultaneous detection of TBEV-specific IgM and IgG or based on a significant increase in the IgG concentration between two samples collected 2 to 4 weeks apart. The sole detection of IgM is not sufficient. In cases with CNS involvement, determination of specific, intrathecally produced IgM and IgG antibodies in the CSF is indicated. Cross-reactivity of anti-TBEV antibodies (especially IgG) with other flaviviruses (yellow fever, dengue, Japanese encephalitis and West Nile virus, including following vaccination) must be taken into account.

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Prevalence

Levels of anti-TBEV IgM antibodies were determined in 500 samples from healthy blood donors (origin: Schleswig-Holstein, Germany, year 2022) aged between 18 and 69 years (252 women, 248 men) using the Anti-TBE Virus ELISA 2.0 (IgM). With a cut-off of 1.0 ratio and excluding borderline results, 0.8% of the blood donors were anti-TBEV positive (IgM).

Cross-reactivity (analytical specificity)

To investigate the cross-reactivity of the test system, samples that had been tested positive for IgM antibodies against dengue, yellow fever, Japanese encephalitis, West Nile or Zika virus were analysed using the Anti-TBE Virus ELISA 2.0 (IgM). It was shown that cross-reactions with antibodies against yellow fever and Japanese encephalitis virus are unlikely, but that cross-reactions with antibodies against dengue, West Nile and Zika virus cannot be ruled out. It should be noted that double infections can occur, particularly in endemic areas. In these cases, positive findings do not result from a cross-reaction of the respective antibodies.

Antibodies against	n	Positive rate in % the Anti-TBE Virus ELISA 2.0 (IgM)
Dengue virus (DENV)	27	11.1
Yellow fever virus (YFV)	21	0.0
Japanese encephalitis virus (JEV)	23	4.3
West Nile virus (WNV)	40	7.5
Zika virus (ZIKV)	19	15.8

Method comparison

142 serologically precharacterised samples (origin: Europe) were investigated using the EUROIMMUN Anti-TBE Virus ELISA 2.0 (IgM) and a commercially available ELISA of another manufacturer as a reference and the results were compared. The positive agreement was 91.5% (95% CI: 79.6–97.6%) and the negative agreement was 96.3% (95% CI: 89.4–99.2%) with a mean concordance of 94.5%. Results in the borderline range were not included in the calculation.

n = 142		Other commercial ELISA		
		positive	borderline	negative
Anti-TBE Virus ELISA 2.0 (IgM), EUROIMMUN	positive	43	4	3
	borderline	2	2	3
	negative	4	4	77

Clinical performance

A total of 297 samples were tested using the Anti-TBE Virus ELISA 2.0 (IgM). For the determination of sensitivity, samples from patients with acute TBEV infection were used. The specificity was determined by analysing samples from healthy blood donors in addition to samples from patients with other diseases relevant for differential diagnostics such as anaplasmosis, Lyme disease, herpes simplex virus infections and SARS-CoV-2 infections. The results are shown in the contingency table.

n = 297		Clinical characterisation	
		positive	negative
Anti-TBE Virus ELISA 2.0 (IgM), EUROIMMUN	positive	59	0
	borderline	0	0
	negative	0	238

Evaluation	n = 297	
	Value in %	95% CI
Specificity	100.0	98.5–100.0
Sensitivity	100.0	93.9–100.0

Positive likelihood ratio: > 1,000, negative likelihood ratio: < 0.001

Literature

1. Robert-Koch Institute. **Frühsommer-Meningoenzephalitis.** RKI guide to TBE and related viral encephalitides. 2022 Apr;16 [in German].
2. Holzmann H. **Diagnosis of tick-borne encephalitis.** Vaccine 2003 Apr;21.
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4. Kaiser R, at al. **Laboratory findings in tick-borne encephalitis – correlation with clinical outcome.** Infection. 2000 Mar-Apr; 28(2);78-84.

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