Vaccines against tick-borne encephalitis (TBE)
WHO position paper 10 June, 2011

Grading of scientific evidence in support of key recommendations

Table III. Do currently available TBE vaccines protect against clinical TBE with all 3 TBE virus subgroups (European, Far-Eastern, and Siberian)?

			Rating	Adjustment to score
Quality Assessment	No of Studies/Starting Score		5 observational	2
	Factors decreasing confidence	Limitation in study design	Serious [1]	-1
		Inconsistency	None serious	0
		Indirectness	Serious[1]	-1
		Imprecision	None Serious	0
		Publication bias	None serious	0
	Factors increasing confidence	Large effect	Very large effect[3]	+2
		Dose-response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	Final Score			**2**
Summary of Findings	**Quality**			Our confidence in the estimate of the effect on the health outcome is limited: The true effect maybe substantially different from the estimate of the effect
	Conclusion			Currently available TBE vaccines protect against clinical TBE with all 3 TBEV subgroups (European, Far-Eastern, and Siberian).

[1] Small number of strains tested. [2] Evidence based on i*n vivo as* well as *in vitro* trials and serological studies, but no direct evidence from RCTs using clinical TBE as endpoint. [3]High protection rates observed and consistent conclusions of studies in animal models as well as in humans.

Evidence that the two Western TBE vaccines induce protective immunity not only against the homologous subtype, but also against the Far Eastern and Siberian subtypes of the virus, is provided by preclinical studies in mice. Thus, *Holzmann H et al, 1992* found no statistically significant difference in the degree of protection when mice were immunized with European prototype vaccine virus and subsequently challenged with three selected Asian isolates and one isolate from the European part of the USSR. *In vivo* (mice) as well as *in vitro* studies by *Hayasaka D et al (2002)* showed that FSME-IMMUN® induced antibody that effectively neutralize Siberian, Far-Eastern, as well as European subtypes of TBEV. *Leonova GN et al 2007* concluded that Encepur®Adult induced a pronounced humoral immune response

towards the genetically and antigenically heterogeneous P-69, P-202, and P-73 strains of the Far Eastern TBEV subtype.

In 2009, *Leonova GN et al* compared the immunogenicity in adults of TBE-Moscow, EnceVir®, and the two Western vaccines FSME-IMMUN® and Encepur® adults . Immunogenicity was measured 2-5 months and 2 years following the administration of 3 doses of the respective vaccine. All vaccines induced neutralizing antibody against the Far Eastern subtype strain P-73. With TBE-Moscow, antibody was detected in 100% and in 94% of the vaccinees after 2-5 months and two years, respectively. With EnceVir® the corresponding figures were 88% and 84%, with FSME-IMMUN® 88.2% and 78.1%, and with Encepur® 100% and 100%.

Recently, Orlinger *KK et al (2011)* showed that a tick-borne encephalitis vaccine based on the European prototype strain induces broadly reactive cross-neutralizing antibodies in humans against the European, Siberian, and Far Eastern TBE virus.

References

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