

**Dissertation review: "Pathogenesis and clinical aspects of tick-borne encephalitis virus infection"
defended by RNDr. Jana Elsterová**

Tick-borne encephalitis virus together with other arbovirus infections is an interesting scientific topic of human and veterinary infectology mainly due to the zoonotic nature of this infection, but also for the current trend of spreading arbovirus infections to new geographical areas due to climate warming and corresponding spread of insect vectors. From this perspective, I consider the choice of the dissertation topic to be well chosen and up to date. I also positively evaluate the multidisciplinary nature of the work, which includes not only classical virology and its procedures, but also interesting clinical aspects of tick-borne encephalitis related to the virus's ability to cross the blood-brain barrier, and even attempts to treat it by hyperimmune serum. Such multidisciplinary focused works provide a guarantee of interesting scientific results.

Formally, the dissertation is organized as a literary overview, followed by the summary of seven manuscripts of impacted publications, which corresponds to the partial goals set by the dissertant and the work ends with a comprehensive chapter "Summary and future perspectives". Each manuscript also clearly defines the participation of the dissertant in the preparation of each of them. The list of references then refers to several dozen mostly recent sources.

Literary review of the work documents that the author is well acquainted with the solved problems and can formulate the acquired knowledge in a professional text. In this part of the work, the author deals with the classification and evolution of the virus, the pathogenesis of the disease in connection with the interaction of the virus with both the host and vector - tick, as well as the clinical course of the disease, its therapy and prevention. It thus provides the reader with a clear overview of the studied issues needed to assess other parts of the dissertation.

The aims of the work are clearly defined and can be considered as fulfilled in the form of submitted manuscripts of publications. Each of the set of objectives is given a brief summary of the issue and its fulfillment is then supported by a set of corresponding publications. I do not have any comments on the choice of targets, they are organically linked to each other and aim to achieve the main objective of the work, ie the study of the pathogenesis of tick-borne encephalitis in terms of virus neuroinvasiveness. The third, last group of partial targets aimed at using positive hyperimmune sera for therapeutic intervention is somewhat out of the scope of this work, but even here we can find a link to the study of pathogenesis of tick-borne encephalitis.

The work as a whole gave me a pleasant reading effect, with only a few misspellings or typographical misdeeds. The obtained results can rightly be considered as a priority, as evidenced by their publication in impacted scientific journals.

I have the following questions or comments:

- Your work suggests that TBEV does not significantly interfere with the cerebrospinal fluid barrier integrity, but this is not conclusive evidence of virus penetration into the CNS by transcellular mechanisms. What is your opinion on the possibility of progression of the virus to the CNS through peripheral nerves or another way?
- What is the current knowledge of the incidence and course of ADE in vaccinated people?
- Do you plan to investigate arbovirus infections, especially TBEV, in the future?

In conclusion I can state that the submitted dissertation thesis meets all the professional requirements required for this type of work and therefore I recommend that RNDr. Jana Elsterová was awarded the corresponding Ph.D. degree

Brno, the 20th April, 2020



prof. MVDr. Vladimír Celer, Ph.D.