THE NATURAL FOCI OF TICK-BORNE ENCEPHALITIS VIRUS: WHAT ARE THE DRIVERS FOR THEIR MAINTENANCE?

Tick-borne encephalitis (TBE) is a viral disease which is caused by the TBE virus (TBEV), a virus of the mammalian tick-borne group in the family *Flaviviridae*. TBEV is endemic in Central Europe, in Eastern Europe, in parts of Northern Europe (especially in the Baltics and Southern Finland, and southern and central Sweden), as well as parts of northern and central Asia, and causes 10,000–12,000 reported cases of TBE each year. TBEV is maintained in so-called natural foci by ticks of the genus *Ixodes* and potentially also by *Dermacentor* and *Haemayphysalis*. Pavlovsky first developed his important „natural focus theory“ based on his experiences during several expeditions into the Russian taiga to study TBEV and its transmission to humans (see also [The TBE Book, Chapter 1]).

Besides *Ixodes (I.) ricinus* as vector, small mammals (*Apodemus* spp., *Microtus* spp., *Myodes* spp.) are believed to be a core factor for maintaining the natural transmission cycle of TBEV in its natural setting. The biology of *I. ricinus* is characterized by three stages, each with a specific ecological optimum for development, virus harboring and survival. There are, however, a number of questions which are still unsolved after 80 years when Pawlowsky first described the natural foci of TBEV in Russia.

The proportion of virus-infected ticks in a natural focus rarely exceeds 1–5%. This makes the stability of TBEV natural foci over decades difficult to explain.

It is still unclear which structure and size a natural focus needs to have to support the transmission cycle.

Furthermore, it is unknown which role the numbers of ticks and small mammals play. Is there a minimal number of mammals and/or ticks for supporting and maintaining the transmission cycle of TBEV?

To better explain the stability of these transmission cycles, the concept of co-feeding (simultaneous feeding of larvae and nymphs in close proximity to each other on the same rodent in the absence of a systemic infection) is of paramount importance in the current understanding of TBEV vector biology. However, this transmission mode has never been proven in a natural setting. Indirect data from statistical models, however, suggest a role of this mechanism in nature, supported by observations that ticks tend to feed on their hosts in clusters. The co-feeding transmission is thought to occur between co-feeding ticks in the absence of a systemic viremia and has been experimentally proven.

As such forms of transmission are difficult to verify under natural settings, the aim of the study was to identify whether the climatic conditions optimal for co-feeding (i.e., rapid increase of temperature in spring or rapid decrease of temperature in autumn which may enforce the blood-sucking of larval and nymphal stages) might cause a significant increase of infected nymphs in the following tick activity season.

The data of tick sampling in a well-known natural TBE focus in Southern Germany over 10 years were statistically analyzed with weather data of the region. The analysis was done with a total of 15,530 ticks, among which were 11,036 nymphs. The monthly TBEV minimal infection rates (MIR) were calculated and correlated with the absolute monthly registered temperature and the temperature increases and decreases of the years studied.

No correlation between TBEV-positive females and positive males, as well as no correlation between the MIR of nymphs and adults, could be detected. The highest MIR in nymphs was consistently seen in September. However, after investigating the MIR in male and female adult ticks, male ticks had the MIR maximum in April and female ticks in May. There was also no significant trend detectable for MIR in nymphs for both male and female adult ticks. Neither was there a trend observed over the study period regarding the overall number of collected ticks.

We performed a regression analysis to investigate a potential influence of temperatures in the months of March and April on the MIRs. However, there was no significant association between temperatures in these months and the MIRs of nymphs collected in the following months of the year. We could not verify that a slower increase in spring temperatures would result in decreased MIRs during the following months.

Our data indicate that an early start of warm temperatures might have negative effects on tick activity and survival in the following months. Notably, no such correlation was found for the MIR, neither in nymphs nor in adult tick stages. It is surprising that MIRs in the nymphal stages were independent of the number of nymphs in the respective years and stable at about 0.5-1% spanning the whole study period. This might further underscore the importance of nymphs, in contrast to adult *I. ricinus* stages, for maintaining the transmission cycle of TBEV in a focus.

Overall, this study shows that even after 80 years the concept of natural focus transmission and the key players in the natural transmission cycle of TBEV are not understood, and that data from laboratory studies might not be transferred to the situation in nature without proof.

Literature

Borde et al.

The complex interplay of climate, TBEV vector dynamics and TBEV infection rates in ticks – Monitoring a natural TBEV focus in Germany, 2009-2018

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