

# There are two common tick-borne diseases in Europe: TBE and Borreliosis

## **Tick-borne encephalitis (TBE):**

The TBE virus can infect the brain and cause tick-borne encephalitis (brain inflammation).

About one in four people infected with the TBE virus fall ill and develop symptoms of encephalitis which include high fever, severe headache, and sometimes paralysis and convulsions.

Most patients with TBE encephalitis will recover but up to one third will suffer long-term complications of the disease.

There is no specific treatment for TBE once you are infected but there is an effective vaccine that prevents infection.



# TBE      Flavi- virus

- It is a flavivirus, an RNA virus with several subtypes.
- Tick-borne encephalitis virus (TBEV) causes human epidemics across Eurasia.
- Western TBEV is endemic in central, northern and eastern Europe
- Far Eastern TBEV exist in parts of Balticum and in Russia and Japan.
- About 10.000 cases are reported yearly

# Vector -ticks

- Ticks are abundant in woodlands all across Europe from early spring to late autumn. They live by sucking blood from animals and occasionally bite humans.
- Ticks themselves do not cause disease but if a tick is infected with a virus or bacterium, then that pathogen can be transmitted through the tick's bite and cause disease in humans - a vector
- *Ixodes ricinus* is the main vector for both borreliosis and TBE in Europe. Climate restricts latitude and altitude distribution of ticks. A certain number of days per season with proper temperatures influencing the development of the ticks and their activity are necessary.

# Climate change

Indirectly, both the tick population size and the virus-infected proportion of ticks will be affected by climate influences on the year-round survival of host and reservoir animals. Ticks may survive freezing temperatures (well below  $-7^{\circ}\text{C}$ ) and become active when night temperatures rise above  $4-5^{\circ}\text{C}$ .

The life span of a tick can be more than 3 years depending on climatic conditions, and includes three blood-sucking stages: larvae, nymphs, and adults.

All three tick stages may be infected as TBE virus is transmitted transovarially in about 1%.

However, nymphs are the major contributors to infection in human beings.

- TBE is a notifiable disease in Sweden and represents a substantial part of the viral encephalitis disease burden in the country.
- In the four-year period leading up to 2009, an average of 177 TBE cases were reported annually, and the number of TBE cases increased by 71% from 131 cases in 2005 to 224 cases in 2008.
- TBE occurs from April to December in Sweden, with the peak incidence between May and July.

Source: ecdc

- Most of the infections were acquired in the counties of Stockholm, Södermanland and Uppsala, and along the southern part of Lake Vänern in the county of Västra Götaland. Every year sporadic cases occur across southern Sweden.
- In 2008, a locally acquired infection was reported from the county of Västerbotten, which is the highest latitude for endemic TBE infection documented in Sweden.

# Surveys

Prevalence surveys:

21% of adult aseptic meningitis in Northern Stockholm (1999 and 2004)

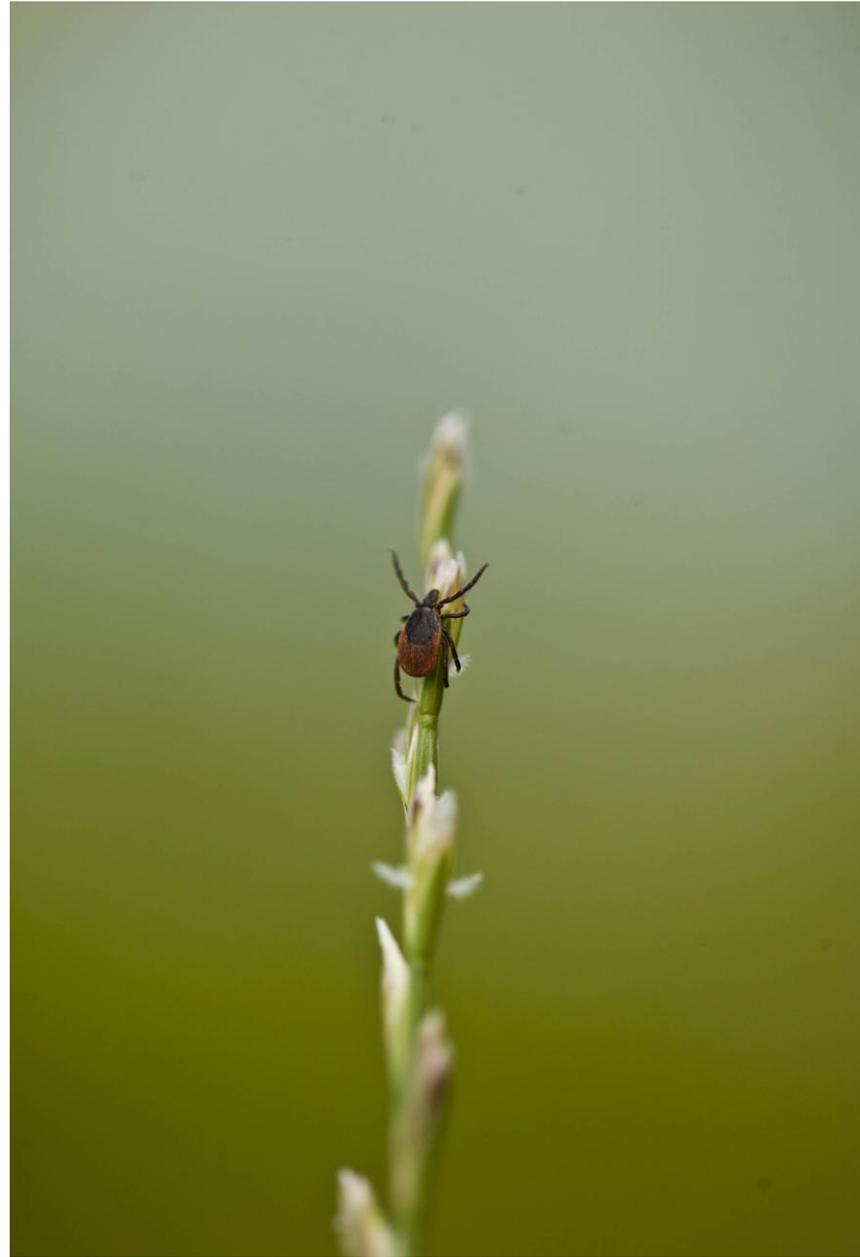
- Seroprevalence surveys:

4% to 22% in endemic areas, and 5% Stockholm

3.5% on the island of Aspö (Southeast Sweden) in 1991; 12% in 2002

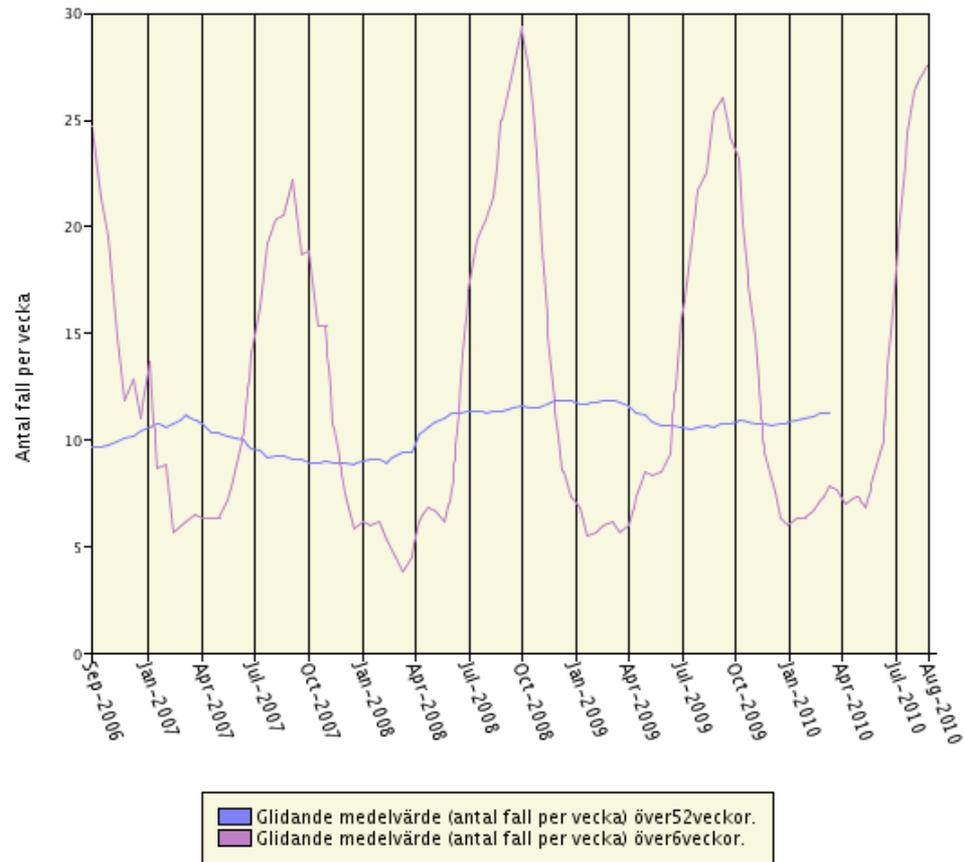
0.8% of persons in northeastern Skåne are seropositive.

Tick-borne encephalitis virus has been identified in *Ixodes ricinus* found on migrating birds.

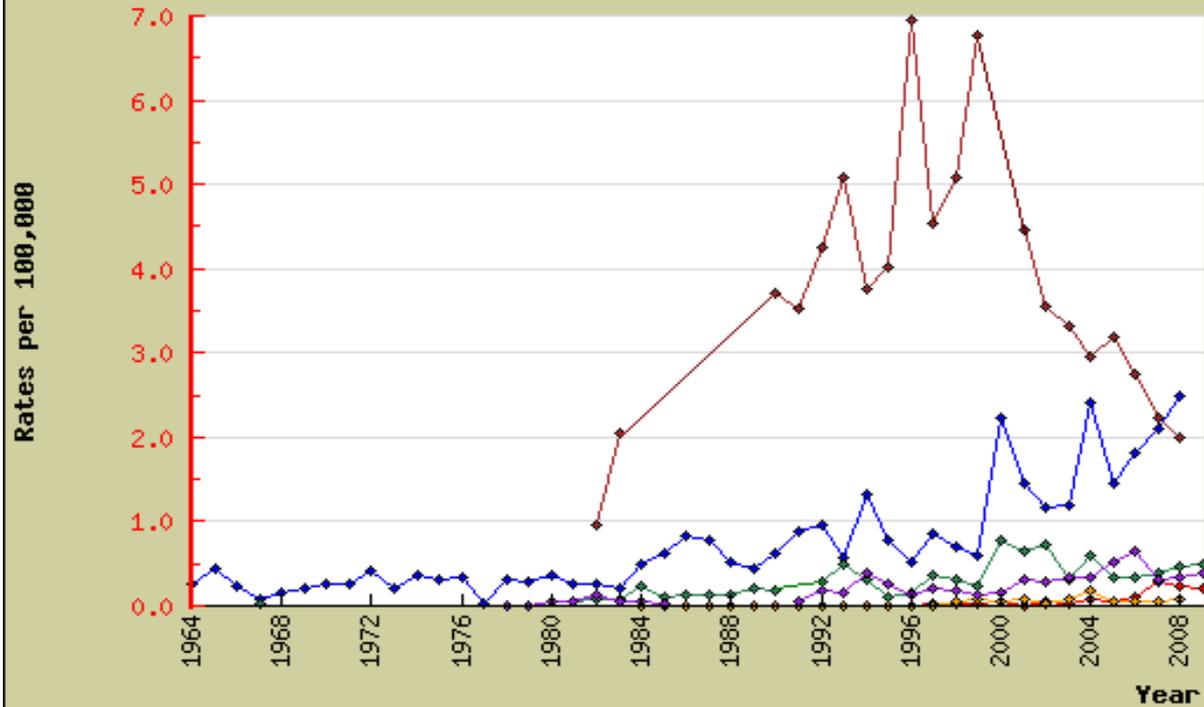


# Reported cases in Sweden

Viral meningoencefalit – Trend

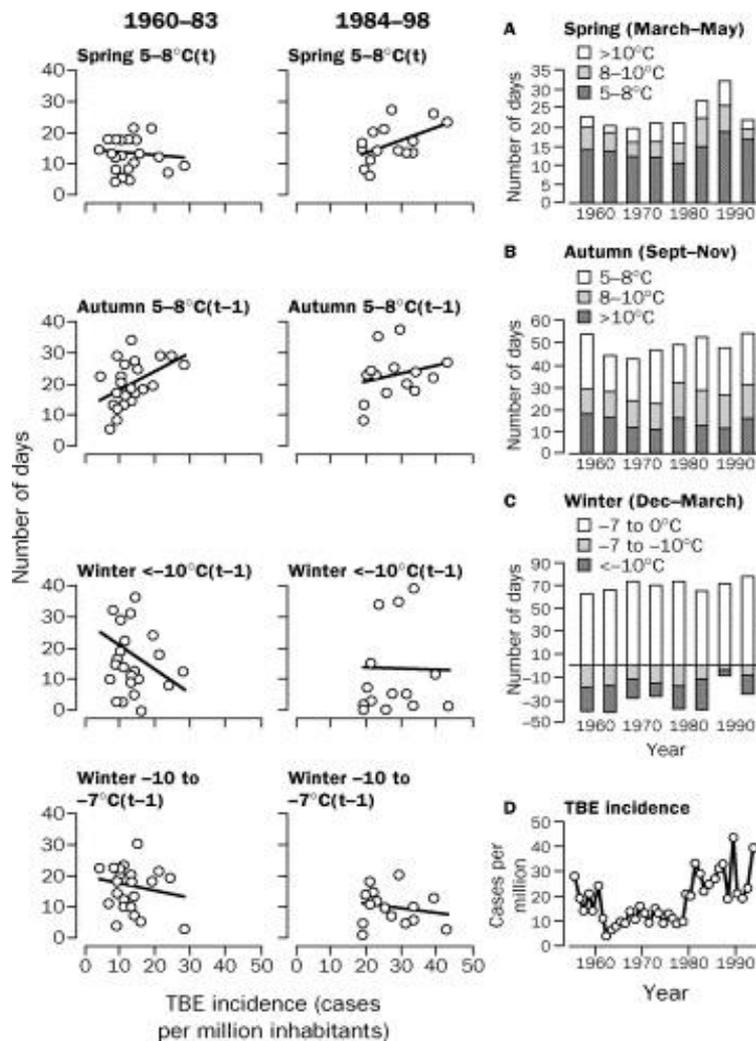


### Disease Comparisons - GIDEON



- ◆ Sweden. Tick-borne encephalitis, cases (Rates per 100,000)
- ◆ Norway. Tick-borne encephalitis, cases (Rates per 100,000)
- ◆ Finland. Tick-borne encephalitis, cases (Rates per 100,000)
- ◆ Denmark. Tick-borne encephalitis, cases (Rates per 100,000)
- ◆ Germany. Tick-borne encephalitis, cases (Rates per 100,000)
- ◆ Russian Federation. Tick-borne encephalitis, cases (Rates per 100,000)

Analysed temperatures and TBE incidence The four charts to the left show the plotted relation between TBE incidence and the number of days with different temperature variables. A, B, and C show average number of days per 5 year periods with the different spring, autumn, and winter temperatures used in our analyses. D shows the annual TBE incidence between 1960 and 1998 in Stockholm County.



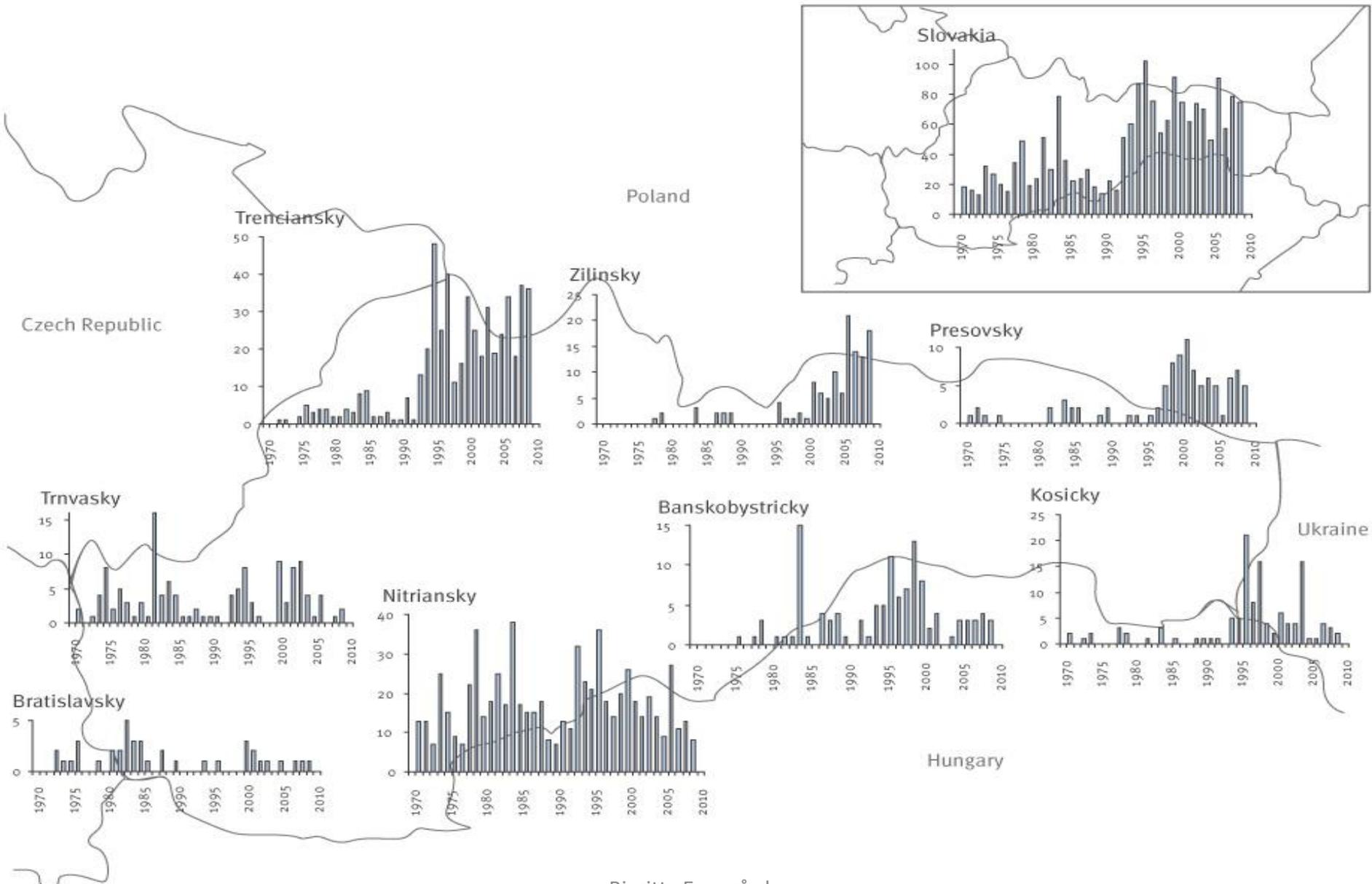
Birgitta Evengård

# Conclusion:

- Increases in disease was signif related to a combination of two consecutive mild winters, temperatures favoring spring development (8-10C) and extended autumn activity (5-8C) in the year prior and temperatures allowing tick activity (5-8C) early in the incidence year.

**FIGURE 1**

Annual numbers of tick-borne encephalitis cases since 1970 in all Slovakia (inset) and each kraj (region), showing the typical spatial and temporal heterogeneity in incidence within one country



Birgitta Evengård

Source: Public Health Authority of the Slovak Republic.

No single factor is likely to cause such a pattern.

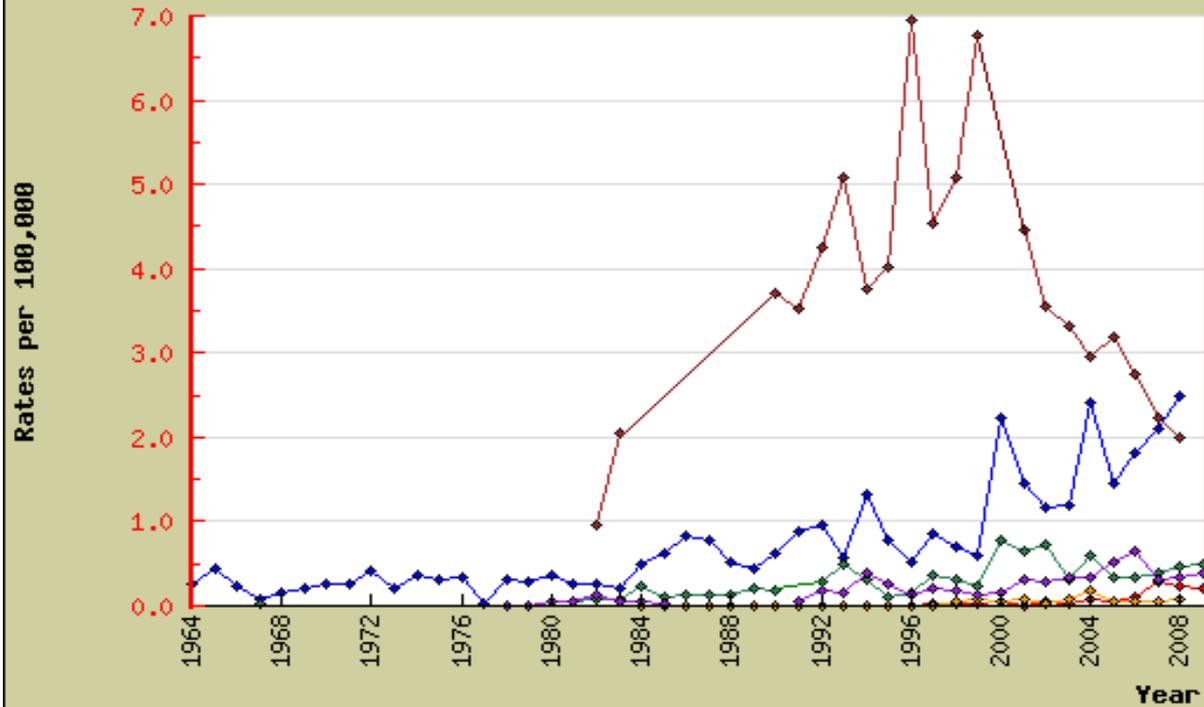
- Instead, a nexus of interacting, independent but synergistic, biotic, abiotic and socio-economic impacts on all four partners within the system (virus, vector, vertebrate wildlife and human) has been proposed and supported by comparative data from five diverse countries (Slovenia, Czech Republic and the three Baltic countries).

Non-Hemagglutinating Flaviviruses: Molecular  
Mechanisms for the Emergence of New Strains via  
Adaptation to European Ticks

- Khasnatinov et al Slovakia, PLoS ONE 4(10): e7295. doi:10.1371/journal.pone.0007295
- TBEV is characteristically a hemagglutinating (HA) virus; the ability to agglutinate erythrocytes tentatively reflects virion receptor/ fusion activity. However, for the past few years many atypical HA-deficient strains have been isolated from patients and also from the natural European host tick, **Ixodes persulcatus**.
- By analysing the sequences of HA-deficient strains we have identified 3 unique amino acid substitutions.
- We genetically engineered virus mutants each containing one of these 3 substitutions; they all exhibited HA-deficiency. Unexpectedly, each genetically modified non-HA virus demonstrated **increased TBEV reproduction** in feeding **Ixodes ricinus**, not the recognised tick host for these strains.
- Moreover, **virus transmission efficiency** between infected and uninfected ticks co-feeding on mice was also **intensified** by each substitution. Retrospectively, the mutation D67G was identified in viruses isolated from patients with **encephalitis**.

- We propose that the emergence of atypical Siberian HA-deficient TBEV strains in Europe is linked to their molecular adaptation to local ticks. This process appears to be driven by the **selection of single** mutations that change the virion surface thus enhancing receptor/fusion function essential for TBEV entry into the unfamiliar tick species. As the consequence of this **adaptive mutagenesis**, some of these mutations also appear to **enhance** the ability of TBEV to cross the human blood-brain barrier, a likely explanation for fatal encephalitis.
- Future research will reveal if these emerging Siberian TBEV strains continue to disperse westwards across Europe by adaptation to the indigenous tick species and if they are associated with severe forms of TBE.

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