

15th ISW-TBE Newsletter

May 2011

Dear colleague,

another tick season is fast approaching, and we hope that you and your family and patients are well prepared to prevent the health risks potentially related with a tick bite. Unfortunately, tick-borne diseases are generally caught when doing the things we like doing most, such as taking a walk or spending the day hiking, picnicking, or mountain-biking. So, when spending time outside, tuck your pants into your socks—and get your TBE shot in time.

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Happy reading!



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Although still young, the year 2011 has already seen a number of conferences dealing with tick-borne diseases, such as the 13th Annual Meeting of the International Scientific Working Group on Tick-Borne Encephalitis (ISW-TBE) in February in Vienna, Austria, or the XI International Jena Symposium on Tick-Borne Diseases in March. Some of the research results presented are summarized below.

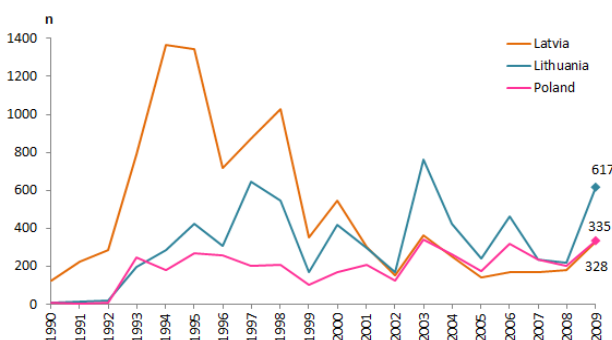
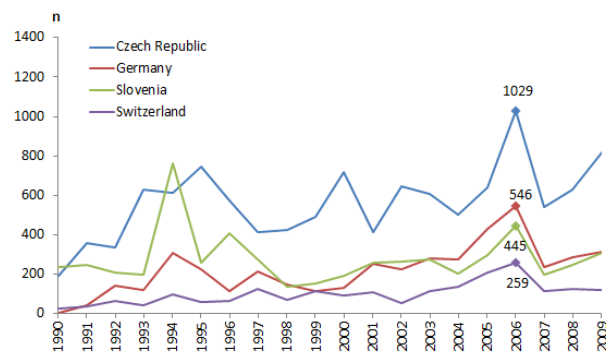


1 TBE—Perfect Example of a Complex System

How changes in human activity and natural wildlife cycles work together to change zoonotic disease incidence

Tick-borne diseases are prime examples of complex systems: Whenever changes in any one of the many biological and human factors occur, the incidence of human infection may vary abruptly.

In 2006, the incidence of TBE increased dramatically in some European countries, notably in Germany, Switzerland, Slovenia, and the Czech Republic (see graph). In 2007, incidences returned to average or below-average levels in these countries. Sarah Randolph and colleagues from the Department of Zoology, University of Oxford, found that the 2006 TBE spike was not caused by weather-induced variations in tick abundance—as may have been expected—but by the unusually warm and dry weather conditions that favored outdoor activities and thereby increased human exposure to virus-infested ticks.¹



The year 2009 saw TBE spikes in Latvia, Lithuania, and Poland (see graph), but not in other countries. Godfrey and Randolph tested the hypotheses that this rise could be due to unusual weather patterns or a reduction in economic well-being as a result of the recession.² 2008 and 2009 showed weather patterns very similar to those seen in 1989–2009. Also, Latvia, Lithuania, and Poland did not differ from other countries. Weather was therefore discounted as an explanatory variable.

To test for an effect of the recession, the predictive power of unemployment in 2009 and a range of socioeconomic indices was assessed. The greatest increases in TBE incidence were correlated with a combination of a marked increase in unemployment and high background levels of poverty. Possible explanations include increased exposure to ticks as a result of food foraging trips, low vaccination uptake, and increased susceptibility to infection due to the physiological and emotional stress caused by conditions of economic vulnerability.

2 When Ticks Travel by Train...

...and Get Off in Sverdlovsk Oblast

Speaking of the interaction between natural wildlife cycles and human behavior—a recent publication from the Russian Federation³ also shows how intricately intertwined human activity and tick exposure are.

In Sverdlovsk, a region located some 1600 km east of Moscow on the border between Europe and Asia and highly endemic for TBE, more than 95% of TBE strains isolated are of the Siberian subtype (S-TBEV). To determine the origin and distribution of S-TBEV strains in the Middle Urals, Romanenko et al.³ partially sequenced the surface glycoprotein E gene in 165 S-TBEV isolates collected in the Middle Urals between 1966–2008 and found 4 types of isolates, which they termed ‘local,’ ‘split,’ ‘corridor,’ and ‘diffuse (see figure).

Distribution of S-TBEV isolates in the Middle Urals



Isolates of cluster A (diffuse type) are presented in the map on the right.

Cluster B (local type) = Δ

Cluster C (split type) = ∇

Cluster D (corridor type) = \blacksquare

--- Trans-Siberian Railway, - - - - local roads

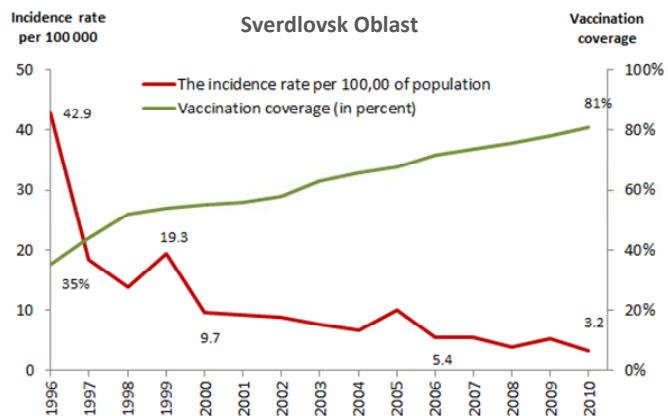
Phylogenetic analysis of the isolates and comparison with historical events suggested that the distribution of S-TBEV strains in the Middle Urals and the European part of Russia originated from 2 different foci in western Siberia. The primary reason for the distribution pattern of S-TBEV strains appears to have been the result of human economic activity during the colonization of new Siberian territories, as evidenced by the first land road into Siberia and the Trans-Siberian Railway.³



3 Sverdlovsk—a Pioneer in TBE Vaccination

Sverdlovsk is noteworthy for yet another reason. At the 13th Annual Meeting of the International Scientific Working Group on Tick-Borne Encephalitis ISW-TBE, Doctor Victor Romanenko from the Center for Hygiene and Epidemiology in Sverdlovsk Region, Russian Federation, presented an excellent example of a successful public health intervention. In Sverdlovsk, vaccination against TBE has been mandatory since 1995. Since 2001, TBE vaccination has been obligatory for children aged 7 years or older, and in 2008, mandatory vaccination was extended to all individuals aged 15 months or older.

Today, the TBE vaccination coverage in Sverdlovsk Oblast is above 80%, and mandatory immunization has led to a more than 10-fold decrease in the incidence rate of TBE, i.e., from 42.9 per 100 000 in 1996 to 3.2 per 100 000 in 2010 (see graph). The rate of deaths due to TBE has seen a similarly impressive decline, i.e., from 0.88 per 100 000 in 1996 to 0.14 in 2010.



Transposed into a graph, the Sverdlovsk experience looks very much like its Austrian counterpart, where vaccination rates have ranged between 85%–88% and TBE case numbers of have dropped to well below 100 (see graph). This is in sharp contrast to the numbers of TBE cases in one of Austria’s neighboring countries, the Czech Republic. There, case numbers have increased steadily, indicating that the natural risk of TBE infection has remained unchanged. Because both countries are geographically similar, the difference in TBE incidence between them can only be explained by the high vaccination coverage of close to 90% in Austria—compared with less than 20% in the Czech Republic.

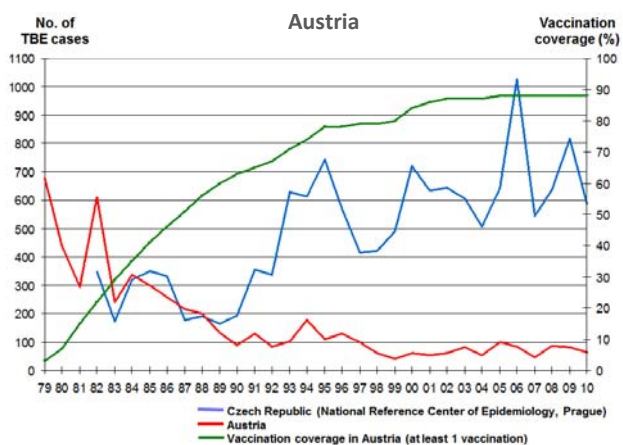


Figure courtesy of Professor Dr Franz X. Heinz, Department of Virology, Medical University of Vienna.



4 Ticks: Wash Them Hot and Tumble them Dry

Common recommendations to prevent tick bites when spending time outside include wearing light-colored clothing, long pants, and long-sleeved shirts, using repellents, doing a body check after potential tick exposure, and removing ticks immediately without crushing them.

Oxygen deprivation or a hot bath: which is more deadly?

Finally, to keep ticks from being imported into our homes, recommendations include throwing our clothes in the wash to kill ticks that might have been hiding in seams and other crooks and crevices. However, is it the oxygen deprivation or the water temperatures that kill ticks having found shelter in our clothing? Hans Dautel and colleagues⁴ kept *Ixodes ricinus* ticks under water with low or high oxygen content for different time periods. Depending on the development stage of the ticks and the oxygen content, *I. ricinus* survived under water for days or even weeks, with some engorged larvae even molting to nymphs. Thus, oxygen deprivation did not limit the survival of submerged ticks.

But then, Dautel put larvae, nymphs, and adult ticks to another stress test by placing them in a washing machine and exposing them to a variety of temperature and program settings. Whereas ticks survived wash programs at 40°C, water temperatures of 60°C were found to be deadly.



Hot air, too, will do the trick

An earlier US study⁵ had shown that lone star ticks (*Amblyomma americanum*) and deer ticks (*Ixodes scapularis*) are able to survive the agitation of a washing machine. Agricultural Research Service (ARS) entomologist John Carroll has been chasing ticks for years. One day, after taking a load of laundry out of his washer, he discovered a live tick sitting on top of the agitator. He set out to determine whether washing and drying clothes were a good way to make sure all ticks were removed from his trekking clothes.

He put lone star and deer ticks into mesh bags and washed them with regular laundry loads using different temperature and detergent combinations. After that, he dried the ticks at different temperatures. Many of them survived the ride in the washing machine, but all of them were killed by 1 hour of high-heat dryer tumbling.

Therefore, whereas most ticks will make it through the delicate wash, they'll unlikely withstand the hot wash cycle and the hot, dry air of a tumble dryer.

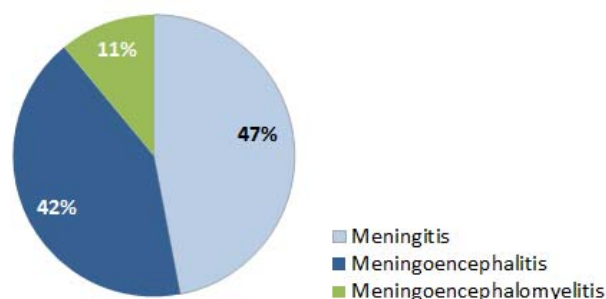
5 New Data on the Long-Term Sequelae of Myelitis After TBEV Infection

Some 30% of patients infected with TBEV develop CNS infection

Of all individuals infected with the TBE virus, an estimated 30%–35% remain free of clinical signs and symptoms, 30%–50% experience only the first (viremic) phase, and up to 30% of patients go on to enter the second phase, i.e., infection of the central nervous (CNS) system.⁶

Some 10% of patients with CNS infection from TBEV develop encephalomyelitis

The clinical course and prognosis of the one third of patients experiencing CNS disease also varies considerably. Between 1994 and 1999, Professor Reinhard Kaiser from the Department of Neurology in Pforzheim, Germany, included 731 patients with TBE in a prospective study on the clinical course of overt TBEV infection.⁷ TBE manifested as isolated meningitis in 47%, meningoencephalitis in 42%, and meningoencephalomyelitis in 11% (see graph). Of the 230 patients who were reexamined 1–5 years after the acute illness, 23% suffered persisting moderate or severe symptoms; the death rate was 1.4%.⁷



Focus on TBEV encephalomyelitis

Whereas a number of studies are available on meningitic and encephalitic courses of TBE, long-term observations on encephalomyelitis are scarce. In a recent publication,⁸ Kaiser reported 10-year follow-up results of those patients included between 1994 and 1999 who had developed encephalomyelitis. Of the 81 patients (11%) who had, 57 agreed to participate in the follow-on study.

Severity of acute disease correlates with prognosis

10 years after the acute phase of the disease, 11 of the 57 patients (19%) had recovered, 29 patients (51%) suffered long-term sequelae, such as pareses, and 17 patients (30%) had died. The most substantial improvements were seen in the first 12 months after acute disease. Also, the clinical findings at the 5- and 10-year follow-up were closely correlated with the severity of acute illness ($r=0.8$, $p<0.01$). Overall, therefore, the clinical picture of acute TBE will often be predictive of the long-term disease course.

Little correlation between MRI findings and severity of acute disease

In contrast, an earlier study⁹ had shown that the clinical findings after TBEV infection and the results of magnetic resonance imaging (MRI) are only weakly related. Thus, although patients with meningoencephalitis and an unfavorable prognosis were somewhat more likely to present with changes on MRI, particularly in the thalamus, some patients with normal MRI scans died from TBE in a matter of weeks.⁹

Why patients with severe paralysis have the worst prognosis

Patients with ataxia, impaired consciousness, double vision, urinary retention, and mild paresis of only one extremity were found to have the best prognosis, whereas patients with tetraparesis and concurrent respiratory paralysis, dysphagia, or dysarthria were among those with the worst prognosis. According to Kaiser, an explanation for this is provided by both post-mortem examinations of TBE patients and animal studies. The TBE virus has a predilection for motor cranial nerve nuclei, the cells of the anterior horn of the spinal cord, the Purkinje cells in the cerebellum, and thalamic cells. Viral infection of neuronal cells causes cell lysis. Because neurons have little regenerative potential, there is only a limited chance for muscle pareses to improve. Therefore, clinical improvements in muscular strength seen in patients with paresis are generally due to the effect of training and physical exercise on neighboring muscle groups. However, if the infection extends over several spinal segments, the resulting neuronal degeneration leads to more generalized muscle atrophy, with little or no chance for regeneration.⁸

Overall, therefore, the likelihood of complete recovery from myelitic disease after infection with the TBE virus is only about 20%, and the chance for clinical improvement decreases substantially after the first 3 years.⁸

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Erratum: A previous version of this newsletter misreported Doctor Victor Romanenko's professional affiliation; this has been corrected in the current version. The figure on Austrian and Czech TBE cases is shown by courtesy of Dr Franz X. Heinz, Department of Virology, Medical University of Vienna.

This newsletter is intended to highlight interesting aspects and issues related to tick-borne encephalitis (TBE). It does not claim to be comprehensive or to provide medical advice. Should you have any questions on issues reported herein, please contact Professor Ursula Kunze at ursula.kunze@meduniwien.ac.at. You receive this email because you have expressed an interest in receiving electronic news updates on TBE and the activities of the ISW-TBE.

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