Int. J. Med. Microbiol. 293, Suppl. 37, 5–15 (2004)

http://www.urbanfischer.de/journals/ijmm

IJMM

Mini-Review

Evidence that climate change has caused 'emergence' of tick-borne diseases in Europe?

Sarah E. Randolph

Department of Zoology, University of Oxford, UK

Abstract

Even though tick-borne disease systems are highly susceptible to climatic influences, climate change to date is not necessarily the cause of the marked increased incidence of a variety of tick-borne diseases in many parts of Europe over the past two decades. To test for causality, rather than coincidence, we need to examine whether the right sorts of climate change have occurred at the right time and in the right places to account for the observed heterogeneous temporal and spatial patterns of tick-borne disease 'emergence'. Tick-borne encephalitis (TBE) incidence, for example, showed a 3-fold step increase from 1983 to 1986 in Sweden, doubled in 1993 in the Czech Republic, increased even more dramatically in the same year in Lithuania and Poland, but declined markedly in 1997 in Hungary, Croatia and Slovenia. Within each country, TBE incidence has changed to different degrees in different regions. Because other tick-borne diseases, notably Lyme borreliosis, has commonly 'emerged' in parallel with TBE, we should first examine climate variables predicted to have a general effect on tick abundance, which has indeed increased in the past decade. These include temperature and moisture stress, which have seasonally differential impacts. Monthly mean records for 1960–2000 from the UK Climate Research Unit's interpolated global climate surface reveal that mean spring, spring-autumn and winter temperatures have all increased gradually over the past 40 years, but apparently most sharply in the late 1980s, when moisture stress also increased. These climate data do not reveal any obvious differences between sites where TBE did or did not 'emerge', and in Sweden increases in TBE pre-dated the onset of warmer springs and winters. If recorded climate changes cannot yet satisfactorily explain the temporal and spatial patterns of tick-borne disease change in Europe, the impact of biotic factors, such as increases in deer abundance and changing habitat structure, and of socio-political changes following the end of communist rule, demand more detailed quantitative analyses.

Key words: Climate change – political change – tick-borne encephalitis – Lyme borreliosis.

Corresponding author: Professor Sarah Randolph, Department of Zoology, South Parks Road, Oxford OX1 3PS, UK, Phone: 0044 1865 271241, Fax: 0044 1865 271240, E-mail: sarah.randolph@zoology.ox.ac.uk

1433-1128/04/293/Suppl.37-5 $ 15.00/0

Introduction – the undeniable impact of climate on tick-borne diseases

Over the past two decades, tick-borne diseases have increased and now constitute a major health problem in many parts of Europe. Principal amongst these are tick-borne encephalitis (TBE) and Lyme borreliosis (LB), both zoonoses caused by agents transmitted by *Ixodes ricinus* and *I. persulcatus*. Effective control depends on identifying the specific and complex causes of this changing zoonotic risk, many of which involve the diverse impact of humans, both direct and indirect. Because climate has changed globally over the same decades, the common assumption is that climate change is the cause of increased incidence of these, and many insect-borne, infections, but this has rarely been tested by appropriate retrospective analyses.

There is no doubt that tick-borne disease systems are very susceptible to influences of climate as many if the parameters and variables of the R_0 model (Randolph, 1998), that determine transmission potential, vary with climate. For example, as ixodid ticks feed only once per life stage, as larvae, nymphs and adults, pathogens must endure a very long delay in the transmission process, equal to the ticks' interstadial development period, during which the vectors suffer significant mortality. Both the delay period and the mortality vary geographically and seasonally with climate. Climate, however, is multifactorial and its effects are not uni-directional. While tick birth and development rates increase with temperature, tick mortality rates increase with moisture stress. At the same time, tick-host relationships may vary with climate; the relative numbers of *I. ricinus* nymphs feeding on transmission-competent rodents increase with moisture stress (Randolph and Storey, 1999). The overall outcome, the tick's seasonal abundance and the pace and rate of pathogen transmission, can only be predicted with fully functional tick population and pathogen transmission models, which we do not yet have. A further complication arises from host responses to climate, especially rodent population dynamics that are differentially susceptible to climate variables at different times of the year. On the basis of biological process-based models, therefore, it is not yet possible to predict whether the incidence of any tick-borne disease will increase or decrease at actual levels of climate change in any one place.

Instead, we can turn the question round and ask: has climate changed at the right time, in the right places and in the right ways, to account for the observed spatial and temporal patterns of increased incidence of tick-borne diseases in Europe over the past 1–2 decades? The epidemiology of TBE and LB has typically been studied at the national rather than the continental level. As a result, explanations for the changing incidence have been specific to each country and not always compatible with events elsewhere. This paper attempts to take a more holistic view to achieve more general conclusions.

What is the right time to look for causality between climate change and tick-borne disease emergence?

The recent history of TBE incidence has been marked by several marked, but asynchronous, discontinuities in many countries. If these have been driven by climatic change, one would expect them to be matched in time by changes in at least one aspect of the regional climate signal. The following examples (Fig. 1) illustrate the range of different scenarios.

In Sweden, the annual case numbers of TBE were typically low from 1960 to 1983 (mean $\pm$ 1 standard deviation $= 24 \pm 7$), then showed a 3-fold step increase between 1983 and 1986, followed by a stable higher incidence (65 ± 20) from 1986. It is too early to say whether there has been a second step increase since 2000 (121 ± 14).

In many parts of Europe, TBE cases did not increase until the early 1990s. In the Czech Republic, annual case numbers were high but variable from 1960 (408 ± 192), consistently lower through the 1980s (256 ± 85), and then approximately doubled from 1993 (583 ± 111). In Lithuania and Poland, there were also fewer cases during the 1980s (14 ± 4, and 13 ± 7, respectively) than during the 1970s (42 ± 15, and 36 ± 11, respectively), but far more dramatic increases from 1993 to the present (365 ± 157, and 190 ± 55, respectively). Thus, whereas the Czech Republic has suffered only about a 50% increase in the past decade over the historic norm, Lithuania (and Latvia) and Poland have suffered increases of an order of magnitude.

Along the southern boundary of the range of TBE, in Hungary, Croatia and Slovenia, recorded case numbers changed very little until the end of the 20th century, when they appeared to have decreased. In Hungary, for example, there was a 75% decrease from 271 ± 60 during 1978–1996 to a 71 ± 21 from 1997–2002.

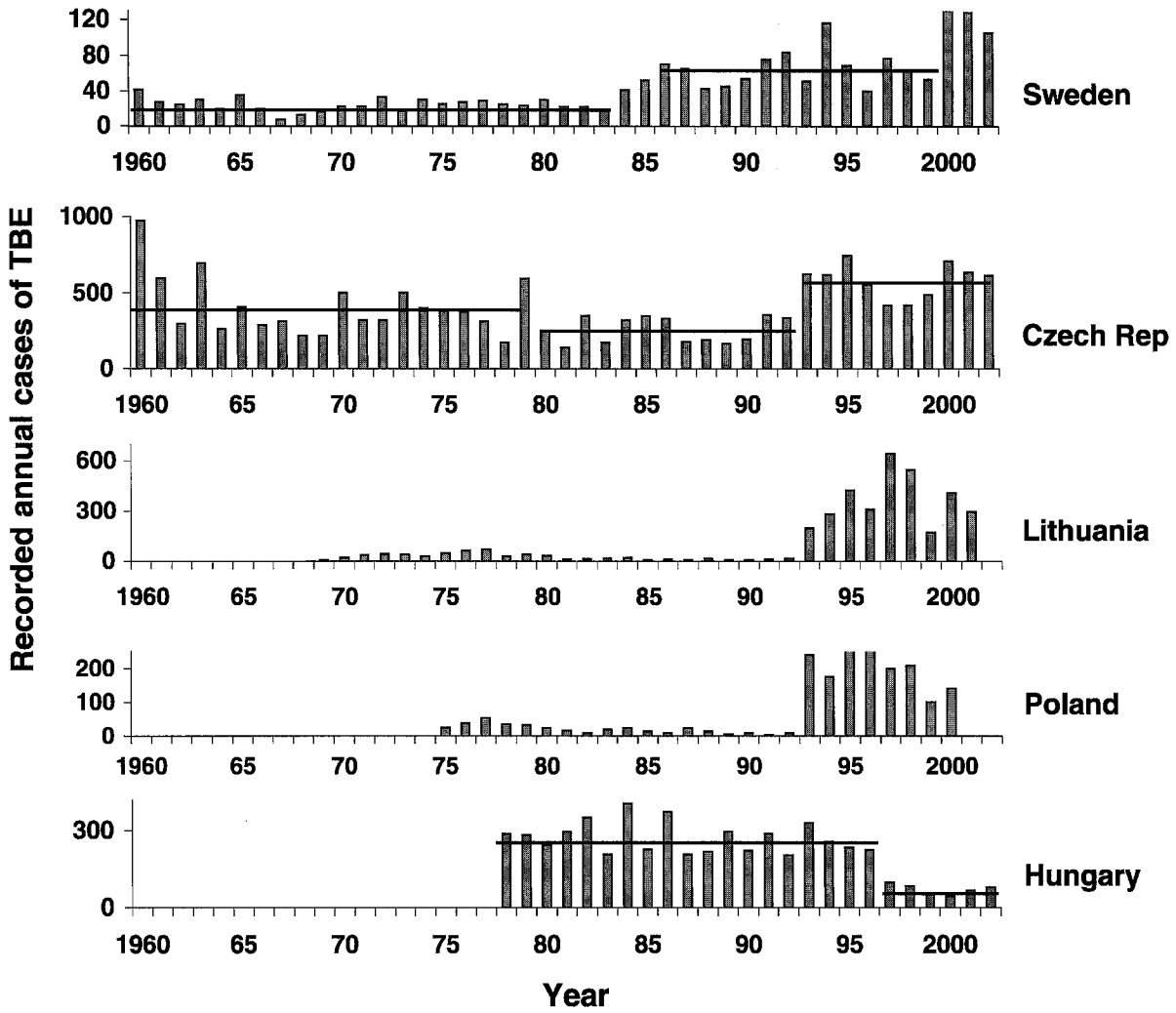

Fig. 1. Recorded annual case numbers of tick-borne encephalitis (TBE) in five European countries, illustrating different patterns of discontinuities in the time series highlighted by the horizontal lines.

What is the right place at which to extract the climate signal?

Neither climate nor disease incidence shows uniform patterns over wide regions. Increases in TBE have occurred to different degrees in different places not only between countries, but also regionally within countries where public health and sociological factors are likely to be more uniform. Maps of the regional incidence of TBE in the Czech Republic show marked geographical variation in the increase between 1989–92 and 1993–96 (Danielová and Benes, 1997). In several regions, TBE was virtually absent (0–1 annual cases/100,000 population) in the first four years, but increased to 11–50 annual cases/100,000 over the second period, while in other regions TBE incidence remained close to zero. In both Lithuania and Poland, high TBE incidence after 1993 has been focussed in certain parts of each country, notably the central regions of Lithuania (Zygutienė, 2001; Vaisviliene et al., 2002) and the extreme northeast (particularly Bialystok) of Poland (Zabicka, 1994). In Hungary, TBE occurs mainly in the Trans-Danubian area, specifically in the counties of Zala, Somogy and Nograd (Vass, 2001). In Sweden, TBE is confined principally to the southeast coastal strip (Haglund, 2001), with >70% of cases occurring in Stockholm county (Lindgren and Gustafson, 2001).

There are three major sources of climate information from which we may extract signals to match these geographically specific epidemiological observations. Each has its own limitations for the purpose of detailed spatio-temporal analyses applicable to complex biological systems.

First there are ground records from meteorological stations. These refer only to local conditions, frequently in sites unrepresentative of tick habitats (such as at airports or close to urban centres) and not necessarily in regions of particular epidemiological interest. Nevertheless, they reveal most directly any changes in general conditions through time, even if not in the precise conditions relevant to tick-borne disease systems. The difficulty lies in gathering together enough individual site records for analyses over continental-scale areas.

Secondly, there are continuous climate surfaces, constructed by interpolating between ground stations, as used by the International Panel on Climate Change (IPCC). The Climate Research Unit (CRU) at the University of East Anglia in the UK has compiled mean monthly records for the last century at a spatial resolution of 0.5^0 longitude/latitude (i.e. pixel sizes of approximately 50×50 km^2) (New et al., 2000), now updated for 1960–2000 (Mitchell T. B. et al., 2003, A comprehensive set of climate scenarios for Europe and the globe, in prep). There are, however, problems of change detection through both space and time. The process of interpolation means that local differences between pixels do not show up adequately. Furthermore, the distribution of ground stations that have contributed to the climate surface is not only uneven, but has also changed over the 40-year period. The net loss of stations in the database towards the end of the series may give rise to artefacts that appear as changes in the climate signal.

Thirdly, there is satellite imagery. Signals from meteorological satellites, such as NOAA's AVHRR sensor, have been processed to provide 10-day or monthly mean climate-related variables for 1982–2000 at 8×8 km^2 resolution (Hay, 2000; Green and Hay, 2001). These small pixels can be composited to give mean conditions over areas in which any epidemiological data are recorded. Within this 19-year period, changes in the sensor platform, and in the precise timing and position of each satellite orbit, must be corrected for before real climate change can be reliably detected (Gutman, 1999).

For this preliminary study, I used the CRU interpolated climate surfaces and identified each pixel that best encompassed regions within the Czech Republic, Lithuania, Poland, Hungary and Sweden where TBE incidence has and has not changed significantly over the past two decades, as detailed above.

What is the right sort of climate change to account for the general 'emergence' of tick-borne diseases?

A variety of different diseases transmitted by ticks of the *I. ricinus* group appear to have 'emerged' recently. Human ehrlichiosis and babesiosis are sporadically, but increasingly, recorded (*inter alia* Petrovev et al., 1997; McQuiston et al., 1999; Grzeszczuk et al., 2002; Foppa et al., 2002), and LB rapidly became the single most abundant vector-borne infection of northern temperate zones since its recognition in the early 1980s. Time series of LB incidence are confounded by the recent and relatively poor reportage of this infection, but where we can make valid comparisons we find certain similarities between LB and TBE. In the Czech Republic, for example, LB is an order of magnitude more prevalent than TBE, in accordance with its much higher transmission potential (Randolph et al., 1996), but shows parallel, highly correlated ($r = 0.855$, $p < 0.001$), annual variation over the past 17 years (Fig. 2). The same is true in Lithuania ($r = 0.920$, $p < 0.001$), and to lesser extent in Switzerland ($r = 0.601$, $p = 0.05$), but in Croatia LB incidence stayed high in the last years of the 20th century, while TBE decreased.

So any search for an appropriate climate change should start with variables that change the general risk factors for all tick-borne diseases. The most obvious one is tick abundance, which is indeed reputed to have increased in many places, although published long-term, standardised data are rare. In Lithuania, the annual average tick index, recorded at nine stationary observation points established through the country in 1987, doubled in 1991, and continued to increase until 1996 (Zygutienė, 2001). Rates of tick demographic processes are sensitive to specific changes in seasonal climate, rather than simply gross changes in annual average temperature or rainfall. Increases in temperature at various times of the year would have different effects on tick populations. Warmer springs (Mar-May) might permit an earlier onset of questing activity, while raised temperatures throughout the spring-autumn period (Mar-Sep) would accelerate inter-stadial development. Temperatures for these two periods are, as expected, highly correlated. Winter temperatures (Dec-Feb) are more variable from year to year and are not strongly correlated with spring temperatures; they might be expected to have less direct effect on ticks which are naturally quiescent at this time, but may have indirect effects via rodent

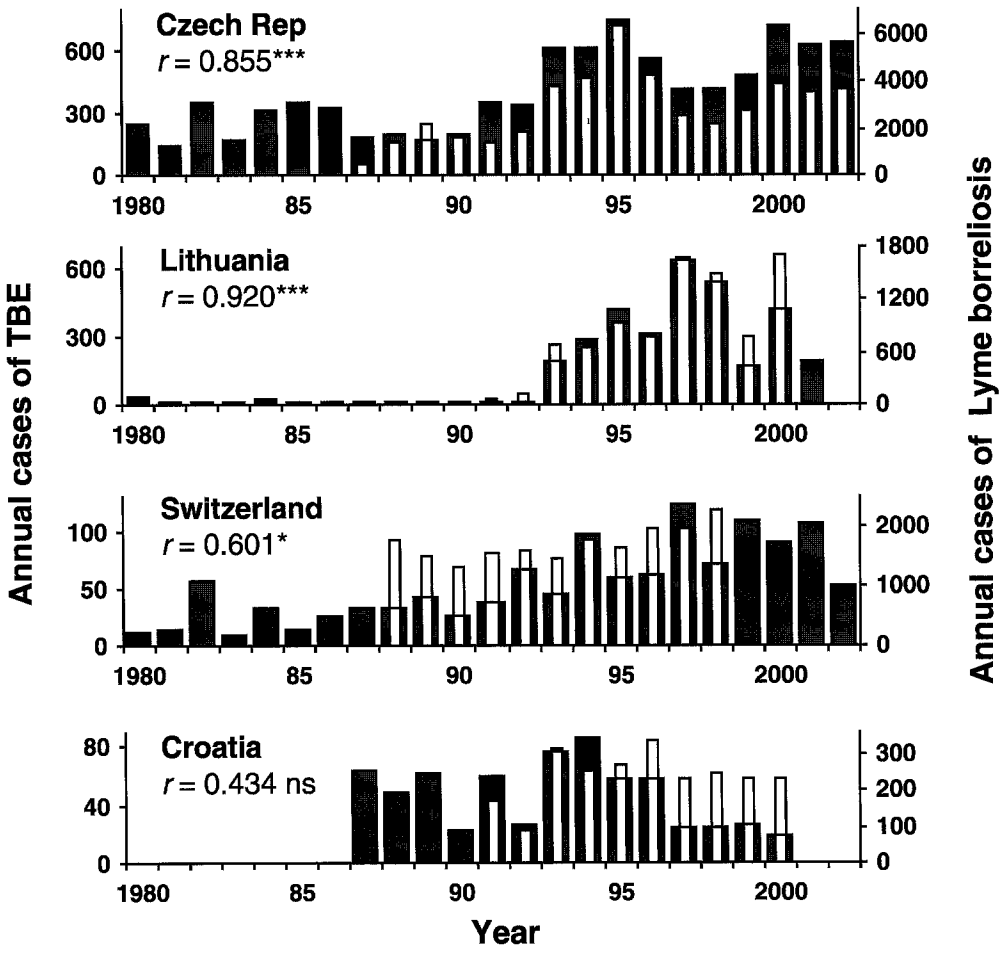

Fig. 2. Recorded annual case numbers of tick-borne encephalitis (TBE) (dark columns) and of Lyme borreliosis (open columns), showing significant correlations (***$p<0.001$, *$p<0.05$) in the Czech Republic, Lithuania and Switzerland, but not in Croatia.

survival and therefore host availability later in the year.

Increased moisture stress is predicted to have different effects at certain critical times of the year. In April-June moisture stress above a certain threshold might cause nymphs to quest lower on the vegetation and so increase the number of nymphs feeding on rodents (Randolph and Storey, 1999), thereby increasing transmission potential. Later in the year, June-Aug, increased moisture stress would decrease tick questing activity and increase mortality as ticks die of fat exhaustion before finding a host (Perret et al., 2000; Randolph et al., 2002). Mean monthly records alone, however, do not identify extreme events, such as heavy rainfall concentrated in short periods, which are likely to have adverse effects on both tick and rodent survival.

Observed changes identified from the CRU interpolated climate data base, 1960–2000

Preliminary results of examining the monthly mean climate variables itemised above show that mean spring temperatures have increased gradually over the past 40 years, with a more marked increase from 1989 (Fig. 3). No statistical analysis has yet been applied to these changes to determine the significance of any trend. The pattern appears to be similar, although the absolute temperature levels were different, in all sites examined in the Czech Republic, Lithuania, Poland, Hungary and Sweden. It was not possible to detect from the CRU climate surfaces any differences in the temporal patterns between those sites where TBE did or did not 'emerge' in the early 1990s, or in 1983–86 (Sweden), nor where TBE declined in incidence (Hungary). This may be due to

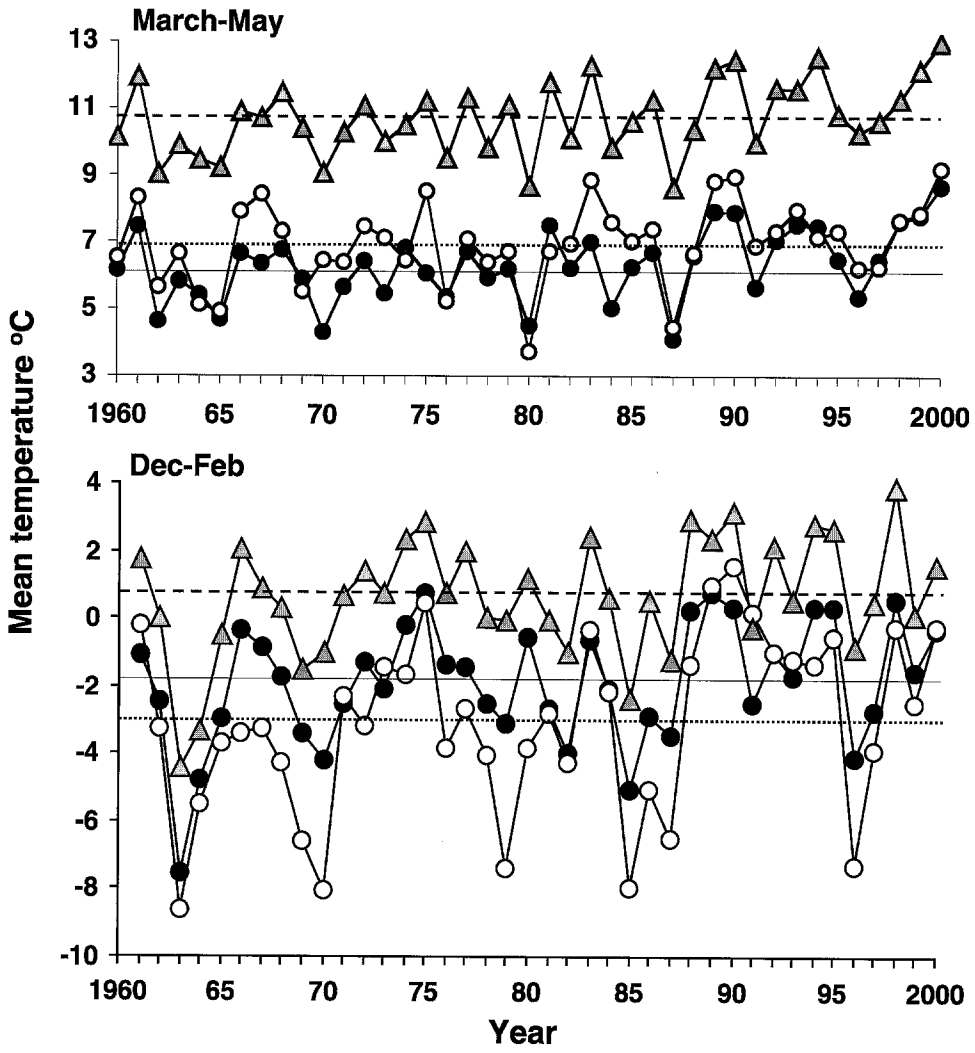

Fig. 3. Mean temperatures in spring (March-May) and winter (Dec-Feb) from 1960 to 2000 in SE Bohemia, Czech Republic (14–14.5°latitude, 49–49.5°longitude) (●), Bialystok county, Poland (23–23.5°lat., 53–53.5°long.) (○), and Zala county, Hungary (17–17.5°lat., 46.5–47°long.) (▲). Data taken from the UK CRU interpolated climate surface – see text. Horizontal lines indicate the 1960–2000 mean levels for each site (Czech – solid, Poland – dotted, Hungary – dashed) to guide the eye.

the nature of the interpolated climate surface which, although presented at 0.5°lat./long. resolution, is not designed to give reliable information on such a scale (http://www.cru.uea.ac.uk/~timm/grid/CRU_TS_2_0.html). It may also reflect the real degree of spatial co-variation in climate variability across Europe. Mean winter temperatures increased most markedly slightly earlier, from 1988 (i.e. the mean of Dec. 87-Feb. 88) (Fig. 3).

Lindgren and Gustafson (2001) identified warmer spring and winter conditions as correlates of increased TBE incidence in Stockholm county, Sweden. The increases in these seasonal temperatures, however, occurred *after* the step increase in TBE cases in Sweden (Fig. 4). The weak statistical correlation with spring temperatures, due entirely to two extreme points, cannot therefore signify causality, and indeed after 1984 there were more cases of TBE in many years despite similar temperature conditions (Fig. 5). However intuitively likely it is that low temperature could be a limiting factor in TBE virus transmission at the northern extreme of its range, evidence that increased temperatures have driven the increase in TBE incidence here is not yet convincing.

Even if the major discontinuities in TBE incidence cannot be explained satisfactorily by the recorded temperature increases, nevertheless a seasonal shift in reported cases of TBE in central and northeast Europe suggests that TBE virus transmission dy-

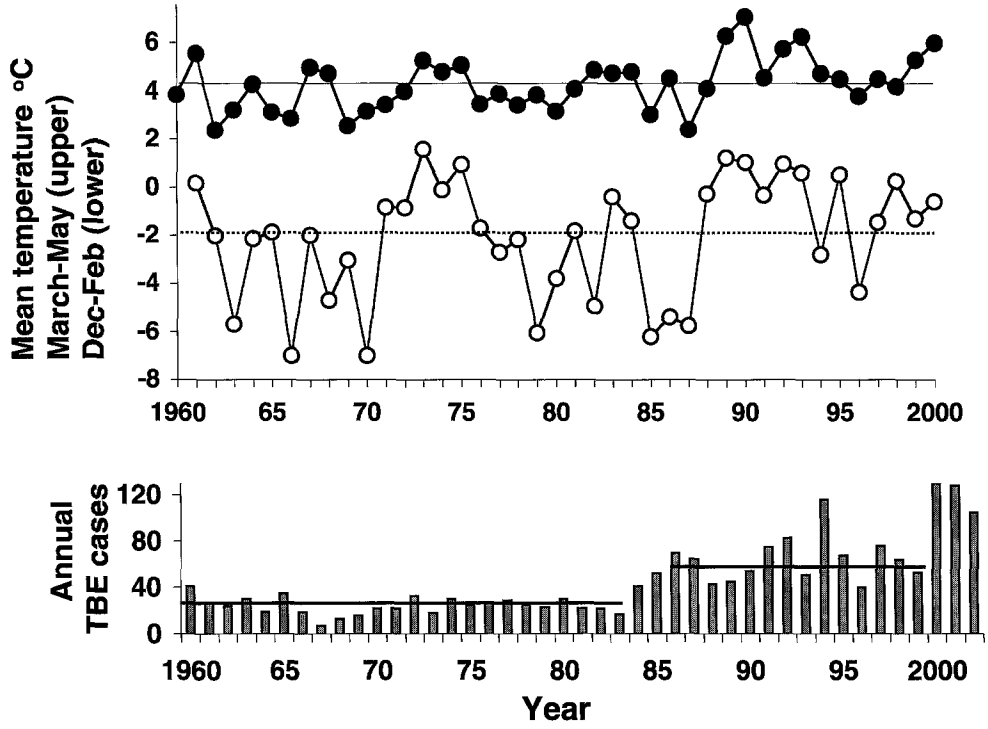

Fig. 4. Mean temperatures in spring (March-May) (●) and winter (Dec-Feb) (○) from 1960 to 2000 in Stockholm county, Sweden (18–18.5°lat., 60–60.5°long.), with overall mean levels indicated by horizontal lines. Data taken from the UK CRU interpolated climate surface – see text. Recorded annual case numbers of tick-borne encephalitis (TBE) in Sweden are shown below for comparison.

namics have changed somewhat, perhaps as a result of warmer temperatures. In the Czech Republic, in 1991 nearly 80% of annual cases were reported in July and August, with < 10% in either early summer or autumn. From 1992 onwards, 20–30% of cases occurred in May and June, and from 1994 onwards 20–30% of cases also occurred in September and October (Danielová and Benes, 1997). Likewise in Poland, the proportion of cases reported in October 1980–92 was double that in 1972–79, and in 1993 the peak occurred in July rather than in August as previously (Zabicka, 1994).

In many parts of Europe, the most common, but not invariable, trend in rainfall has been a slight decrease over the past 1–2 decades, more so in spring (April-June) than in summer (June–Aug) (Fig. 6), although NE Poland and central Lithuania saw large decreases over the past 10 summers. There is no clear spatio-temporal correspondence between rainfall and TBE incidence patterns. Nevertheless, the combination of lower rainfall and warmer temperatures has increased the vapour pressure deficit (VPD), a measure of the overall drying power of the atmosphere (Fig. 7). Although VPD in summer is no higher in Zala, western Hungary, than in some parts of the Czech Republic where TBE has increased, high VPD at the higher temperatures characteristic of Hungarian summers may be more limiting to ticks than at lower temperatures. The complex relationships between atmospheric dryness, temperature and tick questing behaviour and mortality rates deserve more detailed empirical study under natural conditions, rather than in the laboratory where most of the classic studies have been carried out.

Coincident biotic changes

At the same time as the above changes in climate, changes in biotic factors also occurred, notably a significant increase in the density of roe deer across most of Europe, including Scandinavia. Deer are, of course, the principal host for adult *I. ricinus* ticks, and are therefore crucial to tick population maintenance. Data from Denmark offer the best documented evidence for the impact of increasing densities of deer on both temporal and spatial variation in the risk of a tick-borne disease in Europe, this time Lyme borreliosis (Jensen and Frandsen, 2000; Jensen et al., 2000) (data redrawn in Fig. 6 of Randolph, 2003). From 1984 to 1998, an increase in LB paralleled an increase in deer density. Spatial varia-

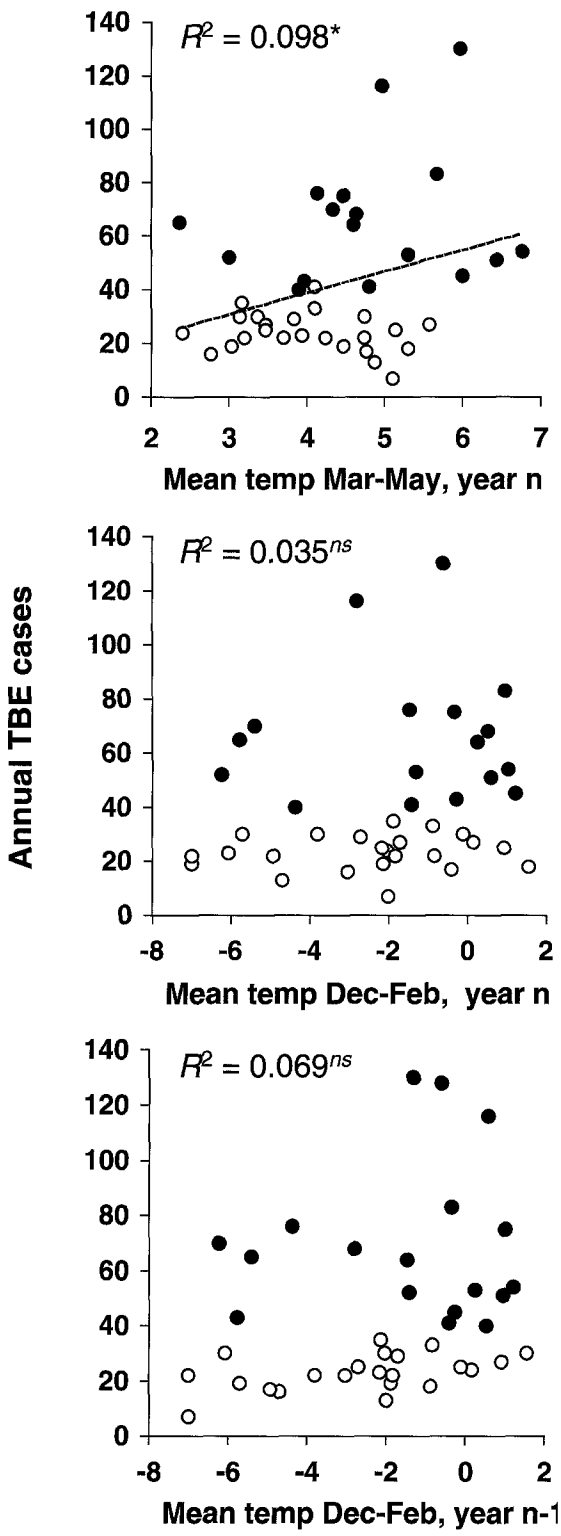

Fig. 5. Recorded annual case numbers of tick-borne encephalitis (TBE) in Sweden from 1960–83 (○) and 1984–2000 (●) in relation to mean spring (March-May) temperatures of the same year (year n), and winter (Dec-Feb) temperatures of the same and preceding years (year n – 1). The regression line and coefficients ($^*p < 0.05$, $^{ns}p > 0.05$) refer to the whole time series, 1960–2000.

tion in tick density across 35 sites in 1996, and in LB cases across 12 counties in 1993–95, was also correlated with deer density. This accords with the seminal role attributed to white-tailed deer in the emergence of LB in the USA (Spielman et al., 1985; Wilson et al., 1985). Associated changes in habitat structure due to shifting agricultural practices may favour tick population growth directly by providing more suitable micro-climates for tick survival.

Conclusions

Climate is just one of many factors, biological and non-biological, that influence tick-borne disease dynamics. Ultimately, all cause variable rates of contact between ticks, transmission hosts and humans, resulting in greater densities of infected ticks and greater incidental spill-over from enzootic cycles to humans. Amongst the biological factors, we have not yet identified changing climatic factors that can explain both the spatial variation and the temporal patterns in tick-borne disease 'emergence'. It is quite different on the one hand to identify climatic forcing factors for relatively minor annual variations in tick-borne disease incidence, although even this has not yet been done satisfactorily, and on the other hand to conclude that climate change has driven the observed variable major discontinuities in time series of these diseases. We have, however, barely started in our search for the right climate change, having only examined the most obvious factors so far. While interpolated climate surfaces may be able to reveal gross trends over wide regions, they are almost certainly too crude, both in their spatial resolution and in the range of variables documented, to provide the subtle climate variables necessary for this task.

With such complex biological systems, it is entirely possible that some minor change in extrinsic factors could have "tipped the balance", setting up the right conditions for enzootic cycles in certain places at one point in time, which have thereafter continued and gained momentum through natural amplification. This is more likely for TBE, with its much lower transmission potential and more specific climate requirements (Randolph et al., 1999; Randolph et al., 2000), and could theoretically result in a sudden increase in incidence. At the same time, while one swallow does not make a summer, the very much lower incidence of TBE in Latvia and Estonia in the past 1–2 years, similar to levels before 1992, warns us that change is not inexorably in one direction only. Other more rare human infections with tick-borne pathogens, ehrlichiosis and babesiosis, are

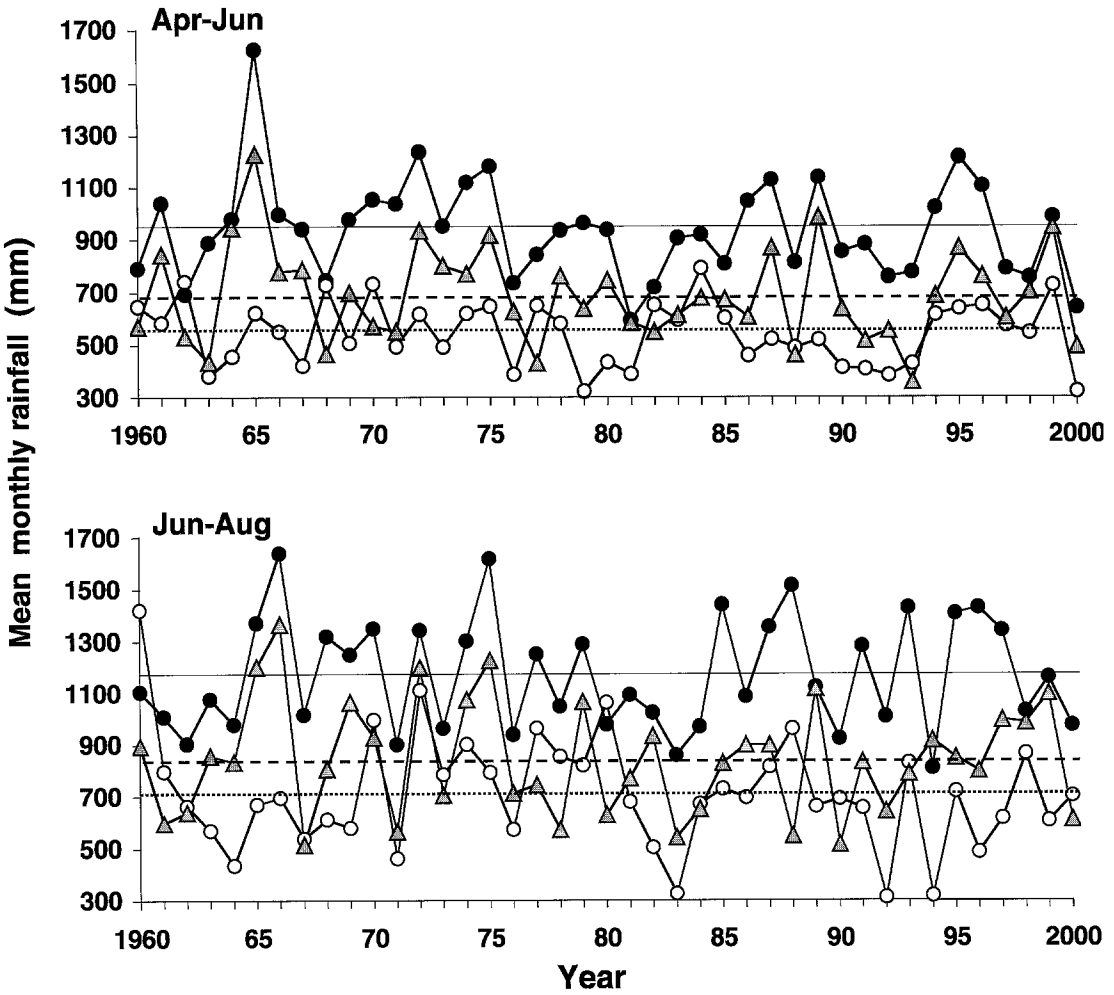

Fig. 6. Total rainfall in spring (April-June) and summer (June-August) from 1960 to 2000 in SE Bohemia, Czech Republic (14–14.5°latitude, 49–49.5°longitude) (●), Bialystok county, Poland (23–23.5°lat., 53–53.5°long.) (○), and Zala county, Hungary (17–17.5°lat., 46.5–47°long.) (▲). Data taken from the UK CRU interpolated climate surface – see text. Horizontal lines indicate the 1960–2000 mean levels for each site (Czech – solid, Poland – dotted, Hungary – dashed) to guide the eye.

also evidently constrained at present by low transmission forces, whose limiting factors we need to understand if we are to be alerted to any further potential 'emergence'.

There is far less doubt that non-biological factors can change very suddenly and result in dramatic changes in disease incidence (Korenberg and Kovalevskii, 1999). It is impossible not to be impressed by the striking coincidence between the extreme increases in tick-borne diseases and the end of communist rule in eastern Europe. A number of epidemiologically relevant sociological changes resulted from this transition, including changes in agricultural practices and in public health services, and the increase in both poverty and wealth with their impact on work and leisure activities. In the absence of demonstrable climate change, the decline in recorded TBE incidence in Hungary may instead be due to the simple fact that the cost of the tests for TBE have had to be paid by the hospitals there since 1997 (Vass, 2001). No such public health changes have occurred in Slovenia, however, where TBE has also declined recently (F. Strle, personal communication). Interwoven political, social and environmental changes can plausibly be invoked to explain the (re-)emergence of a wide range of communicable diseases (MacLehose et al., 2002). According to Engels, the threat posed by infectious disease in the industrial slums stimulated the rise of communism in the 19th century. In a curious twist of history, it appears that the fall of communist rule at the end of the 20th century may have stimulated a dramatic rise in infectious disease in eastern Europe. But before we can safely conclude this, we need good data on sociological factors at resolutions to match our epidemiological observations. Whatever role cli-

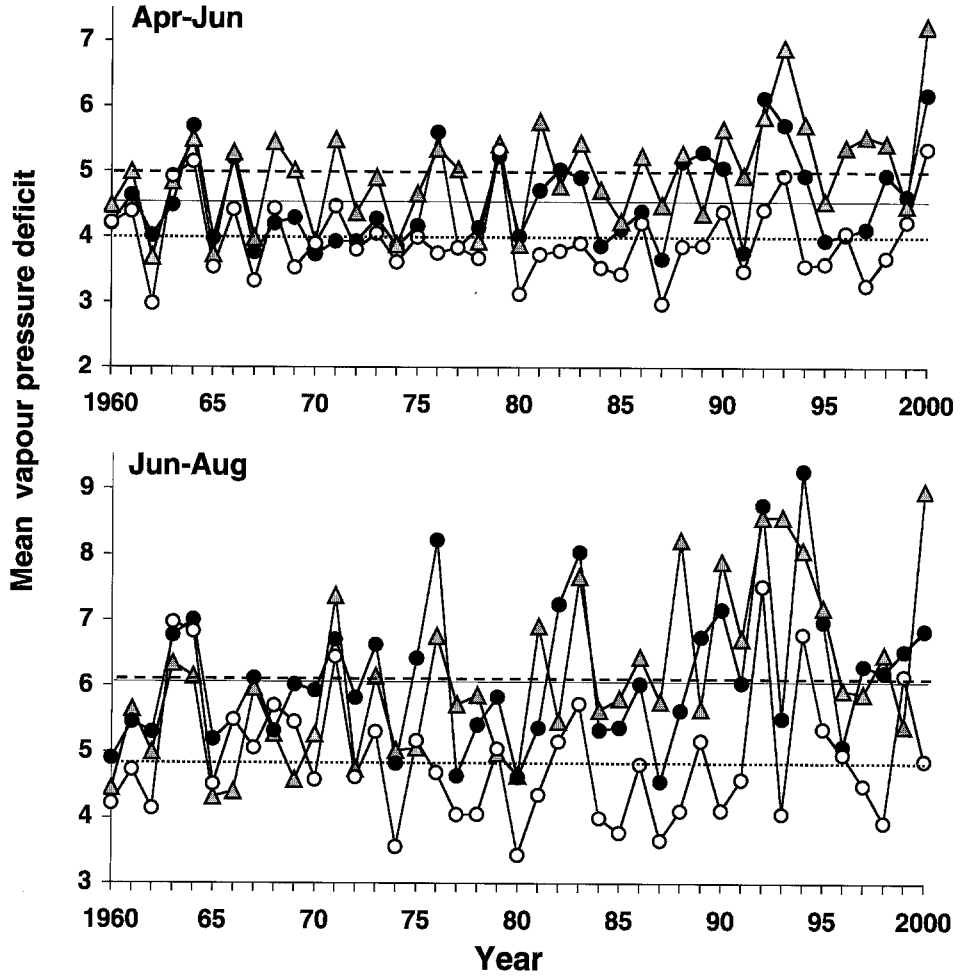

Fig. 7. Mean vapour pressure deficit in spring (April-June) and summer (June-August) from 1960 to 2000 in NW Bohemia, Czech Republic (14–14.5°latitude, 50.5–51°longitude) (●), Bialystok county, Poland (23–23.5°lat., 53–53.5°long.) (○), and Zala county, Hungary (17–17.5°lat., 46.5–47°long.) (▲). Data taken from the UK CRU interpolated climate surface – see text. Horizontal lines indicate the 1960–2000 mean levels for each site (Czech – solid, Poland -dotted, Hungary – dashed) to guide the eye.

mate change may be playing, we should expect a differential impact depending on its starting point, i.e. the regional climate characteristics, and also on the context of specific national socio-political effects.

Acknowledgements. It is a pleasure to acknowledge the contribution made to this paper by David Rogers, and useful discussions with Simon Hay and Wladimir Alonso. This work was funded by the Wellcome Trust and the UK Natural Environment Research Council.

References

Danielová, V., Benes, C.: [Increased incidence of tick-borne encephalitis in the Czech Republic] (in Czech). Prakticky Lekar 77, 580–583 (1997).

Foppa, I., Krause, P. J., Spielman, A., Goethert, H., Gern, L., Brand, B., Telford, S. R.: Entomologic and serologic evidence of zoonotic transmission of *Babesia microti*, eastern Switzerland. Emerg. Infect. Dis. 8, 722–726 (2002).

Green, R. M., Hay, S. I.: The potential of Pathfinder AVHRR data for providing surrogate climatic variables across Africa and Europe for epidemiological applications. Rem. Sens. Environ. 79, 165–175 (2002).

Grzeszczuk, A., Stanczak, J., Kubica-Biernat, B.: Serological and molecular evidence of human granulocytic ehrlichiosis focus in the Bialowieza Primevel Forest (Puszcza Bialowieska), northeastern Poland. Eur. J. Clin. Microbiol. Infect. Dis. 21, 6–11 (2002).

Gutman, G. G.: On the monitoring of land surface temperatures with the NOAA/AVHRR: removing the effect of satellite drift. Int. J. Rem. Sens. 20, 3407–3413 (1999).

Haglund, M.: TBE in Sweden – a review: International Scientific Working Group on TBE. http://www.tbe-info.com/reports/sweden.html (2001)

Hay, S. I.: An overview of remote sensing and geodesy for epidemiology and public health application. Adv. Parasitol. 47, 1–35 (2000).

Jensen, P. M., Frandsen, F.: Temporal risk assessment for Lyme borreliosis in Denmark. Scand. J. Infect. Dis. 35, 539–544 (2000a).

Jensen, P. M., Hansen, H., Frandsen, F.: Spatial risk assessment for Lyme borreliosis in Denmark. Scand. J. Infect. Dis. 35, 545–550 (2000b).

Korenberg, E. I., Kovalevskii, Y. V.: Main features of tick-borne encephalitis eco-epidemiology in Russia. Zentralbl. Bakteriol. 289, 525–539 (1999).

Lindgren, E., Gustafson, R.: Tick-borne encephalitis in Sweden and climate change. The Lancet 358, 16–18 (2001).

MacLehose, L., McKee, M., Weinberg, J.: Responding to the challenge of communicable disease in Europe. Science 295, 2047–2050 (2002).

McQuiston, J. H., Paddock, C. D., Holman, R. C., Childs, J. E.: The human ehrlichioses in the United States. Emerg. Infect. Dis. 5, 635–642 (1999).

New, M., Hulme, M., Jones, P.: Representing twentieth-century space-time climate variability. Part II: Development of 1901–1996 monthly grids of terrestrial surface climate. J. Climate 13, 2217–2238 (2000).

Perret, J.-L., Guigoz, E., Rais, O., Gern, L.: Influence of saturation deficit and temperature on *Ixodes ricinus* tick questing activity in a Lyme borreliosis-endemic area (Switzerland). Parasitol. Res. 86, 554–557 (2000).

Petrovev, M., Lotric-Furlan, S., Avsic Zupanc, T., Strle, F., Brouqui, P., Roux, V. Dumler, J. S.: Human disease in Europe caused by a granulocytic *Ehrlichia* species. J. Clin. Microbiol. 35, 1556–1559 (1997).

Randolph, S. E.: Ticks are not insects: consequences of contrasting vector biology for transmission potential. Parasitol. Today 14, 186–192 (1998).

Randolph, S. E.: Faune, climat et politique: causes possibles aux récents accroissements des zoonoses à tiques. Ann. d'Inst. Past. Actualités 16, 109–120 (2003).

Randolph, S. E., Gern, L., Nuttall, P. A.: Co-feeding ticks: epidemiological significance for tick-borne pathogen transmission. Parasitol. Today 12, 472–479 (1996).

Randolph, S. E., Green, R. M., Hoodless, A. N., Peacey, M. F.: An empirical quantitative framework for the seasonal population dynamics of the tick *Ixodes ricinus*. Int. J. Parasitol. 32, 979–989 (2002).

Randolph, S. E., Green, R. M., Peacey, M. F., Rogers, D. J.: Seasonal synchrony: the key to tick-borne encephalitis foci identified by satellite data. Parasitology 121, 15–23 (2000).

Randolph, S. E., Miklisová, D., Lysy, J., Rogers, D. J., Labuda, M.: Incidence from coincidence: patterns of tick infestations on rodents facilitate transmission of tick-borne encephalitis virus. Parasitology 118, 177–186 (1999).

Randolph, S. E., Storey, K.: Impact of microclimate on immature tick-rodent interactions (Acari: Ixodidae): implications for parasite transmission. J. Med. Entomol. 36, 741–748 (1999).

Spielman, A., Wilson, M. L., Levine, J. F., Piesman, J.: Ecology of *Ixodes dammini*-borne human babesiosis and Lyme disease. Annu. Rev. Entomol. 30, 439–460 (1985).

Vaisviliene, D., Kilciauskiene, V., Zygutiené, M., Asokliene, L., Caplinskas, S.: TBE in Lithuania: epidemiological aspects and laboratory diagnosis. Int. J. Med. Microbiol. S33, S179–181 (2002).

Vass, A.: Tick-borne encephalitis in Hungary: International Scientific Working Group on TBE. http://www.tbe-info.com/reports/hungary.html (2001)

Wilson, M. L., Adler, G. H., Spielman, A.: Correlation between abundance of deer and that of the deer tick, *Ixodes dammini* (Acari: Ixodidae). Ann. Entomol. Soc. Am. 78, 172–176 (1985).

Zabicka, J.: The tick-borne encephalitis in Poland [in Polish]. Przeg. Epid. 48, 197–203 (1994).

Zygutiené, M.: Acarological situation and natural foci of tick-borne encephalitis in Lithuania: International Scientific Working Group on TBE. http://www.tbe-info.com/reports/lithuania.html (2001).