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# Trends in tick population dynamics and pathogen transmission in emerging tick-borne pathogens in Europe: an introduction

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## Introduction

In Europe, tick-borne diseases are the most important group of vector-borne diseases (Heyman et al. 2011; Randolph 2001; Randolph and Šumilo 2007). Research focus has long been on Lyme borreliosis and tick-borne encephalitis (TBE), because of their prevalence and public health impact. However, recently, new pathogens have emerged or re-emerged and geographical distributions of pathogens are changing. Also new techniques and developments in statistical and mathematical modelling have become available which allow for more accurate identification of risk areas as well as for conducting scenario studies. This special issue aims at bringing together some of the latest results on (re)emerging tick-borne diseases and putting them in the perspective of the trends and developments in the ever-changing research field of tick-borne pathogens, with emphasis on the European continent. We see that for some disease systems, such as louping ill, TBE and Lyme disease, intensive studies over the last decades have increased our understanding of the relationship between population dynamics of the various tick-host species, tick populations and pathogen transmission. This is much less the case for other pathogens, including many emerging pathogens, and these knowledge gaps still have to be filled in order to obtain a true understanding of the role of population dynamics, land use, changes in climate, etc. Knowledge and understanding of the underlying mechanisms driving the dynamics of these complex disease systems are of vital importance if we want to minimize the burden of tick-borne diseases now and in the future.

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## Trends and changes in tick population dynamics and pathogen transmission

The population dynamics of ticks, their hosts and tick-borne pathogens are naturally closely intertwined. Ticks depend on vertebrate hosts for their blood meals, and tick-borne pathogens are maintained in a cycle between ticks and hosts. The probability of a tick to find a host for a blood meal, and hence tick survival, will depend on local host density (van Duijvendijk et al. 2015), but in some host species, a density-dependent tick resistance may develop (Randolph 1994), which may create a negative feedback loop. Also, not all host species are equally competent for transmission of each type of pathogen, which means that the composition of the local host population will also affect the transmission opportunities. At least theoretically, a larger proportion of non-competent hosts will reduce the number of bites on infectious hosts and thereby the number of infected ticks. This so-called 'dilution effect' has been demonstrated for some ecosystems (LoGiudice et al. 2003; Ostfeld and Keesing 2000). However, as non-competent hosts (e.g., deer in the case of Lyme borreliosis) provide blood meals for (adult) ticks, they also facilitate tick survival (Pacilly et al. 2014). Therefore, non-competent hosts may have a 'diluting' effect on disease transmission as well as a 'facilitating' effect on tick populations. The net effect may depend on the local species composition (Pugliese and Rosà 2008; Wilson et al. 1988). Recent work by Mannelli et al. (2012), who analyzed various multi-host systems, suggests that even hosts that are not capable of transmitting *Borrelia burgdorferi* sensu lato to the tick vector, *Ixodes ricinus* (Acari: Ixodidae), or that are secondary reservoirs for these agents, contribute to the intensity of transmission and to the overall risk of Lyme borreliosis, through the process of vector augmentation and pathogen amplification (Mannelli et al. 2012. On the other hand, above certain threshold densities, or in the presence of competition with primary reservoir hosts or low attachment rate of ticks to reservoir hosts, incompetent or less competent hosts may reduce transmission through dilution.

Tick population dynamics and pathogen transmission dynamics are also determined by abiotic factors, such as temperature and humidity. Not only do these factors determine the vegetation type and the associated host population, but they also affect the survival and questing activity of ticks (Gassner 2010; Randolph and Storey 1999). This may, for instance, determine the onset of the transmission season, or the degree of synchrony in activity of the tick life stages, which determines the co-feeding opportunities between nymphs and larva, an important factor in TBE epidemiology (Randolph et al. 2000). Altogether, population dynamics of ticks and their hosts and the resulting pathogen transmission dynamics form a highly complex system, determined by a combination of biotic and abiotic factors.

## Changes in geographical distribution and drivers of change

Land use changes and climate are known to have impact on tick ecology and therefore also on tick-borne pathogen dynamics, but due to the complex interactions and feedback loops, effects may be different for each pathogen.

A recent review paper describes the drivers of latitudinal and altitudinal spread of the important tick vector *I. ricinus* in Europe, as well as of changes in the distribution within its prior endemic zones. It discusses the many climatic, ecological, landscape and anthropogenic drivers, based on published literature and unpublished expert opinion from the

VBORNET network (Medlock et al. 2013). The authors divide the drivers into (1) those directly related to climatic change, contributing to an expansion in the tick's geographic range at extremes of altitude in central Europe, and at extremes of latitude in Scandinavia; (2) those related to changes in the distribution of tick hosts, particularly roe deer and other cervids; (3) other ecological changes, such as habitat connectivity and changes in land management; and (4) human-induced changes. Management of habitats on a landscape scale, and changes in the distribution and abundance of tick hosts are important considerations for management of public health risks associated with ticks and tick-borne disease issues in the future. The authors state that a better understanding and mapping of the spread of *I. ricinus* (and changes in its abundance) are essential to assess the risk of the spread of tick-borne infections.

Another trend in the (research of the) distribution of ticks is that more attention is being paid to habitats other than forested areas, the classic habitat. Conditions of modern urban and especially suburban environment in developed European countries adequately meet tick requirements (Uspensky 2014). A review by Rizzoli et al. (2014) indicates that urbanized areas in Europe harbor ticks infected with tick-borne encephalitis virus (TBEV) and have a high prevalence of borrelia-infected ticks. Emerging pathogens, including bacteria of the order Rickettsiales (*Anaplasma phagocytophilum*, Candidatus *Neoehrlichia mikurensis*, *Rickettsia helvetica*, and *R. monacensis*), *Borrelia miyamotoi*, and protozoans (*Babesia divergens*, *B. venatorum*, and *B. microti*) have also been detected in urban tick populations (Rizzoli et al. 2014). Understanding the ecology of ticks and their associations with blood hosts in a European urbanized environment is important for risk assessment and identification of public health strategies for control and prevention of tick-borne diseases (Rizzoli et al. 2014). Concrete control measures in urban areas could include better risk communication to the urban population, control of reservoir populations and changing other environmental conditions in parks and green areas to make them less suitable for ticks (Uspensky 2014).

The paper by Špitalská et al. (2016, this issue) also considers ticks in a non-traditional habitat in Slovakia. Previous studies have investigated ticks and rickettsiae prevalence in mountain forest, recreational areas and urban areas in Slovakia, but this is the first study to report the prevalence of *Rickettsia* species in ticks (7.3 % for nymphs, 15 % for females) in an agricultural site. Considerable temporal fluctuations in densities of questing nymphs and adults were found, and a bimodal activity pattern was observed, with peaks in spring/early summer and autumn. The results indicate that pathogenic *Rickettsia* species circulate in agricultural areas and that there is a potential risk for humans to encounter infected ticks (Špitalská et al. 2016).

Human-induced changes are of course also important. Besides the obvious effect of human activities on tick-borne disease risk via human exposure (e.g., hiking or berry-picking in forest may put people at risk of acquiring infected tick bites), humans may also affect the suitability of the landscape for ticks via their impact on land cover and land use. For instance, land abandonment may lead to more bushes, which provide good habitat for ticks and their hosts. For example, it was recently reported that the increase in *I. ricinus* population density in The Netherlands was associated with the expansion of forest areas and an increase in roe deer population, both environmental changes benefiting the resident tick population (Knap and Avšič-Županc 2015; Sprong et al. 2012). The effect of bush encroachment on tick density is the topic of the study of Vanwambeke and co-authors in this issue (Vanwambeke et al. 2016).

## Emerging tick-borne pathogens in Europe

Of the many tick-borne pathogens in Europe, *B. burgdorferi* s.l. and TBE virus are best known because of their relatively high and widespread prevalence. Other pathogens include *Babesia* spp., *Borrelia miyamatoi*, *Bartonella henselae*, *A. phagocytophilum*, Candidatus *N. mikurensis*, *Rickettsia* spp. and *Francisella tularensis*. Although many of these pathogens have been known to circulate in European ecosystems for a long time, they appear to have become more prevalent in recent years, and their geographical distribution is expanding.

On the eco-epidemiology of Lyme borreliosis and its causative agent, *B. burgdorferi* s.l., a vast body of literature has been published in the last few decades. In Europe, several of the at least 18 genospecies of the *B. burgdorferi* s.l. complex are pathogenic to humans: *B. afzelii, B. garinii, B. burgdorferi* sensu stricto, *B. bavariensis* (previously *B. garinii* OspA serotype 4) and *B. spielmanii*. For other genospecies, such as *B. lusitaniae*, *B. valaisiana* and *B. bissetii*, the pathogenicity is still uncertain. Lyme borreliosis has been present in Europe for a long time, and is not an emerging pathogen in the sense of having emerged in Europe recently. However, a review by Rizzoli et al. (2011) on the situation regarding Lyme borreliosis in Europe indicates that even though the overall prevalence of Lyme borreliosis may be stabilizing, its geographical distribution is still increasing. Also, Lyme borreliosis incidence has increased significantly in recent decades in specific areas, such as The Netherlands and Belgium (Gassner and Overbeek 2007; Hofhuis et al. 2015). A particular reason for concern is the high prevalence of *B. burgdorferi* s.l. infected ticks that has been reported from urbanized areas (Rizzoli et al. 2014). Due to the high human population density in these areas, the risk of people being exposed to infected tick bites is high.

The most important European tick-borne viruses from public health perspective are Crimean–Congo haemorrhagic fever virus (CCHFV) and TBEV (Hubalek and Rudolf 2012). The dynamics of TBE has been studied extensively in the last decades (Amicizia et al. 2013; Jaenson et al. 2012). The importance of co-feeding for the transmission cycle has been highlighted (Labuda et al. 1993; Randolph et al. 1999, 2000), and has also been modelled (Hartemink et al. 2008). Climatic factors, such as rapid spring warming has been linked to the distribution of TBE (Randolph et al. 2000), but cannot explain the whole spatio-temporal pattern (Šumilo et al. 2007). In later work by the same group, several socio-economic parameters have been suggested to explain TBE upsurges in eastern Europe (Šumilo et al. 2008). Still, the spotty distribution and the fact that TBE does not occur everywhere where *I. ricinus* is present (or even abundant, as is the case in The Netherlands) are not sufficiently explained.

Crimean–Congo haemorrhagic fever virus is an emerging tick-borne virus, with a high case-fatality rate in humans. Even though in the last decade immense progress has been made on knowledge of the biology of the virus, the clinical aspects of the disease, and the establishment of rapid and sensitive diagnostics, there are still many gaps to be filled (Papa et al. 2015). One of these is the lacking knowledge of the exact distribution of CCHFV in Southeastern Europe, and this is partly a result of a lack of proper tests. The work by Schuster and co-authors (2016, this issue) aims at investigating which ruminant species is best suited as indicator for the detection of a CCHFV circulation in an area. The prevalence rates in sheep, goats and cattle in various regions of Albania and the Former Yugoslav Republic of (FYRO) Macedonia were investigated. As there are no commercial tests available for the detection of CCHFV-specific antibodies in animals, two commercial tests

for testing human sera were adapted for the investigation of sera from sheep and goats, and new in-house enzyme-linked immunosorbent assays (ELISAs) were developed. The investigation of serum samples with these highly sensitive and specific assays (94–100 %) resulted in an overall prevalence rate of 23 % for Albania and of 49 % for FYRO Macedonia. As sero-prevalence rates were significantly lower for cattle than for small ruminants, the latter are considered to be more suitable indicator animals for CCHFV infections and should therefore be tested preferentially, when risk areas are to be identified.

Much crucial information on the eco-epidemiology of CCHFV is not yet available, but considerable progress has been made (Papa et al. 2015), also within the framework of EDENext, where much emphasis was put on getting more insight in the public health aspects of the disease (Mertens et al. 2013, 2015). Furthermore, a model for CCHFV has been developed and presented in this issue (Hoch et al. 2016).

For Louping ill, another tick-borne virus, much research and modelling has been done on the system in the UK, where the pathogen is endemic. In this issue, the current knowledge on the reservoir hosts, their effect on the dynamics of tick populations and on pathogen transmission has been reviewed by Gilbert (2016, this issue). Louping ill virus (LIV) is part of the tick-borne encephalitis complex of viruses, but differs from TBE in terms of eco-epidemiological aspects. Whereas western TBEV is found primarily in woodlands, in small rodents as reservoir, LIV is generally circulating between sheep, red grouse and mountain hares and, therefore, associated with upland heather moorland and rough grazing land. This overview also highlights the usefulness of mathematical modelling for scenario studies, assessing the effect of control measures.

This issue features a review of the emerging pathogen *Candidatus* Neoerhlichi mikurensis (Silaghi et al. 2016). It summarizes the current state of knowledge on its geographical distribution and clinical importance. Most urgent research needs are the in-vitro cultivation of the pathogen, the development of specific serological tests, the determination of the full genomic sequence, and the routine implementation of molecular diagnosis in diseased patients with a particular panel of underlying diseases. The authors also advocate promoting the knowledge about neoehrlichiosis among general practitioners, hospital physicians and the risk groups such as forest workers or immune-compromised people, to raise awareness about this disease that can easily be treated when correctly diagnosed.

The work by Berthová et al. (2016, this issue) focuses on the role of birds in the circulation of rickettsiae and *Coxiella burnetii* in natural foci (Berthová et al. 2016). They studied the natural infection of birds and (mostly immature) *I. ricinus* ticks that fed on birds with *Rickettsia* spp. and *C. burnetii* in three sites of Slovakia. Sixteen out of 43 caught bird species were infested by ticks and some birds carried more than one tick. Of the 347 birds, *C. burnetii* was detected in 0.9 %, *Rickettsia* spp. in 8.9 % and *R. helvetica* in 4.2 % of bird blood samples. Of the in total 594 specimens of bird-attached ticks (451 larvae, 142 nymphs, 1 adult female), 6.6 and 2.7 % were infected with *Rickettsia* spp. and *C. burnetii*, respectively. The study is a first step towards a better understanding of the circulation of rickettsiae and *C. burnetii* in natural foci in Slovakia, but the role of birds as reservoir is still not proven.

*Babesia* spp. are tick-borne protozoan parasites that have been reported in many European countries and are considered to be emerging pathogens. In the study of Capligina and co-authors (2016, this issue), *Babesia* spp. were detected in 1.4 % of the *I. ricinus* ticks and in 1.9 % of *I. persulcatus* ticks in Latvia. *Babesia microti*, *B. capreoli*, and *B. venatorum* were detected, with *B. microti* as the most prevalent species. The results suggest that

both *I. ricinus* and *I. persulcatus* ticks play a role in the epidemiology of these zoonotic pathogens in Latvia (Capligina et al. 2016).

## Trends in research and future directions

It is clear that for many emerging tick-borne pathogens, knowledge on the exact geographic distribution, the reservoir hosts and their relative importance in the transmission cycles, and on many other aspects of the eco-epidemiology is still lacking. Information on tick population dynamics and its influence on tick-borne pathogen transmission can only be acquired via long-term systematic field work. Standardized methods, such as the standard sampling method for questing ticks that has been used within the framework of EDEN and EDENext, ensure that all tick collections are conducted in a similar way, with similar cloth and over the same distance. This is essential in obtaining comparable field work outcomes – only then can results be compared among countries and regions, so that patterns on a larger geographic scale can be assessed and local outliers be studied in more detail. Of course, reliable tests for detection of pathogens in ticks and hosts are crucial, and for some pathogens, such as CCHFV, the development of tests in still work in progress (see also Schuster et al. 2016, this issue). Whereas the spatial geographic distribution of pathogens like babesia, rickettsia and anaplasma is still under study, as can be seen from the contributions to this special issue, the temporal dynamics are often even less well known. Also, the pathogenicity to humans is often not known. For example, in The Netherlands prevalence of rickettsia in ticks appears to be high, but no clinical cases have been reported.

Furthermore, the notion that ticks and their hosts may carry more than one pathogen at the same time should be incorporated in our thinking about tick-borne diseases. More focus on co-infection and shifting from the 'one-pathogen-one-disease' vision to the pathobioma paradigm may help to get a better understanding of the dynamics of the various pathogens and their interactions. The pathobioma paradigm entails considering the pathogenic agent integrated within its abiotic and biotic environments and taking into account the complexity of the tick microbiome, which may affect its vectorial capacity (Vayssier-Taussat et al. 2015).

## Increased use of mathematical models, statistical models and satellite data

The use of models in research on tick-borne pathogens has become increasingly popular. Mathematical models have been developed to describe the dynamics of tick populations and of tick-borne pathogens. These models are often very complex, because the population dynamics of the ticks, their hosts and the tick-borne pathogens are closely intertwined. Abiotic as well as biotic factors are known to play a role and need to be taken into account in order to capture the essential mechanisms driving the dynamics. Mechanistic mathematical models are an important tool for scenario studies; that is, assessing the potential effect of control measures, or of changes in land use or environmental conditions. This has, for instance, been demonstrated by the work of Dobson and Randolph (2011), who modelled the effect of changes in climate, host densities and acaricide treatments on *I. ricinus* population dynamics, based on a matrix model (Dobson et al. 2011). In this issue, the paper by Hoch et al. (2016) shows how $R_0$ models can be used to test potential

scenarios for the control of CCHF. As mentioned above, CCHF is an emerging zoonotic disease caused by a virus (CCHFV) and is mainly transmitted by ticks of the species *Hyalomma marginatum* in Eastern Europe and Turkey. The $R_0$ model is based on a tick population dynamics model and also considers the influence of abiotic (meteorological variables) and biotic factors (host densities). The model was used to test control strategies and especially the effect of acaricide treatment. The paper is a typical example of how modelling can help to get insight into the ability of a variety of strategies to prevent and control disease spread. Modelling has also been particularly useful in unraveling the dynamics of LIV, as was demonstrated in the paper by Gilbert (2016, this issue).

The use of species distribution models or environmental niche models for the prediction of suitable habitat for ticks, or for tick-borne pathogens, is now one of the standard tools in tick-borne disease eco-epidemiology (Randolph 2000). This type of statistical model matches observed presence/absence or abundance data to often satellite-imagery-derived environmental data, such as climatic factors, seasonality, vegetation indices or fragmentation indices (Rogers 2006). Examples of techniques and toolboxes are logistic regression, random forest, non-linear discriminant analysis, MaxEnt, and (boosted) regression trees. These modelling techniques have been applied to numerous tick-borne disease systems, such as TBE (Daniel et al. 1998; Randolph et al. 2000), CCHFV (Estrada-Peña et al. 2007), and Lyme borreliosis (Brownstein et al. 2005; Randolph and Rogers 2000; Swart et al. 2014). A recent modelling attempt yielded a map of the global distribution of CCHFV (Messina et al. 2015). As there is no description of the underlying mechanisms, these techniques are usually not suitable for predicting the effect of changes. Also, because they are based on observed presence or abundance data, they are less applicable for emerging/invasive species. There are methodological caveats, that can only partly be avoided by removing collinear variables (Estrada-Peña et al. 2015) and model outputs should, as always, be interpreted with caution. Still, these techniques enable us to form new hypotheses and to determine possible areas of higher risk, which can help direct future studies or indicate where preventive measures should be considered.

## Public health and one health

Tick-borne pathogens pose a clear public health issue, even though the impact on public health may differ substantially among pathogens, both in terms of morbidity/severity of the disease and in numbers of cases (or people at risk). For example, in The Netherlands >24,000 cases of Lyme borreliosis are reported annually, whereas reports of other tick-borne pathogens are rare in spite of their presence in *I. ricinus* (Hofhuis et al. 2015). Tick-borne diseases are a classic example of a disease system where humans and wild or captive animals share pathogens and where a 'one health' approach is needed to control the disease. Multi-disciplinary approaches have to be applied, combining expertise from a variety of disciplines, such as veterinary medicine, human medicine, ecology, acarology and public health. Combining field work, experimental work and modelling, in an iterative manner, where field work and experimental work yield parameter estimates for models, and models yield hypotheses for mechanisms and indications of putative higher- and lower-risk areas, that then can be verified via field work, has yielded useful insights in dynamics of, e.g., LIV (Gilbert 2016, this issue) and Lyme borreliosis.

For CCHFV, a 10-year research roadmap has already been sketched in a recent review (Papa et al. 2015), highlighting the need for a better understanding of the vector-virus

interaction, the impact of infection on livestock and other animals, the role of various host species in disease transmission, and the development of vaccines and treatment strategies for humans and animals. Priority future goals were identified, including the study on CCHFV dynamics in reservoirs and vectors, the study of the role of birds, climate change and reservoir/host abundance for the distribution of ticks and the establishment of new CCHFV endemic areas, the creation of an epidemiological predictive risk map and the development of countermeasures such as vaccines and treatment options.

Tick-borne diseases are clearly widely present in Europe, and their circulation can continue as long as the principle tick hosts, especially *I. ricinus*, *I. persulcatus* and *H. marginatum*, remain present. As the survival of tick*s* depends mostly on the occurrence of wildlife, and environmental and societal change can change habitat suitability for ticks and their principle blood hosts, European countries should be aware of the potential health risk(s) that these pathogens pose to their societies. Research should focus on the cause of disease emergence and tick-pathogen-host interaction, so that more effective preventive measures can be developed.

# References

Amicizia D, Domnich A, Panatto D, Lai PL, Cristina ML, Avio U, Gasparini R (2013) Epidemiology of tick-borne encephalitis (TBE) in Europe and its prevention by available vaccines. Hum Vaccines Immunother 9:1163–1171

Berthová L, Slobodník V, Slobodník R, Olekšák M, Sekeyová Z, Svitálková Z, Kazimírová M, Špitalská E (2016) The natural infection of birds and ticks feeding on birds with *Rickettsia* spp. and *Coxiella burnetii* in Slovakia. Exp Appl Acarol. doi:10.1007/s10493-015-9975-3 (this issue)

Brownstein JS, Skelly DK, Holford TR, Fish D (2005) Forest fragmentation predicts local scale heterogeneity of Lyme disease risk. Oecologia 146:469–475

Capligina V, Berzina I, Bormane A, Salmane I, Vilks K, Kazarina A, Bandere D, Baumanis V, Ranka R (2016) Prevalence and phylogenetic analysis of *Babesia* spp. in *Ixodes ricinus* and *Ixodes persulcatus* ticks in Latvia. Exp Appl Acarol. doi:10.1007/s10493-015-9978-0 (this issue)

Daniel M, Kolar J, Zeman P, Pavelka K, Sadlo J (1998) Predictive map of *Ixodes ricinus* high-incidence habitats and a tick-borne encephalitis risk assessment using satellite data. Exp Appl Acarol 22:417–433

Dobson ADM, Randolph SE (2011) Modelling the effects of recent changes in climate, host density and acaricide treatments on population dynamics of *Ixodes ricinus* in the UK. J Appl Ecol 48:1029–1037

Dobson ADM, Finnie TJR, Randolph SE (2011) A modified matrix model to describe the seasonal population ecology of the European tick *Ixodes ricinus*. J Appl Ecol 48:1017–1028

Estrada-Peña A, Zatansever Z, Gargili A, Aktas M, Uzun R, Ergonul O, Jongejan F (2007) Modeling the spatial distribution of Crimean–Congo hemorrhagic fever outbreaks in Turkey. Vector Borne Zoonotic Dis Larchmt N 7:667–678

Estrada-Peña A, Estrada-Sánchez A, Estrada-Sánchez D (2015) Methodological caveats in the environmental modelling and projections of climate niche for ticks, with examples for *Ixodes ricinus* (Ixodidae). Vet Parasitol 208:14–25

Gassner F (2010) Tick tactics. Interactions between habitat characteristics, hosts and microorganisms in relation to the biology of the sheep tick *Ixodes ricinus*. PhD thesis, Wageningen University, The Netherlands

Gassner F, Overbeek LSV (2007) Lyme disease in Europe: facts and no fiction. In: Takken W, Knols BJG (eds) Emerging pests and vector-borne diseases in Europe. Wageningen Academic Publishers, Wageningen, pp 207–223

Gilbert L (2016) Louping ill virus in the UK: a review of the host, transmission and ecological consequences of control. Exp Appl Acarol. doi:10.1007/s10493-015-9952-x (this issue)

Hartemink NA, Randolph SE, Davis SA, Heesterbeek JAP (2008) The basic reproduction number for complex disease systems: defining $R_0$ for tick-borne infections. Am Nat 171:743–754

Heyman P, Cochez C, Hofhuis A, van der Giesen J, Sprong H, Porter SR, Losson B, Saegerman C, Donoso-Mantke O, Niedrig M, Pappa A (2011) A clear and present danger: tick-borne diseases in Europe. Expert Rev Anti Infect Ther 8:33–50

Hoch T, Breton E, Josse M, Deniz A, Guven E, Vatansever Z (2016) Identifying main drivers and testing control strategies for CCHFV spread. Exp Appl Acarol. doi:10.1007/s10493-015-9937-9 (this issue)

Hofhuis A, Harms M, van den Wijngaard C, Sprong H, van Pelt W (2015) Continuing increase of tick bites and Lyme disease between 1994 and 2009. Ticks Tick-Borne Dis 6:69–74

Hubalek Z, Rudolf I (2012) Tick-borne viruses in Europe. Parasitol Res 111:9–36

Jaenson TG, Hjertqvist M, Bergström T, Lundkvist Å (2012) Why is tick-borne encephalitis increasing? A review of the key factors causing the increasing incidence of human TBE in Sweden. Parasit Vectors 5:184

Knap N, Avšič-Županc T (2015) Factors affecting the ecology of tick-borne encephalitis in Slovenia. Epidemiol Infect 143:2059–2067

Labuda M, Danielova V, Jones LD, Nuttall PA (1993) Amplification of tick-borne encephalitis virus infection during co-feeding of ticks. Med Vet Entomol 7:339–342

LoGiudice K, Ostfeld RS, Schmidt KA, Keesing F (2003) The ecology of infectious disease: effects of host diversity and community composition on Lyme disease risk. PNAS 100:567–571

Mannelli A, Bertolotti L, Gern L, Gray J (2012) Ecology of *Borrelia burgdorferi* sensu lato in Europe: transmission dynamics in multi-host systems, influence of molecular processes and effects of climate change. FEMS Microbiol Rev 36:837–861

Medlock JM, Hansford KM, Bormane A, Derdakova M, Estrada-Peña A, George J-C, Golovljova I, Jaenson TG, Jensen J-K, Jensen PM et al (2013) Driving forces for changes in geographical distribution of *Ixodes ricinus* ticks in Europe. Parasit Vectors 6:1

Mertens M, Schmidt K, Ozkul A, Groschup MH (2013) The impact of Crimean–Congo hemorrhagic fever virus on public health. Antiviral Res 98:248–260

Mertens M, Vatansever Z, Mrenoshki S, Krstevski K, Stefanovska J, Djadjovski I, Cvetkovikj I, Farkas R, Schuster I, Donnet F et al (2015) Circulation of Crimean–Congo hemorrhagic fever virus in the former Yugoslav Republic of Macedonia revealed by screening of cattle sera using a novel enzyme-linked immunosorbent assay. PLoS Negl Trop Dis 9:e0003519

Messina JP, Pigott DM, Golding N, Duda KA, Brownstein JS, Weiss DJ, Gibson H, Robinson TP, Gilbert M, William Wint GR et al (2015) The global distribution of Crimean–Congo hemorrhagic fever. Trans R Soc Trop Med Hyg 109:503–513

Ostfeld RS, Keesing F (2000) Biodiversity and disease risk: the case of lyme disease. Conserv Biol 14:722–728

Pacilly FCA, Benning ME, Jacobs F, Leidekker J, Sprong H, Van Wieren SE, Takken W (2014) Blood feeding on large grazers affects the transmission of *Borrelia burgdorferi* sensu lato by *Ixodes ricinus*. Ticks Tick-Borne Dis. 5:810–817

Papa A, Mirazimi A, Köksal I, Estrada-Pena A, Feldmann H (2015) Recent advances in research on Crimean–Congo hemorrhagic fever. J Clin Virol 64:137–143

Pugliese A, Rosà R (2008) Effect of host populations on the intensity of ticks and the prevalence of tick-borne pathogens: how to interpret the results of deer exclosure experiments. Parasitology 135:1531–1544

Randolph SE (1994) Density-dependent acquired resistance to ticks in natural hosts, independent of concurrent infection with *Babesia microti*. Parasitology 108:413–419

Randolph SE (2000) Ticks and tick-borne disease systems in space and from space. Adv Parasitol 47:217–243

Randolph SE (2001) The shifting landscape of tick-borne zoonoses: tick-borne encephalitis and Lyme borreliosis in Europe. Philos Trans R Soc Lond B Biol Sci 356:1045–1056

Randolph SE, Rogers DJ (2000) Satellite data and disease transmission by vectors: the creation of maps for risk prediction. Bull Soc Pathol Exot 1990(93):207

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

Randolph SE, Šumilo D (2007) Tick-borne encephalitis in Europe: dynamics of changing risk. In: Takken W, Knols BJG (eds) Emerging pests and vector-borne diseases in Europe. Wageningen Academic Publishers, Wageningen, pp 187–206

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

Randolph SE, Green RM, Peacey MF, Rogers DJ (2000) Seasonal synchrony: the key to tick-borne encephalitis foci identified by satellite data. Parasitology 121:15–23

Rizzoli A, Hauffe H, Carpi G, Vourc HG, Neteler M, Rosa R (2011) Lyme borreliosis in Europe. Euro Surveill Bull Eur Sur Mal Transm Eur Commun Dis Bull 16:1–8

Rizzoli A, Silaghi C, Obiegala A, Rudolf I, Hubálek Z, Földvári G, Plantard O, Vayssier-Taussat M, Bonnet S, Špitalská E et al (2014) *Ixodes ricinus* and Its transmitted pathogens in urban and peri-urban areas in Europe: new hazards and relevance for public health. Front Public Health 2:251

Rogers DJ (2006) Models for vectors and vector-borne diseases. Adv Parasitol 62:1–35

Schuster I, Mertens M, Mrenoshki S, Staubach C, Mertens C, Bruening F, Wernike K, Hechinger S, Berxholi K, Mitrov D et al (2016) Sheep and goats as indicator animals for the circulation of CCHFV in the environment. Exp Appl Acarol. doi:10.1007/s10493-015-9996-y (this issue)

Silaghi C, Beck R, Oteo JA, Pfeffer M, Sprong H (2016) Neoehrlichiosis: an emerging tick-borne zoonosis caused by Candidatus *Neoehrlichia mikurensis*. Exp Appl Acarol. doi:10.1007/s10493-015-9935-y (this issue)

Špitalská E, Stanko M, Mošanský L, Kraljik J, Miklisová D, Mahríková L, Bona M, Kazimírová M (2016) Seasonal analysis of *Rickettsia* species in ticks in an agricultural site of Slovakia. Exp Appl Acarol. doi:10.1007/s10493-015-9941-0 (this issue)

Sprong H, Hofhuis A, Gassner F, Takken W, Jacobs F, van Vliet AJ, van Ballegooijen M, van der Giessen J, Takumi K (2012) Circumstantial evidence for an increase in the total number and activity of borrelia-infected *Ixodes ricinus* in the Netherlands. Parasit Vectors 5:294

Šumilo D, Asokliene L, Bormane A, Vasilenko V, Golovljova I, Randolph SE (2007) Climate change cannot explain the upsurge of tick-borne encephalitis in the baltics. PLoS One 2(6):e500

Šumilo D, Bormane A, Asokliene L, Vasilenko V, Golovljova I, Avsic-Zupanc T, Hubalek Z, Randolph SE (2008) Socio-economic factors in the differential upsurge of tick-borne encephalitis in central and Eastern Europe. Rev Med Virol 18:81–95

Swart A, Ibañez-Justicia A, Buijs J, van Wieren SE, Hofmeester TR, Sprong H, Takumi K (2014) Predicting tick presence by environmental risk mapping. Front Public Health 2:238

Uspensky I (2014) Tick pests and vectors (Acari: Ixodoidea) in European towns: introduction, persistence and management. Ticks Tick-Borne Dis. 5:41–47

van Duijvendijk G, Sprong H, Takken W (2015) Multi-trophic interactions driving the transmission cycle of *Borrelia afzelii* between *Ixodes ricinus* and rodents: a review. Parasites Vectors 8:643. doi:10.1186/s13071-015-1257-8

Vanwambeke S, Van doninck J, Artois J, Davidson RK, Meyfroidt P, Jore S (2016). Forest classes and tree cover gradient: tick habitat in encroached areas of southern Norway. Exp Appl Acarol. doi:10.1007/s10493-015-0007-0 (this issue)

Vayssier-Taussat M, Kazimirova M, Hubalek Z, Hornok S, Farkas R, Cosson J-F, Bonnet S, Vourch G, Gasqui P, Mihalca AD et al (2015) Emerging horizons for tick-borne pathogens: from the "one pathogen–one disease" vision to the pathobiome paradigm. Future Microbiol 10:2033–2043

Wilson ML, Telford SR, Piesman J, Spielman A (1988) Reduced abundance of immature *Ixodes dammini* (Acari: Ixodidae) following elimination of deer. J Med Entomol 25:224–228