Invited Review

The ecology of tick-borne diseases

Miriam Pfäffle *, Nina Littwin, Senta V. Muders, Trevor N. Petney

Zoological Institute, Department of Ecology and Parasitology, Karlsruhe Institute of Technology, Kornblumenstrasse 13, 76131 Karlsruhe, Germany

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ABSTRACT

Zoonotic diseases are major causes of infection related morbidity and mortality worldwide. Of the various arthropods capable of transmitting pathogens that cause such diseases to humans, ticks, which are vectors of more kinds of pathogens than any other group of invertebrate, have become an increasing focus of attention. This is particularly the case in the temperate northern hemisphere where they are a significant vector of human disease. Here, we provide an overview of the complex ecological systems defining the various epidemiological cycles of tick-borne diseases. We highlight the abiotic and biotic factors influencing the establishment and persistence of tick populations and their associated pathogens. Furthermore, we emphasize the dynamic nature of such systems, especially when they are under the influence of both small and large-scale anthropogenic changes to the environment. Although a great deal of work has been done on ticks and the diseases which they transmit, the very dynamism of the system means that new factors are continually arising which shift the epidemiological pattern within specific areas. We therefore consider that more detailed, long-term (i.e. at least 10 years), multidisciplinary studies need to be carried out to define why and how these pattern shifts take place and to determine their public health significance.

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1. Introduction

1.1. Zoonotic diseases and ticks

Ticks transmit more pathogen species than any other group of blood-feeding arthropods worldwide (Durden, 2006), affecting humans, livestock and companion animals. Probably all tick-borne diseases (TBDs) are zoonotic while anthropogenic diseases including mosquito-transmitted diseases such as malaria, caused by *Plasmodium falciparum* and *Plasmodium vivax*, do not appear to have evolved into zoonoses. There is one possible exception in the relapsing fever pathogen, *Borrelia duttoni*, which was long considered to be anthropogenic. Recent evidence, however, has shown that this species can infect domestic pigs and chickens and that it is probably also zoonotic (McCall et al., 2007).

Tick-borne zoonoses have been known since the second half of the 19th century (Hoogstraal, 1967; Hoogstraal, 1977. Tick-borne diseases of humans – a history of environmental and epidemiological changes. Medical Entomology Centenary. Symposium Proceedings, pp. 48–55.) and represent some of the world's most rapidly expanding arthropod-borne diseases (Committee on Lyme Disease and Other Tick-Borne Diseases: The State of the Science; Institute of Medicine, 2011). Diseases such as tick-borne encephalitis

(TBE) and Rocky Mountain spotted fever, although known for many years, were either locally confined and/or showed a low prevalence of infection (e.g. Wolbach, 1919; Chumakov and Seitlenok, 1940). The major impact of TBDs on the general public in Europe and North America first became evident with the detection of *Borrelia burgdorferi* as the causative agent of Lyme disease (LD)) in the 1980s (Burgdorfer et al., 1982; Granström, 1997) and the recognition of its medical significance, wide distribution and high prevalence (O'Connell et al., 1998; Sood, 2002). Since then the number of recognized, medically important TBDs has increased dramatically, undoubtedly due to the stimulus generated by the impact of LD. For instance, more than 10 new *Rickettsia* spp. pathogenic to humans have been described since 1984, and the notifiable TBDs in the United States of America (USA) increased from two in 1990 to five in 1998 (Paddock and Telford, 2011). Not only is the number of newly recognized TBDs increasing, but also the number of case reports. For instance, the reported numbers of LD in the USA increased by 101% in a 14 year period between 1992 and 2006 (Bacon et al., 2008). In Germany, TBE is notifiable country-wide and cases of borreliosis have become notifiable in nine federal states over the last few years (Robert Koch Institute, http://www.rki.de/DE/Content/Infekt/EpidBull/Merkblaetter/Ratgeber_LymeBorreliose.html#doc2398672bodyText13, accessed 22 July 2013). During the last two decades, new endemic foci of TBE and an increase in the number of cases have been reported throughout Europe. Even in Austria, where the coverage of vaccination is high and incidence has decreased by 90%, the risk of an unvaccinated person

* Corresponding author. Tel.: +49 721 608 42701; fax: +49 721 608 47655.
E-mail address: miripfaeffle@web.de (M. Pfäffle).

contracting TBE is likely to be higher now than 30 years ago (Lindquist and Vapalahti, 2008).

In this review our aim is to provide a broad overview of the abiotic and biotic factors which influence the distribution and abundance of predominantly ixodid ticks, to consider how these factors influence the transmission dynamics of tick-borne pathogens (TBPs), and finally to consider how the anthropogenic changes to the environment, both at small and at large scales, influence these dynamics. We will also highlight certain controversial aspects of the complex, dynamic host-tick-pathogen system and point out the need for strong interdisciplinary cooperation in order to elucidate the reasons for current changes in tick distribution and abundance.

Although the number of publications on tick ecology and tick-borne disease in increasing rapidly, most of these are short-term studies, only considering a single aspect within the complex host-tick-pathogen system, and are often based on limited data sets. For a full understanding of the epidemiology of these diseases, it is essential to understand the complex interaction between ticks, their hosts, their environment and the pathogens which they transmit over a long enough period to be able to determine annual variation (Ostfeld et al., 2006). This cannot be done by ecologists alone because geological, geoecological and climatic factors, including global climate change, are important, as are changes in landscape, land use and human behaviour leading to increased (or decreased) contact times with infected ticks.

1.2. Ticks as vectors

To date, almost 900 tick species have been described. These are divided into three families: the Argasidae or soft ticks (191 species), the Ixodidae or hard ticks (701 species) and the Nuttalliellidae consisting of only one species, *Nuttalliella namaqua* (Guglielmone et al., 2010). The generic taxonomy of argasid ticks is currently highly controversial with different authorities listing between four and 10 valid genera (Guglielmone et al., 2010). The genera *Argas*, *Ornithodoros* and *Carios*, if recognized, are all of medical importance for humans. *Argas monolakensis*, for example, transmits Mono Lake virus, while various relapsing fever *Borrelia* spp. are transmitted by a variety of *Ornithodoros* spp. (Estrada-Peña and Jongejan, 1999; Jongejan and Uilenberg, 2004). The Ixodidae consist of 13 current genera of which the most important for humans are *Amblyomma*, *Dermacentor*, *Haemaphysalis*, *Hyalomma*, *Ixodes* and *Rhipicephalus* (Estrada-Peña and Jongejan, 1999; Guglielmone et al., 2010).

Each ecological, physiological and behavioral characteristic of a tick determines the likelihood and route of contact with its host, as well as its ability to survive and transmit a pathogen, therefore directly affecting its performance as a vector (Randolph, 1998). Ticks differ from other arthropod vectors in various ways and they open up habitats for pathogens in areas where, for example, mosquitoes are not able to transmit diseases due to constraining abiotic factors (L'vov and Gostinshchikova, 1970). Their low mobility forces them into a way of life which makes them more vulnerable to a wide range of changing climatic conditions (questing on vegetation) or to specialized protective host responses (living in or near nests or the burrows of their hosts) (Randolph, 1998). They usually invest less energy in finding a host than flying vectors but can use their energy reserves to survive for relatively long periods, in some cases for many years (Oliver, 1989). They also use, compared with other arthropod vectors, more energy in the uptake of a usually large blood meal, which enhances the tick's potential as a vector (Randolph, 2004a). Unlike other blood-feeding arthropods, with some exceptions, every life history stage of a tick feeds only once before moulting or oviposition (female argasids feed several times and lay eggs after each blood meal), but feeding occurs over a

prolonged period, in some ixodid species up to 14 days (Kröber and Guerin, 2007). While insect vectors approach many different host individuals per generation, members of the Argasidae feed on very few hosts and members of the Ixodidae on a maximum of three individual hosts per lifetime (Oliver, 1989).

In order to use a tick as a vector, a pathogen must survive trans-stadially (from one life history stage to the next) or, more rarely, trans-ovarially from female to egg. Thus the pathogen has to maintain itself through the tick's developmental phases, which can last several months to years depending on the species and environmental conditions, and then through transmission to a new host. This means that a pathogen depends heavily on the development, survival and reproductive rate of its tick vector and the tick's developmental, stage-specific host relationships (Randolph, 1998). A tick's way of life usually precludes the pathogen's use of alternative transmission routes and therefore limits the distribution of TBDs to areas where its tick vector and its hosts are able to survive and establish stable populations.

2. Factors influencing tick distribution and abundance

Tick-borne diseases such as LD occur in environments where the presence of vector-competent ticks, the aetiological agent and reservoir hosts overlap (Barbour and Fish, 1993). Human exposure to tick-borne pathogens, in turn, can only occur within these geographic locations (Gage et al., 2008; Jaenson et al., 2012). Therefore, a habitat suitable for the presence and propagation of tick-borne pathogens has to primarily meet the basic requirements of the ticks and their hosts.

2.1. Microclimate and climate

The microclimate is composed of the suite of micro-scale climatic conditions measured in defined areas, for example, near the ground surface (Geiger, 1965; Chen et al., 1999), including temperature, wind speed, degree of exposure, saturation deficit (SD) and soil moisture. Variations in microclimate can increase or decrease the survival chances and the developmental rate of a tick, induce changes in population growth, behavior, susceptibility to pathogens, incubation period of pathogens, seasonality of activity and pathogen transmission (Norval, 1977; Campbell and Glines, 1979; Koch and Dunn, 1980; Fujimoto, 1989; Peavey and Lane, 1996; Hunter, 2003; Süss, 2003; Brownstein et al., 2005; Dantas-Torres and Otranto, 2011).

This applies not only to hard ticks but also to soft ticks, both of which show very narrowly defined temperature and SD tolerance ranges for development, activity and survival (Vial, 2009). The measure of water content and therefore the drying power of the air, which is a measure of the likelihood/length of tick survival, are best expressed as SD. Many studies also use relative humidity (RH), which, when it reaches a certain threshold, is an indication of the tick's ability to rehydrate. For example, *Ixodes ricinus*, *Dermacentor variabilis* and *Amblyomma cajennense* only survive when the RH in their microhabitat is not lower than 80% for extended periods of time (Kahl and Knülle, 1988). The longevity of these species is drastically shortened when the equilibrium humidity drops below 80% (Knülle, 1966).

The overall tolerance to temperature extremes and desiccation, however, varies with species, developmental stage, sex, age and physiological condition (Needham and Teel, 1991). Unfed larvae of *Rhipicepalus sanguineus* sensu lato (Kolonin, 2009; Dantas-Torres, 2010; Guglielmone et al., in press) show a higher heat stress resistance and tolerate 1 h of exposure to temperatures up to 50 °C at a RH of 97% while*Ixodes scapularis*, a tick which is associated with high humidity and mild winter temperatures, displays

high mortality rates at temperatures of only 30 °C (Yoder et al., 2006). Madder et al. (2005) compared the survival of adults of two African ticks in relation to different temperature and RH conditions. The survival rate of *Rhipicephalus zambesiensis*, a tick adapted to hot and dry conditions, was higher under extreme conditions with higher temperatures and lower RH than that of *Rhipicephalus appendiculatus*, which is found in cooler and wetter areas.

Interstadial development, such as pre-oviposition, pre-eclosion and premoult periods, depends on the ambient temperature, with very low and very high temperatures and high SDs potentially preventing successful hatching and development by increasing mortality (Ogden et al., 2004, 2008a; Petney et al., 2011). For *I. ricinus*, climate plays an important role at the northern limit of its distribution (Dautel and Knülle, 1997). The damaging effects of very cold temperatures are cumulative and increase the winter mortality rate, especially in diapausing engorged larvae and nymphs (Gray, 1981; Dautel and Knülle, 1997). Additionally, the moulting stages of this tick are very vulnerable to cold temperatures, meaning that if summer temperatures do not favour complete development before the onset of winter, they are unlikely to survive moderate frosts (Gray et al., 2009). The southern limit of the distribution of this species is determined by high temperatures and SDs leading to unsuitable environmental conditions (Estrada-Peña, 2001b).

For *I. scapularis*, the colder the environment, the longer the interstadial developmental periods, the total generation time and the greater the proportion of ticks that die before reproduction (Ogden et al., 2006b). Additionally, in an 8 year study on *I. scapularis* populations in a LD focus in Illinois, USA, Jones and Kitron (2000) related extreme weather events such as drought in 1 year with decreasing larval density on both the vegetation and the tick's most important host, the white-footed mouse (*Peromyscus leucopus*). In contrast cumulative rainfall was positively correlated with larval density.

Questing ticks are exposed to variable climatic conditions, which often do not correspond to their equilibrium humidity and thus lead to water loss (Knülle and Rudolph, 1982). To prevent desiccation, ticks leave their questing spot occasionally and return to the leaf litter, where the RH is higher, in order to rehydrate. The questing duration is negatively correlated with the SD in the case of *I. ricinus* (Perret et al., 2004), which means that the hotter and drier the environment, the less time ticks spend questing on the vegetation.

The preferred questing conditions vary between the nymphs of two tick species which can be found in similar habitats in the USA. *Amblyomma americanum* and *I. scapularis* differ in the time of day and microclimatic conditions at which they prefer to quest. *Ixodes scapularis* is predominantly found early and late when temperatures and SD are lower (higher humidity), while *A. americanum* is more often found in the late morning and early afternoon, when temperatures and SD are higher (Schulze et al., 2001; Schulze and Jordan, 2003). *Ixodes scapularis* is substantially less tolerant to higher SDs than *A. americanum*. Its activity period thus occurs at a time when the danger of desiccation is lowest, which at the same time is correlated with the main activity period of one of its main hosts, the white tailed deer, *Odocoileus virginiana*. The reasons for the daytime questing of *A. americanum* are much less clear. Although much more tolerant to high temperatures and SDs, it also attaches predominantly to nocturnal and crepuscular hosts. Schulze and Jordan (2003) suggested that this tick may actively seek out its hosts when they are resting during the daylight hours.

Both species transmit zoonotic disease to humans but the spectrum of these diseases differs. *Amblyomma americanum* is a vector of *Ehrlichia chaffeensis*, the causative agent of human monocytic ehrlichiosis, *Ehrlichia ewingii* (human and canine granulocytic ehrlichiosis), *Borrelia lonestari*, which has been associated with a rash,

Francisella tularensis (tularemia) as well as various *Rickettsia* spp. (Goddard and Varela-Stokes, 2009). *Ixodes scapularis* is the most important vector of *B. burgdorferi* (LD) in North America and also transmits *Anaplasma phagocytophilum* (human anaplasmosis) and *Babesia microti* (human babesiosis) (De la Fuente et al., 2008). Thus, the pattern of human activity, whether mornings, evenings or at midday, will determine the likelihood of which diseases can be contracted.

Most ticks show seasonal variation in activity, differing between species and developmental stages. Nymphs of *Ixodes pacificus* show different seasonal activity patterns, depending on the type of habitat and the related climatic factors. Under dryer and warmer conditions, nymphs begin to quest earlier and have an overall shorter activity peak than under colder and more moisture-rich conditions (Eisen et al., 2002). A similar pattern exists for *I. ricinus* in Europe. In central Europe, northern England and Scotland, nymphs and adults (sometimes larvae) show a bimodal pattern, with activity peaks in spring and autumn, while *I. ricinus* from Ireland and southern England have only one peak in spring or early summer (Kurtenbach et al., 2006). This is related to a milder climate in Ireland and southern England provided by the Gulf Stream. Burri et al. (2011) point out in a study on *I. ricinus* in Switzerland that milder temperatures allow activity earlier in the year, whereas questing behavior is delayed in areas with lower average temperatures (e.g. in higher altitudes) due to delayed development caused by colder climatic conditions (Jouda et al., 2004). Such changes in development lead to changes in the patterns of seasonal activity making tick cohorts available to different diapause windows (Gray et al., 2009). Randolph (2002) quantitatively analyzed the population dynamics of *I. ricinus* in England, providing a model for such work in other areas within the distributional range of *I. ricinus* where climatic and habitat conditions vary substantially from those found in the UK.

2.2. Habitat characteristics

Ixodid ticks spend up to 99% of their lives off the host, except for one- and two-host ticks which normally live in arid, harsh environments where off-host survival is difficult (Oliver, 1989). The microclimatic characteristics discussed above are directly dependent on the characteristics of the habitat in which the tick and their hosts live (Norval, 1977; Chilton and Bull, 1994; Adeyeye and Phillips, 1996; Chilton et al., 2000; Gage et al., 2008). The canopies of woody plants, for example, modify the microclimate beneath and around them by intercepting precipitation and by shading, which influences the soil moisture (Breshears et al., 1998). In contrast to intercanopy patches, canopy patches normally have lower soil temperatures during warmer and higher soil temperatures during colder days as a result of shading and leaf litter accumulation (insulation effect). They additionally receive less rainfall due to foliar interception (Pierson and Wight, 1991; Breshears et al., 1997, 1998). The soil temperature itself has an influence on soil evaporation, with increasing temperatures leading to an increase in evaporation rates (Hillel, 1980). Therefore, more shielded habitats with a permanent leaf litter layer providing a more constant microclimate benefit the development of ticks and the establishment of tick populations. It is this specific microclimate that must be considered when discussing tick survival (Daniel and Dusabek, 1994). SD and RH also depend on the soil water content and soil pore size, which can influence the ticks' ability to hide from direct sunlight, for example in desert environments (Fielden and Rechav, 1996; Schwarz et al., 2009).

For *I. ricinus*, undergrowth and shrub cover provide an intermediate temperature but a high humidity, and more ticks are found in deciduous than in coniferous forests (Schwarz et al., 2009; Williams and Ward, 2010). Lindström and Jaenson (2003) investigated

the influence of different vegetation types on the abundance of *I. ricinus* in Sweden. The abundance of nymphs was significantly higher in forest areas compared with open fields, while the highest abundance was found in beech forests (40 nymphs/100 m^2). In warmer Mediterranean climates, *I. ricinus* is more abundant in habitats with secondary plant growth such as river canopies, heterogeneous pine forests or deciduous heterogeneous forests, as Estrada-Peña (2001a) revealed in a study from Spain. This was attributed to the shrub cover and litter depth in forest habitats creating more favorable microclimatic conditions than open fields.

A study on *I. scapularis* in Wisconsin, USA showed that the presence and abundance of this tick varied in different habitats, although the host populations were adequate (estimated by small mammal trapping) (Guerra et al., 2002). Here too, tick presence correlated positively with deciduous forests and negatively with grasslands. This applies for a number of other tick species (see e.g. Semtner et al., 1971; Kolonin et al., 1981; Fourie et al., 1996).

Altering suitable habitats by either mechanical and/or chemical treatment can change the microclimate in a way that negatively affects tick populations and their development (Hoch et al., 1971). This was nicely demonstrated by Meyer et al. (1982) who investigated the potential for habitat modification, which changed both microclimatic temperature and humidity conditions, together with animal control and standard spraying as control methods against *A. americanum*. Of these, only habitat modification was successful in reducing both free-living nymphs and tick burdens on cattle.

The "Normalized Difference Vegetation Index" (NDVI), which gives a measure of photosynthetic activity on the ground, derived from a combination of the red and near-infra-red channels of satellite data, has been shown to be a good predictor of tick (and TBD) abundance and can explain more than 50% of the variation in tick abundance in an area (Estrada-Peña, 2001b). Kitron and Kazmierczak (1997) used the NDVI to identify vegetation and differentiate between agricultural land and wooded areas in Wisconsin. They found that high NDVI values in spring and fall were strongly correlated with both *I. scapularis* distribution and human disease incidence. Using the NDVI to predict the future distribution of *I. scapularis* in Canada, Ogden et al. (2006a) suggested that tick populations would be able to establish in more northern woodland areas, in contrast to Carolinian forests where most populations now occur. Nevertheless, it is not possible to use the NDVI as a universal index to predict tick distribution. *Rhipicephalus appendiculatus* distributions correlated with NDVI values in Kenya, while in the neighboring Ethiopia this tick does not occur (Kolonin, 2009), despite suitable vegetation (NDVI) and climatic values (CLIMEX) (Perry et al., 1991). Although the CLIMEX model is outdated – it cannot capture fine-scale suitable habitats and is not able to simulate local specific population dynamics – other statistical analyses and more recent models also detected the habitat suitability of the Ethiopian Highlands for *R. appendiculatus* (see Randolph, 1999; Leta et al., 2013). The most likely cause for the absence of this species in the Ethiopian Highlands, despite suitable habitat and host populations, is that this tick is has not been introduced from eastern African countries, where it is endemic, due to natural, physical barriers between these countries which are unsuitable for tick survival (Leta et al., 2013).

2.3. Hosts

2.3.1. Host suitability and tick dispersal

Access to potential hosts species and their population densities are critical for the development and survival of ticks (Kirstein et al., 1997; Gray et al., 1999; Estrada-Peña, 2001b; Wood and Lafferty, 2012). For some tick species, such as the generalist *I. ricinus*, which occurs on hundreds of different hosts including reptiles, birds and mammals, the presence of a potential host is likely in most habitats, whereas other species may only be found on one or a few host species, e.g. *Ixodes lividus* which is specific for sand martins, *Riparia riparia* (Ulmanen et al., 1977; Petney et al., 2011). The persistence of specialist ticks therefore relies on the presence of these host species and can be severely threatened if their hosts are endangered, probably leading to co-extinction if their host should die out (Durden and Keirans, 1996; Miller et al., 2007; Mihalca et al., 2011).

The behaviour of hosts is an important factor in the distribution and dispersal of ticks (Estrada-Peña, 2001b; McCoy et al., 2001), which have only limited independent movement (McCoy et al., 1999; Miller et al., 2007; Petney et al., 2011). The movement of hosts through the landscape facilitates dispersion, including invasion into new regions (Léger et al., 2013). The chance of being picked up by a suitable host is increased by high population densities and diverse communities of hosts, which might be a reason for the predominant association of many species of hard tick larvae and nymphs with small mammals (Krasnov et al., 2002; Kiffner et al., 2011b). Such mammals, in particular, offer the immature stages of ixodid ticks the advantage of reaching suitable feeding sites (Schwarz et al., 2009; Kiffner et al., 2011b), wheareas big game animals offer large blood meals, serving as key hosts for adult ticks and more strongly influencing tick distribution (Wilson et al., 1984; Duffy et al., 1994; Estrada-Peña, 2001b; Léger et al., 2013).

Red deer (*Cervus elaphus*) and roe deer (*Capreolus capreolus*) are common and well-studied species in Europe (De la Fuente et al., 2004; Kiffner et al., 2010) which are frequently parasitized by *I. ricinus*, *Dermacentor marginatus* and *Hyalomma marginatum* (Pichon et al., 1999; Ruiz-Fons et al., 2006; Kiffner et al., 2010). Roe deer is the most synanthropic and widespread deer species in Europe and plays an outstanding role as a host for ticks (Rizzoli et al., 2009; Vor et al., 2010; Kiffner et al., 2011a). Tick abundance is positively correlated with deer abundance and hence zones with a high density of cervids are considered areas with a higher disease risk (Pichon et al., 1999). The most important cervid species in North America is the white-tailed deer (*Odocoleus virginianus*) which is a suitable host for the tick species *I. scapularis* (Smith et al., 1990; Fish and Childs, 2009). Deer numbers have increased significantly over the last century throughout Europe (Fuller and Gill, 2001) and North America (Nelson et al., 2000).

Besides the high population densities of these hosts, ticks may also profit from their social activities: adult roe deer are territorial in spring and summer, which involves the dominant male chasing away subadult or subdominant individuals, providing the chance for ticks to be distributed quickly and effectively over long distances. Roe deer are known to migrate more than 100 km, although distances up to a few kilometres are usual (Mysterud, 1999; Vor et al., 2010). White-tailed deer have been documentend to travel 23–45 km in 31–356 h (minimum 2.1–18.6 km/day) over two to four periods of travel (Nelson et al., 2004), increasing the range and distribution of associated ticks such as *I. scapularis*.

Since birds are highly mobile and can travel great distances in a relatively short time, they are also likely to play a major role as dispersers of ticks and TBD agents (Olsen et al., 1995; Bjöersdorff et al., 2001; Gern, 2008). Ogden et al. (2008b) estimate that migratory birds disperse 50–175 million *I. scapularis* ticks across Canada each spring, implicating migratory birds as significant in tick range expansion.

Once introduced into a new and appropriate ecosytem, ticks may infest suitable local animals or even evolve associations with new hosts. In New Caledonia, for example, the cattle tick *Rhipicephalus* (*Boophilus*)*australis* (previously recognized as *R.* (*B.*) *microplus*; *R. australis* was reinstated for Australia and New Caladonia by Estrada-Peña et al. (2012a,b) has evolved in contact with two sympatric host species into two differentiated genetic pools: on cattle, its original host and on rusa deer (*Rusa timorensis*), a new host for the tick (De Meeus et al., 2010). This genetic isolation, while in

sympatry, has occurred over a relative short period of time, within fewer than 244 tick generations (De Meeus et al., 2010).

2.3.2. Acquired resistance against ticks

Tick infestation and the development of pathogens in both ticks and their vertebrate hosts are mediated by species-specific molecular mechanisms (Rubaire-Akiiki, 1990; De la Fuente et al., 2008), but are also modified by the host individual's age, sex and immune status (Kazmierczak and Burgess, 1989; Szep and Moller, 1999).

The immune system of the host is stimulated by both the infestation of the tick and infection with TBPs (Brossard and Wikel, 2004). The immune system of the host activates innate and acquired host defenses against infestation, the latter involving humoral and cellular immunoregulatory and effector pathways (Wikel and Bergman, 1997). Tick feeding induces a complex array of host immune regulatory and effector responses involving antigen-presenting cells, cytokines, immunoglobulins, complement and T-lymphocytes (Wikel et al., 1997). The development of acquired resistance can lead to an influx of cells into the dermis and the epidermis surrounding the tick's mouthparts (Wikel and Bergman, 1997). Basophils together with eosinophils are recruited to the site of tick attachment and induce tick rejection by local basophil degranulation (Brown et al., 1982). Basophil infiltrates also increase the vascular permeability at tick feeding sites, causing enhanced oedema formation, providing only a protein-low serum (Ribeiro, 1989). Histamine produced by the host inhibits tick salivation and engorgement (Wikel, 1996). Langerhans cells trap salivary antigens and migrate to the lymph nodes where they act as antigen-presenting cells for specialized lymphocytes. Antibodies against tick-specific antigens are produced and contribute, together with the complement, to acquired resistance (Allen et al. 1979; Nithiuthai and Allen, 1985).

Although ticks have evolved countermeasures to suppress host immune reactions and to facilitate blood ingestion, the balance between host defense and tick induced modulation of host defense is quite an important factor for tick survival and pathogen transmission (Brossard and Wikel, 2004). The bank vole (Myodes glareolus) is a natural host for I. ricinus but develops acquired resistance to these ticks, which can be generally expressed by reduced attachment success, engorgement size and weight, and tick survival (Wikel and Bergman, 1997; Hughes and Randolph, 2001b). This is also the case for infestations of M. glareolus with Ixodes trianguliceps (Randolph, 1994). However, acquired resistance to I. ricinus or I. trianguliceps does not develop in the yellow-necked mouse, Apodemus flavicollis, which is another natural host for these species (Randolph, 1994; Dizij and Kurtenbach, 1995).

Acquired resistance has also been shown in other host-tick systems, e.g. the resistance of European (Bos taurus) and zebu cattle (Bos indicus) to R. (B.) australis (= microplus) (Riek, 1962) or of rabbits to R. appendiculatus (Dobbelaere et al., 1987; Fivaz et al., 1991). Nevertheless, acquired resistance and the intensity of reaction depend on host species and the rate of exposure to tick infestation (Randolph, 2001). As an additional complicating factor, host hormone status may also influence the development of immunity. Hughes and Randolph (2001b) showed that testosterone affects the acquired resistance to I. ricinus in M. glareolus. High testosterone levels lead to reduced innate and acquired resistance against the ticks and their associated pathogens in the hosts.

3. Factors influencing transmission dynamics

In order for an infection to become established or a pathogen to be transmitted at least two ticks have to feed on the same individual host, not necessarily at the same time, one infecting the host (this infection has to become established in the host) and one

becoming infected via the host. This pattern may be modified by tick-to-tick transmission (co-feeding). One characteristic of ticks or parasites in general, is their tendency to occur in an aggregated or overdispersed pattern, both in a host population as well as on an individual host (e.g. Andrews et al., 1982; Petney and Fourie, 1990; Petney et al., 1990). This facilitates the co-feeding process in which the host does not become infected but an uninfected tick ingests the pathogen when an infected tick introduces the pathogen to the host via its saliva and an uninfected tick feeding alongside the infected tick ingests the pathogen (Labuda et al., 1993a,b). Thus even if the host itself does not become infected, it is required for disease transmission between the different tick life history stages. For example, in contrast to B. burgdorferi sensu lato (s.l.), where patent infections can persist in a susceptible host over weeks and months, the viraemia caused by infections with TBE virus (TBEV) is less persistent, making it less likely that the pathogen is transmitted through an infected host but through ticks in which an infection can persist throughout their life (Nosek et al., 1967). Transmission of TBEV normally occurs via co-feeding, with infected nymphs feeding on the same host at the same time as uninfected larvae (Labuda et al., 1993a,b). Therefore, the maintenance of TBE foci depends on large numbers of uninfected larvae feeding next to infected nymphs on a rodent host.

3.1. Abiotic conditions

3.1.1. Climate

The close relationship between pathogens and their tick vectors makes the pathogens susceptible to the abiotic factors affecting ticks. For instance, the likelihood of R. sanguineus, a vector of Rickettsia conorii (the causative agent of Mediterranean spotted fever) and Rickettsia rickettsii (Rocky Mountain spotted fever), attaching to hosts other than dogs, including humans, increases with warmer summer temperatures. This is related to a warming-mediated increase in the host-seeking behaviour of R. sanguineus leading to a higher risk of infection with Rickettsia spp. (Parola et al., 2008; Socolovschi et al., 2009).

Bioclimatic threshold temperatures affect the transmission of TBDs (Lindgren et al., 2000). The occurrence of LD in the northeast of the USA is correlated with monthly precipitation, drought events and temperature, with late spring and early summer precipitation being the most significant climatic factors related to the disease incidence (Jones and Kitron, 2000; Estrada-Peña, 2002; McCabe and Bunnell, 2004).

If the activity of I. ricinus begins earlier in the year or indeed continues throughout winter there will be an increase in the duration over which transmission can occur (Burri et al., 2011). However, climatic conditions and thus transmission likelihood are also dependent on altitude. Thus the prevalence of B. burgdorferi s.l. infections in nymphs was negatively correlated with altitude in a Swiss study, reducing the likelihood of transmission in higher areas (Jouda et al., 2004). Locally, focal warm and dry climatic conditions reduce the questing density of I. ricinus, the proportion of hosts with co-feeding larval and nymphal ticks and, therefore, the transmission efficiency of enzootic TBEV (Burri et al., 2011).

From the standpoint of the pathogen, infection with B. burgdorferi spirochetes in nymphs kept at temperatures of 27 °C or less for 6 months was persistent, while only 10% of nymphs kept at 30 °C and 0% of nymphs kept at 37 °C maintained their infections (Shih et al., 1995). Nymphs were already unable to infect rodent hosts after being incubated at temperatures higher than 27 °C for 2 weeks (Shih et al., 1995).

Estrada-Peña et al. (2012a,b) discussed the limited literature currently available on the direct role of temperature on disease transmission and suggested that tick stress response (TSR), questing behavior and pathogen transmission are interconnected. TSR

can be initiated by temperature changes and works against the negative effects of heat shock and pathogen infection on the questing behavior as well as the longevity of ticks.

3.1.2. Habitat characteristics

Ticks find their hosts either passively by questing on vegetation, waiting in a host's nest or burrow or actively by moving toward more distant stimuli. Micro- and macroclimatic factors influence this behavior (Knap et al., 2009) and are therefore likely to decrease or increase the human risk of becoming infected with a TBP (Rizzoli et al., 2009).

As ticks are passive dispersers, not every habitat that is basically suitable for the establishment of tick populations actually harbours ticks and thus TBP transmission is not possible in these areas. A variety of other landscape parameters, such as habitat connectivity, also contribute to the potential establishment of a stable vector population and, therefore, habitat suitability for the occurrence of TBPs (Estrada-Peña, 2003).

The requirements of *I. ricinus* for specific temperature and SD conditions are consistent with the factors stated by Montomoli (2009, A new seroepidemiological survey in Italy. Lecture, ISW Vienna, http://www.isw-tbe.info, accessed 24 April 2013), providing optimal habitat and microclimatic conditions for TBEV infection of ticks, namely an average annual temperature of approximately 8 °C, a high RH and earth moisture ⩾92%. Infected ticks are frequently found in areas where different types of vegetation are located in close proximity (Montomoli, 2009. A new seroepidemiological survey in Italy. Lecture, ISW Vienna, http://www.isw-tbe.info, accessed 24 April 2013), such as around the edges of forests with neighbouring vegetation such as grassland, forest clearings, river meadows and marshlands, forest plantations with thick undergrowth and shrubs, and in transient areas between deciduous and coniferous forests (Süss, 2003).

Lindström and Jaenson (2003) stated that reforestation in Sweden was likely to increase *I. ricinus* abundance and, in addition, the risk of TBP transmission because forest ecosystems act as a buffer and prevent climatic extremes and excessive microclimatic variability. A study carried out in the State of New York, USA, showed that the composition of fine scale structures such as understory vegetation may steer vector density and allow prediction of the prevalence of infection in small mammals, with an increasing understory density of herbaceous foliage and underbrush shrubs leading to increasing prevalences of *B. burgdorferi* in small mammal hosts (Prusinski et al., 2006).

The distinction between the wide range of vegetated land cover types included in such habitats in Europe and North America, especially between arable and abandoned fields, confirms the negative impact of agricultural land on TBE incidence (Vanwambeke et al., 2010). An examination of land cover variables such as landscape composition revealed that a greater area, larger patch size of forest, and known habitat for vectors and hosts were related to higher disease incidence (Vanwambeke et al., 2010). Conversely, TBE incidence was lower not only where there were relatively large areas of unfavorable land cover, such as arable land, but also where forests were surrounded by more agricultural land (Vanwambeke et al., 2010).

3.2. Hosts

Although both the host and the tick can serve as reservoirs for a wide range of viral, bacterial and protozoan pathogens (Socolovschi et al., 2012), vector potential is severely constrained by the contact rates between hosts and ticks per blood meal (Randolph, 2004a). In addition, host competence is determined by complement sensitivity or resistance. This is both host as well as pathogen-specific and is one of the crucial factors governing host-pathogen relationships, as complement-mediated killing determines the reservoir competence of a host species (Bhide et al., 2005). Thus, the species-specific pattern of viability and/or lysis of pathogens determine the reservoir competence of hosts and, hence, play a key role in the tick infection rate (Kurtenbach et al., 1998; Gern, 2008). In the case of specific host-pathogen relationships this might result from an adaptation to complement-mediated killing, so that certain pathogen species exploit the molecules of their host which protect them from an alternative pathway of complement killing (Richter et al., 2004; Richter and Matuschka, 2010). Conversely, pathogens which are not adapted to the host are exposed to complement-mediated lysis soon after attachment of the tick (Kurtenbach et al., 1998).

3.2.1. Reservoir hosts

Tick infection rate strongly depends on the population density and susceptibility of the most important tick hosts, their infection rate, duration of infection and the immune status of the individual host (Wilson et al., 2002; De la Fuente et al., 2004; Speck et al., 2013). Therefore, the reservoir status of the main tick hosts harboring pathogens, as well as the intensity of infection, is extremely important for the persistence of a pathogen in an area (Wilson et al., 1984, 2002; Humair and Gern, 1998; Bjöersdorff et al., 2001; Ostfeld and LoGiudice, 2003; Perkins et al., 2003; Pfäffle et al., 2011).

In the case of LD, a few dozen vertebrate hosts have been identified as reservoirs for the *B. burgdorferi* s.l. complex (Kirstein et al., 1997; Gern and Humair, 2002; Rauter and Hartung, 2005). The endemic areas of this disease are maintained through complex interactions among different tick species, a variety of *Borrelia* strains and the large number of vertebrate hosts upon which ticks feed, with specific associations between hosts, ticks and *Borrelia* genospecies (Richter et al., 2004; Gern, 2008). Such specific associations have been confirmed between rodents and *B. afzelii* and *B. burgdorferi* sensu stricto (s.s.), as well as between birds and *B. garinii* and *B. valaisiana* (Kirstein et al., 1997; Gray et al., 1999; Gern, 2008). Several studies in Europe have confirmed that particularly small rodents (e.g. wild mice and voles) are key hosts in the epidemiological cycle of LD, not only due to the high susceptibility of this group (Ogden et al., 1997; Humair and Gern, 1998; Humair et al., 1999; Hughes and Randolph, 2001a; Hanincova et al., 2003; Randolph, 2004a; Tonteri et al., 2011), but also due to the preference of some tick species, such as *I. ricinus* and *D. marginatus*, during their immature stages (Kiffner et al., 2011b).

Once a susceptible host is present, it can also act as a factor in the dispersal of pathogens. The St. Louis encephalitis virus, for example, was probably introduced during the past few centuries into South America from Africa by migrating birds, and gradually dispersed to North America using the same transport pathway (Gould et al., 2006). Ogden et al. (2008b) investigated the role of northward-migrating birds and the northward range expansion of LD and human granulocytic anaplasmosis. Ticks on these birds harboured different *Borrelia* genospecies, including those species which are known to cause LD in humans and alleles that are rare in the northeastern USA. Olsen et al. (1995) examined the prevalence of *Borrelia* spp. in ticks of migrating birds in Scandinavia and observed five different species of ticks harbouring various strains of *B. burgdorferi* s.l. *Borrelia garinii* was most prevalent in ticks from birds arriving from the south or southeast in the spring, whereas the distribution of *Borrelia* spp. was more heterogeneous in ticks from birds migrating from the southwest. Thus, birds may partly be responsible for the heterogeneous distribution of LD in Europe and North America.

3.2.2. Epidemiological sub-cycles

Another area about which we know relatively little is epidemiological sub-cycles. For example, *I. ricinus* is a generalist species

using a large number of mammalian, avian and reptilian hosts. Some of these host species are susceptible to TBDs and have their own, more specialist, tick fauna which can also transmit TBPs. Thus the European hedgehog (*Erinaceus europaeus*) serves as a host for *I. ricinus* and *Ixodes hexagonus* and is known to harbor a variety of different pathogens (Gern et al., 1997; Skuballa et al., 2007, 2010, 2012). Although *I. hexagonus* is a nest-dwelling species, and moreover largely a specialist associated primarily with hedgehogs (Pfäffle et al., 2011), the species could serve as a vector within hedgehog populations, thus leading to high infection rates (Skuballa et al., 2010; Speck et al., 2013). This increases the probability of *I. ricinus* becoming infected by feeding and/or co-feeding on the same host, and consequently the transmission of pathogens crossing the species barrier to include humans (Wikel and Bergman, 1997; Estrada-Peña and Jongejan, 1999; Mahy and Brown, 2000; Taylor et al., 2001; Skuballa et al., 2010).

Such sub-cycles have also been suggested for *I. trianguliceps* in the UK, which has an endemic cycle involving field voles, *Microtus agrestis* (Bown et al., 2006). These common hosts are often infested with both *I. trianguliceps* and *I. ricinus* nymphs and larvae. Both ticks have been found infected with *A. phagocytophilum* (Bown et al., 2006).

3.2.3. Dilution hosts

Disease risk is reduced by the presence of hosts with a low capacity to infect feeding vectors (incompetent reservoirs) which dilute the effect of competent reservoir hosts (Schmidt and Ostfeld, 2001; LoGiudice et al., 2003). Domestic ruminants seem to be dilution hosts for some TBPs, especially *B. burgdorferi* s.l. Sheep for example are not susceptible to *B. burgdorferi* s.l., although transmission of pathogens is considered to occur via tick co-feeding (Ogden et al., 1997). Richter and Matuschka (2010) also indicated the zooprophylactic characteristics of ruminants. Engorged ticks from cattle and goats showed no infection with LD spirochetes, although approximately 25% of those ticks found on vegetation were infected with *B. burgdorferi*. Therefore it seems that the more immature ticks that are diverted from reservoir hosts such as rodents to zooprophylactic ruminants, the lower is the risk of LD (Richter and Matuschka, 2010). This does not account for other *Borrelia* spp. such as *Borrelia miyamotoi*, for which no zooprophylactic ability of ruminants could be detected (Richter and Matuschka, 2010).

Although the dilution effect reduces vector infection rates, it does not necessarily reduce the population densities of ticks. The European bison (*Bison bonasus*), red deer, roe deer and fallow deer (*Dama dama*) are considered to be reservoir-incompetent for *Borrelia* spp. (Nelson et al., 2000; Bhide et al., 2005; Gern, 2008; Pound et al., 2010; Alonso et al., 2012), but these are important hosts for a variety of tick species positively influencing population density (Smith et al., 1990; Pichon et al., 1999; Ruiz-Fons et al., 2006; Gern, 2008; Pound et al., 2010). Big game seems to be favored by adult females, because continuous and large blood meals support the production of large numbers of eggs (Dobson et al., 2006).

In nature, this dilution effect is most likely supported by an increased biodiversity (Daszak et al., 2000, 2001; Ostfeld and Keesing, 2000; Wood and Lafferty, 2012). Schmidt and Ostfeld (2001) showed that increasing species richness, but not evenness, leads to a reduced disease risk, since dilution effects are most pronounced when alternative hosts have negative influences (e.g. predation or competition) on dominant reservoir hosts within the community. It is also possible that species which are expected to be dead-end or dilution hosts for TBPs potentially provide a platform for non-systemic pathogen transmission among co-feeding ticks (Kiffner et al., 2010). This may explain why, for instance, at large spatial scales there is a positive relationship between LD inci-

dence in humans and roe deer density, which are not competent hosts for *B. burgdorferi* (Vor et al., 2010).

The dilution effect theory has, however, been challenged by different studies which show that the loss of biodiversity in some communities led to a decrease in disease risk (Ostfeld and LoGiudice, 2003; Foley et al., 2009). This happens when pathogen transmission is greater within species than between species, particularly when a suitable host species is dominant, highly abundant and widespread (Keesing et al., 2006; Foley et al., 2009).

Recently, the generality of this concept was strongly attacked by Randolph and Dobson (2012) who, based on theoretical and empirical evidence, argued that the dilution effect theory applies only in certain, limited circumstances. In a pointed rejoinder, Ostfeld (2013) argued that, at least with respect to LD in the eastern USA, Randolph and Dobson had distorted and omitted relevant information and included information which was not applicable, thus biasing their analysis.

Salkeld et al. (2013) conducted a meta-analysis with 16 biodiversity-diseases relationships including two studies on LD and one on *A. phagycatophilum*. The authors found only very weak support for the dilution effect theory but they did find strong evidence for heterogeneity in the effects. This implies that different processes were acting during different studies. The dilution effect does not simply depend on biodiversity itself but on the composition of a specific community, which might dilute or amplify disease risk, because individual species have specific and contingent effects on other species within the community (LoGiudice et al., 2003). The relationship between biodiversity and zoonotic disease risk is therefore a specific rather than a general phenomenon and the understanding of ecological dynamics of specific disease systems is critical for predicting zoonotic disease risk (Salkeld et al., 2013).

3.2.4. Acquired resistance against pathogens

Although some pathogens may benefit from suppression of the host's immune defenses by ticks, the complement present in the blood of several host species has been shown to be the active component in pathogen-host specificity (Gern, 2008). Wikel et al. (1997) indicated that tick infestation can lead to resistance against pathogens by infesting BALB/c mice, first with uninfected and then with *B. burgdorferi*-infected *I. scapularis* ticks. The control group was only infested with infected nymphs and all host individuals became infected with *B. burgdorferi*. The experimental group, which had been previously infested with uninfected ticks, showed an infection prevalence of only 16.7% after being infested with infected ticks. The acquired resistance against ticks can also cause resistance to pathogens, which might be caused by a stimulated immune system (Wikel and Bergman, 1997).

Rubaire-Akiiki (1990) tested the effects of acquired resistance against tick infestation on the susceptibility of vectors to infection with pathogens. They infested two *B. taurus* calves with *Hyalomma anatolicum* nymphs and used a third calf as a control without primary tick infestation. All calves were inoculated with a stabilate of *Theileria annulata*, the agent of bovine theileriosis, and became infected. After that, nymphs were applied and examined after engorgement. Nymphs from the calves which developed a certain level of tick resistance after previous *Hyalomma* infestation were significantly less susceptible to infection by *T. annulata* than nymphs from the control calf, which indicates that acquired resistance against ticks leads to a reduced vector capacity in the ticks. Acquired resistance at the individual level and circulating tick-reactive antibodies determine the persistence and transmission likelihood for TBD agents (Wikel et al., 1997; Gern, 2008).

4. The influence of anthropogenic changes to the environment and host-tick-pathogen dynamics

Superimposed on natural environmental dynamics such as seasonal changes, there are major anthropogenic influences such as habitat fragmentation, urbanization, de- and reforestation, other land use changes and climate modification which influence host-tick-pathogen interactions (Barbour and Fish, 1993; Patz et al., 2004; Olson and Patz, 2010). These factors span a wide range of disciplines, including physical and human geography, meteorology, sociology, veterinary and human medicine, as well as ecology. Their relative importance, although currently an area of intensive study, remains largely obscure.

4.1. Small scale dynamics

4.1.1. Habitat fragmentation

Fragmentation describes the loss of large tracts of connected habitat caused by dividing continuous areas into smaller fragments which are isolated from each other, for example through road construction or building development (Watling and Donnelly, 2006). This has a substantial impact both on the populations and communities of organisms living in an area (Bennett and Saunders, 2010; Bergerot et al., 2010). The fragmented patches are scattered through a matrix of modified habitats, while the conditions surrounding the fragment, including connectivity between patches, determine the extent to which exterior environmental conditions penetrate the patch (Baskent, 1999). The unaffected grain of the area, called the core habitat, is determined by the fragment size and shape and the ecosystem of the surrounding matrix. The environmental characteristics of the affected bordering zones (edges) have numerous important effects on climate and organisms (Ewers and Didham, 2006; Vogt et al., 2006). Fragment size is not the only factor defining the community structure of fragment-dwelling organisms; in fact it is a functional interaction of numerous factors of the core-zones and edges of the patch influenced by the surrounding matrix, habitat area and edge effects (Vogt et al., 2006).

Traditionally edges have been considered beneficial to wildlife, including tick hosts, because diversity generally increases near habitat edges. Explanations for this edge effect include greater vegetation complexity or the simultaneous availability of more than one landscape element, as well as microclimatic factors (Gray et al., 1999; Nelson et al., 2000; Ewers and Didham, 2006). However, edges can have negative effects on wildlife due to disturbance, the possible isolation of patches and corridors modifying distribution and dispersal, increasing predation and parasitism (Yahner, 1988; Gray et al., 1999). How the dynamics of the individual host populations change is therefore variable, depending on the circumstances. Large herbivores such as deer profit from the vegetative complexity delivered by edge effects, but also from nearby, accessible field crops, reduced hunting pressure near suburban or urban habitats, and the presence of ornamental vegetation as winter forage and cover (Alverson et al., 1988; Fuller and Gill, 2001; Rooney, 2001; Allan et al., 2003; Vor et al., 2010).

Habitats of mosaic-shaped landscapes are considered to experience higher tick densities than homogeneous forested landscapes, which may be in part due to high host numbers for adult tick feeding and reproduction (Wilson et al., 1984). In highly fragmented landscapes of the eastern USA, the density of nymphal *I. scapularis*, the incidence of *Borrelia*-infections, as well as the density of infected nymphs was significantly negatively correlated with forest patch size resulting in a higher risk of LD in smaller patches (Allan et al., 2003). This also involved an elevated risk of humans entering tick habitat (Allan et al., 2003). Forest fragmentation leads to the loss of many vertebrate species from the remaining habitat patch,

whereby white-footed mice (*P. leucopus*), the typical nymphal host and reservoir for a variety of pathogens in the eastern USA, appears not to be negatively affected by fragmentation and consequently mouse abundance in small patches tends to be higher than in larger habitat areas, leading to high densities of infected nymphs (Lewellen and Vessey, 1998; Nupp and Swihart, 1998; Allan et al., 2003). Furthermore, the lack of other vertebrate species occurring as predators or competitors can lead to high absolute densities of mice and therefore potentially to an increase in the number of infected nymphs (Allan et al., 2003).

Trying to characterize the environmental factors driving the distribution of Crimean-Congo hemorrhagic fever (CCHF) in Turkey, Estrada-Peña et al. (2010) found that neither single climatic nor vegetation variables, nor any individual seasonal component, were key factors in the distribution of the TBP, but that high habitat fragmentation with well-connected patches was positively correlated with case incidence.

4.1.2. Urbanization

The human population has more than doubled since the second part of the 20th century and this expansion is expected to continue through the forthcoming decades before reaching 10 billion around 2070 (Bongaarts, 2009). As a result of this increase, associated with social and economic changes, there has been a strong migration into cities (Sutherst, 2004).

The enormous expansion of urban areas corresponds with the rapid and dramatic conversion of landscape from natural to anthropogenic, hallmarked by built-up areas, industry and its associated infrastructure (Bradley and Altizer, 2007). The consequences that arise from these environmental changes include dramatic alterations in faunal and floral diversity and abundance, degradation and loss of natural habitat and shifts in (micro-) climatic conditions (e.g. heat island effects) (Uspensky, 2008, Ticks (Acari: Ixodoidea) as urban pests and vectors with special emphasis on ticks outside their geographical range. Proceedings of the 6th International Conference on Urban Pests, Hungary, pp. 333–348.)

Due to the intense landscape modifications resulting in a complex mosaic pattern of heterogeneous landscapes (Klausnitzer, 1993), habitats within urban and suburban areas are often unsuitable for many species, leading to an overall loss of wildlife biodiversity and abundance and, therefore, to a decline in sources of TBP reservoirs (Zygutiene et al., 2008). Some species, however, are capable of adapting to the new environment. Populations of urban-adapted hosts can reach densities in urban and suburban areas that are much higher than observed in undisturbed areas (Riley et al., 1998; Deplazes et al., 2004). Moreover, an abundance of certain resources is available in the city areas throughout the year via human waste or intentional feeding by citizens (Contesse et al., 2004). These can additionally support thriving urban-adapted animal populations (Deplazes et al., 2004; Bradley and Altizer, 2007) and can lead to increased contact with humans.

In the developed world, urbanization is typically implemented in a structured way, often with green areas, whereas in developing countries the expansion of urban areas happens much faster, is less structured and can lead to poor infrastructure, poor housing, high human density, impoverished suburbs and highly polluted city centres (Gubler, 1998; Sutherst, 2004). Both types of expansion can create conditions suitable for tick and host existence and thus lead to the emergence of TBDs (Patz et al., 2004; Bradley and Altizer, 2007; Uspensky, 2008, Proceedings, see above).

Within urban areas in the developed world green zones such as parks, forest patches and gardens are kept up to elevate the living standards of citizens. Tick populations such as those of *I. ricinus* are mainly restricted to these areas within cities, as this is where they find favorable microclimatic conditions (Dautel and Kahl, 1999, Ticks (Acari: Ixodoidea) and their medical importance in the urban

environment. Proceedings of the 3rd International Conference on Urban Pests, Czech Republic, pp. 73–82.), substrate for questing and abundant hosts (Prusinski et al., 2006).

European hedgehogs, for example, are a common, well-adapted component of urban ecosystems (Pfäffle et al., 2009). As indicated in Section 3.2.2 they are frequently infested with two species of ticks, *I. ricinus* and *I. hexagonus* (e.g. Gern et al., 1997; Pfäffle et al., 2011), which are both proven vectors of several tick-borne pathogens (Skuballa et al., 2009; Silaghi et al., 2012) and are known to host a variety of zoonotic TBPs, including TBEV, *A. phagocytophilum* and several *B. burgdorferi* s.l. genospecies (Skuballa et al., 2007, 2010). These pathogens have been found in hedgehogs from Berlin, (Germany) Budapest (Hungary) and Hamburg (Germany) and are thus involved in the urban cycle of TBDs (Skuballa et al., 2007, 2009, 2010; Földvari et al., 2011; Silaghi et al., 2012; Speck et al. 2013).

Populations of white footed mice in North America tend to reach high densities in fragmented areas, especially in small, isolated woodland patches surrounded by urban environments (Nupp and Swihart, 1998; Lewellen and Vessey, 1998; LoGiudice et al., 2003), thus providing a basis for both the feeding of immature ticks and the maintenance of pathogens.

Another factor facilitating completion of the tick life cycle in urban areas is the availability of medium to large-sized hosts. As deer species, the main hosts for the adult stages of *I. ricinus*, are typically absent from city centres, hedgehogs might act as surrogate hosts for adult *I. ricinus* in central European urban habitats (Földvari et al., 2011). This establishment of a shift in the core host–parasite association can in turn lead to changes in pathogen prevalence and composition in urban areas, as has been shown by the unusually high prevalences of *Borrelia spielmanii* found in the English Garden in Munich, Germany (Fingerle et al., 2008).

Deer, as well as wild pigs, however, are abundant in less disturbed suburban areas, and populations thrive in areas closely associated with human habitations. As a result, deer- associated ticks such as *A. americanum* and *I. scapularis* have become endemic in many suburban areas in the southern USA, together with the pathogens they transmit, such as *E. chaffeensis* (Comer, 2001). European wild boar (*Sus scrofa*) are also associated with a variety of TBPs (e.g. *Anaplasma* spp. and *Rickettsia* spp.), as well as ticks such as *H. marginatum*, *Rhipicephalus bursa* and *D. marginatus* (Hubalek et al., 2002; De la Fuente et al., 2004; Meng et al., 2009). Through the intersection of deer and wild pig habitats with suburban and urban areas the disease risk for humans increases (De la Fuente et al., 2004; Ruiz-Fons et al., 2006; Meng et al., 2009).

In some cases, the original transmission dynamics of TBPs can even shift towards urban adapted ticks and therefore cause a change in disease distribution. Rocky Mountain spotted fever is a TBD persistent in the USA and caused by *R. rickettsii*. It originally occurred in the northwestern and northern-central states of the USA (Wolbach, 1919). Typically, the disease was transmitted by the Rocky Mountain wood tick, *Dermacentor andersoni*, but there has been a geographical shift in the disease distribution to the more highly populated areas in the southern-central, southern and eastern parts of the USA, facilitated by a change in the main vector in these regions to *D. variabilis*, the American dog tick (Gratz, 1999), thus increasing the risk of infection by urban ticks.

It is not only the landscape but also the mean temperature in urban environments that differs from the surrounding areas, being between 1 and 6.5 °C higher on warm days (Santamouris, 2001; Frumkin, 2002). This heat island effect is presumably caused by heat absorption from dark surfaces in built-up areas and its subsequent re-radiation as thermal infrared radiation, together with the lack of vegetation (Frumkin, 2002). This temperature pattern might influence the survival, activity and distribution of ticks in cities, with a possible impact on reproductive success, the period of tick

activity both from a daily and an annual perspective, and thus have an effect on pathogen prevalences. *Borrelia burgdorferi* s.l. has been shown to impart survival advantages to *I. ricinus* ticks under challenging thermohygrometric conditions (Herrmann and Gern, 2010), which might lead to an increase in the number of infected ticks and an increased risk of transmission at the edges of tick-suitable habitat patches within cities. Unfortunately, research in this area is scarce (Bradley and Altizer, 2007).

The contamination of tick habitats by increased environmental pollution with heavy metals from industry and cars can lead to exoskeleton abnormalities in ticks (Zharkov et al., 2000). Ticks bearing such cuticular anomalies are more susceptible to infection with a variety of TBPs, including a higher prevalence of multi-infection, while also showing behavioural changes, such as enhanced activity, that increase the risk of human infection (Alekseev and Dubinina, 2008).

As cities expand, human populations encroach upon their rural, peri-urban and suburban surroundings, invading natural and semi-natural environments such as forests and former agricultural land (Frumkin, 2002). This urban sprawl (Brueckner, 2000) can lead to an increased exposition of humans to vector ticks and TBPs due to the general increase of contact zones between wildlife and humans or domestic animals (Meerburg et al., 2009; Munderloh and Kurtti, 2011; Tack et al., 2012). Even though urbanization decreases the abundance and diversity of wildlife parasites, pathogen transmission can increase among urban-adapted hosts (Bradley and Altizer, 2007), resulting in the emergence of urban zoonotic disease cycles and the spread of infectious agents such as TBPs in urbanized areas (Lederberg et al., 1992; Reye et al., 2010). A number of studies in the northeastern part of the USA have confirmed the hypothesis of human-made infection risk in suburban areas by showing that the likelihood of infection with *B. burgdorferi* s.l. is especially high in suburban residential areas (e.g. Falco and Fish, 1989; Allan et al., 2003; LoGiudice et al., 2003). The creation of ecotones between human-altered and natural landscapes represents an ecological setting of special importance, favoring the transmission of LD by the aggregated and overlapping presence of host and vector species within relatively restricted spatial limits (Estrada-Peña, 2001a; Despommier et al., 2006).

This pattern of expansion and associated risk of infection with TBPs seems to be consistent for other parts of the world: it is thought that in the Sagar-Sorab area in India, the central focus of Kyasanur forest disease (KFD) was established mainly due to the encroachment of human settlements on forest areas (Pattnaik, 2006). The ecotones generated provide a suitable habitat for both the tick vector, *Haemaphysalis spinigera*, as well as large populations of reservoir hosts such as wild monkeys, enhancing the likelihood of the establishment of stable enzootic transmission cycles in this area (Pattnaik, 2006).

4.1.3. Land use

Human interventions in the natural balance of landscapes started in prehistoric times with land tillage, forest clearing and irrigation, with growing human population densities exacerbating the situation (Misana et al., 2003; Foley et al., 2005). Yet even such a limited human impact on natural ecosystems can lead to new habitats for animals and plants. In Europe, extensive pasture in former times formed important habitats for thermophilic species in the northern part and in the central and southern regions of Germany, serving as refuges for pre-glacial relict species until now (Beierkuhnlein, 2007). Large-scale harvesting of forests in the first half of the 19th century created large open areas of heathland and farmland providing a suitable environment for many native steppe elements, such as the European brown hare (*Lepus europaeus*) (Ellenberg, 2010; Petney et al., 2012).

Today reforestation, together with habitat fragmentation, may lead to an increase in tick-suitable habitats and thus potentially to a rise in pathogen prevalence (Estrada-Peña et al., 2010). In Europe, the first large-scale forest harvesting started during the 7th century with the aim of gaining arable farmland and space for settling, followed by a second phase of deforestation as a result of increased commodity demand by a growing human population (Ellenberg, 2010). In North America, many areas were degraded due to European settlement during the 17th and 18th centuries, showing a complex east–west gradient of disturbance (Hall et al., 2002). Large-scale deforestation increased during the green revolution when agricultural production dominated in many countries of the world (Tilman, 1999), followed by agricultural intensification and reforestation in the 20th century (Daszak et al., 2001). The re-colonization of abandoned land and reforestation to ensure sustainability of forests are also considered as key factors in the emergence of TBDs via the creation of suitable tick habitats, for example for *I. ricinus* and *I. scapularis* (Fish and Childs, 2009; Committee on Lyme Disease and Other Tick-Borne Diseases: The State of the Science; Institute of Medicine, 2011; Léger et al., 2013).

In addition to the conversion of non-agricultural ecosystems into arable land, the exponential rise in the demand for food could only be ensured by the intensification of farming methods using monocultures (Misana et al., 2003). The loss of herbs is related to a substantial loss of biodiversity not only of plants but also of animals (Pegel, 1986). Wild ungulates, such as deer and wild boars, however, benefit especially from the cultivation of crops including wheat, and the expansion of farmland (Pegel, 1986; Daszak et al., 2001; Foley et al., 2009).

In general, land use change influences both the microclimate and the potential host species for ticks in an area. In cases of monoculture with hostile microclimatic conditions, tick populations are likely to suffer. Indeed, agricultural land is highly unsuitable for *I. ricinus* (Sumilo et al., 2006). Reforestation, however, is likely to open up new areas with a suitable microclimate and host populations allowing the establishment of ticks and the epidemiological cycle of TBDs (Allan et al., 2003; Estrada-Peña et al., 2010; Léger et al., 2013).

4.1.4. Domestic animals

Animal husbandry is assumed to have been a source of human exposure to zoonoses since ancient times (Munderloh and Kurtti, 2011). Among the large variety of vertebrates that can act as amplification hosts for different zoonotic TBDs, pets and livestock represent some of the largest reservoirs for human infection (Jongejan and Uilenberg, 2004; Chomel et al., 2006). In developing countries, densely populated urban and peri-urban slums are a common side effect of urbanization which often harbour high densities of domestic animals such as poultry, pigs or small ruminants (Foeken and Mwangi, 2000). These are bred in small-scale private farms and serve, amongst others things, as a source of food, income and security. They live in close contact with humans (Ghirotti, 1999). This scenario with plenty of hosts, especially for adult ticks, provides excellent conditions for tick existence (Uspensky, 2008. Ticks (Acari: Ixodoidea) as urban pests and vectors with special emphasis on ticks outside their geographical range. Proceedings of the 6th International Conference on Urban Pests, Hungary, pp. 333–348), and the close contact to humans can result in the emergence of TBDs.

As human contact with livestock typically takes places among farmers and associated occupational groups, it is not surprising that people at highest risk of contracting Crimean-Congo hemorrhagic fever (CCHF) infection comprise agricultural workers, and in particular farmers living in endemic rural areas in various parts of the world (Whitehouse, 2004; Ergönül, 2006) where vector ticks, including those of the genus *Hyalomma*, are abundant. For example, high CCHF antibody prevalences in a South African rural community were predominantly found in farmers and this has been shown to correlate with handling lambs (Fisher-Hoch, 1992).

In the context of close contact to animals and exposure to TBDs, argasid ticks play a special role: a number of soft tick species, such as *Ornithodoros moubata*, can be found in close association with humans and within human dwellings (McCall et al., 2007). This and certain other species of the genus are capable of transmitting tick-borne relapsing fevers (TBRF), caused by at least 15 different *Borrelia* spp. (Barbour and Hayes, 1986; Parola and Raoult, 2001; Dworkin et al., 2008). TBRF *Borrelia* in Central Tanzania can use domestic animals (chickens and pigs) as reservoir hosts and *Ornithodoros* tick populations may act as a bridging vector between animals and humans in this region (McCall et al., 2007). However, humans can also benefit from the vicinity of domestic animals: goats and cattle can eliminate spirochete infection from ticks (Richter and Matuschka, 2010), thus holding the potential to decrease the risk of infection with LD *Borrelia*.

Besides the role of livestock, close contact with companion animals can also change the human risk of TBD acquisition as these animals represent potential reservoirs for several zoonotic TBD agents and thus can alter the rate of human exposure to TBDs. These include borreliosis, ehrlichiosis, rickettsiosis including Rocky Mountain spotted fever, and TBE (Shaw et al., 2001). However, the relative contribution to increased human risk of disease infection also depends on the transmission cycle of the respective pathogen and especially the behavioural traits of the vector tick. Shaw et al. (2001) defined three different epidemiological scenarios, posing different extents of threats of TBD infection in humans. The first involves the transmission of a pathogen by exophilic ticks with a broad host spectrum, such as that found for *I. ricinus* (Süss, 2003). In this setting, pets can serve as sentinels for human infection risk. The second involves the transmission of pathogens by exposure to tick contents due to damaging ticks by the grooming of infested animals or inappropriate removal of ticks by humans. Transmission of *Coxiella burnetii*, the agent of Q-fever, occurs relatively frequently in shearers who can cut open the ticks or cause an aerosol of tick faeces in the process of removing wool from sheep (Schulz et al., 2005; Runge and Ganter, 2008). The third and putatively most important form of increased exposure, with the greatest potential for transmission of zoonotic pathogens, involves pets as hosts for nidiculous or endophilic tick vectors such as *R. sanguineus*. These ticks live in close association with dogs and can reach high densities within kennels or animal shelters, and even in human homes occupied by dogs (Peter et al., 1984). Another important aspect relating to *R. sanguineus* is its ability to produce up to four generations per year under optimal conditions and the fact that males can take up several blood meals on different dogs, which adds to the potential frequency of pathogen transmission (Dantas-Torres, 2010). In this scenario, dogs can significantly increase the human-tick interface, thus leading to an increased risk of transmitting zoonotic pathogens such as *R. conorii* and *R. rickettsii* (Dantas-Torres, 2010; Nicholson et al., 2010).

Cats are abundant throughout the world (Denny and Dickman, 2010), being amongst the most common companion animals, predominantly in developed countries (Gratz, 1999). They usually live in close association with their owners (Day, 2011), where they represent another source of human infection with pathogens (Gage et al., 2000; Elmore et al., 2010). Cats have been shown to be capable of harboring a variety of different TBPs, including *Borrelia* spp., *Bartonella* spp., *Ehrlichia* spp. and *Rickettsia* spp. (Day, 2011), and cat ownership was associated with LD risk even before this diseases was known to be tick-borne (Fish, 1995). *Bartonella henselae*, which causes cat-scratch disease (Jameson et al., 1995), has long been known as a flea-transmitted disease but recently it was shown to be transmitted by cat-infesting *I. ricinus* ticks as well

(Cotté et al., 2008). Additionally, *B. henselae*-infected ixodid ticks were shown to have the ability to carry co-infections with the human pathogenic *B. burgdorferi* s.l. and *A. phagocytophilum* (Holden et al., 2006).

4.1.5. Human behavior

In addition to parameters such as the population density of ticks and the prevalence of infected ticks, the incidence of human TBD in a particular area depends on social factors that determine the likelihood of contact between infected ticks and humans (Bröker and Gniel, 2003; Bayles et al., 2013). Therefore, the way in which humans interact with their environment plays an important role in determining the risk of a tick bite and infection (Stoddard et al., 2009).

Employment is one way in which humans are confronted with tick-infested habitats, often on a regular and/or frequent basis. Rangers, hunters or lumberjacks, for whom the forest is the designated place of work, are among the highest-risk occupations for contracting TBDs (Fingerle et al., 1997; Deutz et al., 2003; Cisak et al., 2005; Lindgren and Jaenson, 2006; Thorin et al., 2008). The most important factor contributing to the high levels of seropositivity for various TBDs in these working groups is most likely the close contact with vegetation (Thorin et al., 2008), especially the areas within a tick infested habitat in which a tick bite is most likely to occur. A study from Austria (Deutz et al., 2003) indicated that even when compared with other risk groups, hunters seem to be particularly prone to contracting TBPs, as they showed comparably high levels of seropositivity for *B. burgdorferi* s.l., *Ehrlichia* spp. and *F. tularensis*. This pattern is consistent with findings from Schwartz and Goldstein (1990), where seropositivity for LD among several groups of outdoor workers was compared and found to be present most frequently in hunters. The authors considered that this was likely to be the result of the amount of time spent in tick habitats in general, together with vicinity to the carcasses of tick hosts, and the duration of stay within brushy vegetation where the risk of contact with ticks is high.

Besides encountering tick-infested habitats on a professional basis, domestic activities such as walking the dog or collecting firewood in tick habitat are regarded as sources of increased exposure to ticks in their natural habitat (Pattnaik, 2006; Piesman, 2006). Villagers in the Karnataka state of India frequently become infected with Kyasanur forest disease through the bites from *H. spinigera* ticks when they visit nearby forests to collect firewood (Pattnaik, 2006).

Leisure activities such as fishing, jogging or hiking that typically take place in natural tick habitats have also been identified as risk factors for infection (Smith et al., 1988). Seropositivity for LD has been found to increase in proportion to the hours per week spent outdoors during recreational activities such as fishing and hiking (Schwartz and Goldstein, 1990). However, compared with the occupational risk of infection, leisure activities are likely to pose a minor threat to human beings, due to the low duration and frequency of stay, as well as the spatial focus of activity within the tick habitat (Sumilo et al., 2008b). Hikers and joggers spend most of their time on trails and not within the coppices and shrubbery where ticks are typically found questing during their active period.

The rapid and extensive growth of urban areas all over the world, together with the vast increase in people living in built-up environments, has contributed a great deal to an increasingly "nature-hungry" population and the rising popularity of outdoor recreation (Ibrahim and Cordes, 2008) with the potential to provide a source of social and health benefits (Godbey, 2009). These activities typically take place in natural and semi-natural habitats such as forests or parks. Green areas within cities are frequently visited and intensively used for a large variety of recreational activities including barbecues, picnics, sunbathing or ball games. As mentioned in the section on urbanization, ticks can, under appropriate environmental circumstances, establish stable populations within cities, even in the absence of large hosts (Falco and Fish, 1989; Dautel and Kahl, 1999. Ticks (Acari: Ixodoidea) and their medical importance in the urban environment. In: Proceedings of the 3rd International Conference on Urban Pests, Czech Republic, pp 73–82.; Uspensky, 2008, Ticks (Acari: Ixodoidea) as urban pests and vectors with special emphasis on ticks outside their geographical range. Proceedings of the 6th International Conference on Urban Pests, Hungary, pp. 333–348), and pathogen prevalences can reach high levels (Fingerle et al., 2008), not least due to the patchy environmental characteristics present (Estrada-Peña et al., 2010).

Changes in human behavior caused by war, social disruptions and conflicts, together with their environmental consequences, are assumed to be among the major factors that lead to CCHF outbreaks in the past (Hoogstraal, 1979). When Soviet troops during World War II began to reoccupy the Crimean steppe, they encountered large areas of fallow land where agricultural properties had been abandoned in reaction to fighting. As a result, large wild hare populations had established together with *Hyalomma* ticks, respectively hosts and vectors of CCHF. It is assumed that these conditions contributed to the CCHF epidemic among military personnel, affecting signalmen and surveyors in particular, who frequently moved within thick undergrowth and coppices (Hoogstraal, 1979; Leblebicioglu, 2010).

Later, changing human activities due to the socio-economic transition that followed the end of the soviet leadership were widely associated with epidemiologically relevant sociological changes in relation to increases in both wealth and leisure as well as unemployment and poverty (Randolph, 2004b, 2010b), impacting on work and leisure activities. This was accompanied by a significant increase in the incidence of human TBE from 2- to 30-fold in many central and eastern European (CEE) countries around the early 1990s (Sumilo et al., 2008b). In addition, people progressively started individual farming for economic reasons, leading to an increase in sheep and goat numbers (Randolph, 2002). These animals often grazed in tick-infested areas at the edges of forests (Kohl et al., 1996). The consumption of raw milk from TBE-infected stock animals is a special, but rather rare (Kriz et al., 2004), source of TBE infection for humans (Labuda et al., 2002). Nevertheless, there is an epidemiological significance of alimentary TBEV infections, for example in Slovakia (Kohl et al., 1996) and probably in other CEE countries. The same is potentially true for Q-fever which can also be caused by the consumption of raw milk products (Runge and Ganter, 2008).

Other, and perhaps more important, consequences of the vast upheavals in large parts of eastern Europe during the 1990s included increasing outdoor activities for either recreation or economic reasons such as the gathering of wild fruit and mushrooms, which are both associated with frequent visits to tick-infested habitats (Randolph, 2002).

With increasing levels of awareness of TBDs, the self-perception of risk allows people to actively avoid exposing themselves and companion animals to habitats where ticks and TBPs are abundant. There is increasing evidence that when faced with potentially lethal or novel pathogens, people change their behavior to try to reduce their risk of contracting disease (Ferguson, 2007). This pattern is consistent with observations from several studies that have shown that the risk of disease can attenuate over time in risk groups, as well as in the general public, due to behavioural changes and vaccination (Piacentino and Schwartz, 2002). The latter has proven to be effective in Austria, where extensive vaccination efforts have helped to drastically reduce the number of TBE cases (Bröker and Gniel, 2003; Heinz et al., 2013).

Following the independence from Soviet rule, the increase in TBE cases observed in the Baltic States was followed by a steep

decrease, exceeding vaccination rates and acquired immunity in the population (Sumilo et al., 2008a). Together with the fact that high exposure rates to TBDs had been found to coincide with unemployment and a low income as well as not being vaccinated, Sumilo et al. (2008a) concluded that behavioural changes for risk avoidance must have driven the decrease in TBE incidence.

In the developing world, where public health efforts are low compared with Europe or the USA, the establishment of avoidance behavior can also be observed. In rural areas in central Tanzania some people prefer to sleep outdoors during the hot season to avoid being bitten by soft ticks living in their homes. These *Ornithodoros* ticks are the vectors of TBRF *Borrelia* spp. including *B. duttoni* (Kisinza et al., 2003).

4.2. Global scale changes

4.2.1. Climate change

The role of climate change for TBD epidemiology is a controversial topic (Harvell et al., 2009; Randolph, 2010a). As we have seen, TBD systems are very sensitive to, and limited by, climatic and linked microclimatic conditions. Over the last century, precipitation worldwide has increased by approximately 1% and the trend for maximum temperature shows an increase of approximately 0.88 °C and that of minimum temperatures of 1.86 °C per 100 years (Easterling et al., 1997; Khasnis and Nettleman, 2005) indicating that these conditions are changing systematically.

There are several studies which indicate that the distribution of ticks and TBPs in Europe and North America is increasing. Incidences of TBE have considerably increased since the early 1980s in Sweden. This has been associated with climatic changes, mostly to higher average temperatures, milder winters and spring temperatures favoring the development of ticks (Lindgren et al., 2000). The milder winters, which are due to stronger global warming effects in winter in the north, might have led to a reduction in overwintering mortality of tick hosts and the extension of the active period of ticks (Githeko et al., 2000). *Ixodes ricinus* has apparently also spread to higher latitudes in Sweden, which might have affected the dynamics of TBE transmission and, therefore, increased the risk of infection in these regions. However, these studies have been limited in their scope and the changes reported could also been have due to other factors such as an increase in roe deer density and increased human activity in tick habitats (Githeko et al., 2000; Jaenson et al., 2012).

Although winter activity of *I. ricinus* is common at the southern limit of its distribution (Gray, 1991), only limited information on this topic is available for central and northern Europe (e.g. Szell et al., 2006). Dautel et al. (2008) provided the first systematic study of the winter activity of questing *I. ricinus* larvae and nymphs in central Europe. They found more or less continuous activity in *I. ricinus* throughout the winter from October 2006 to March 2007 in a forest in Berlin, Germany. This was related to a mild winter with only 2 days in the whole period with temperatures below 0 °C, while mean daily temperatures were approximately 4.6 °C higher than the long-term mean, resembling a Mediterranean winter. The daily maximum temperatures for December, January and February were 7.5, 7.7 and 6.6 °C, respectively (Dautel et al., 2008), which approximate the threshold for questing activity of *I. ricinus* (Süss et al., 2008). Increased winter temperatures in central Europe might therefore prolong the annual length of questing of *I. ricinus* and shift the seasonality of this tick towards earlier in the year.

From 1993 to 2001, a twofold increase of TBE incidence was observed in the Czech Republic compared with the years 1984–1992, with a total increase in cases in known TBE areas, an increase in TBE cases in areas where it had not occurred before and a re-emergence of the disease in areas where TBE cases had been only

sporadically observed since the 1970s (Daniel et al., 2003). Additionally, an increase in the distribution of *I. ricinus* to higher altitudes was observed, thereby expanding the range of TBE into Bohemian mountain areas. Danielova et al. (2008) were not able to ascribe this change to socio-economic shifts or land use changes but it was correlated with increased monthly temperatures, especially in the period of maximum *I. ricinus* activity. Daniel et al. (2008) reported that similarly to the situation in Sweden, milder winters were slightly correlated with an increase in TBE incidence in Bohemia, which the authors related to the decreased winter mortality of small mammal hosts during milder winters, leading to a higher probability of larvae finding a suitable host. Nevertheless, human outdoor activities are also weather-dependent, providing a possible source of confusion.

Given the lack of long-term studies which incorporate systematic global climate change, modeling is a major option in attempting to understand potential changes in the host-tick-pathogen system. Dobson and Randolph (2011) modeled the potential role of climate change and the impact of increasing numbers of roe deer hosts on tick population density and concluded that both abiotic and biotic environmental changes may have contributed to recent increases in tick populations.

In the USA, the Rocky Mountain wood tick, *D. andersoni,* serves as a vector of several human pathogens including *F. tularensis* (tularemia), *R. rickettsii,* as well as the Colorado tick fever virus in its natural range in North America (Hopla, 1974; Burgdorfer, 1977). Based on climate change estimates in Colorado (USA), climate warming is expected to result in rapid changes in the spatial patterns of abundance and distribution of *D. andersoni* (Eisen, 2008), which is likely to expand the risk areas for pathogens transmitted by this vector.

Although climate change will affect the distribution of vectors and TBDs in one way or the other, for example by opening up new territories for vectors (Brownstein et al., 2005) or altering the timing and duration of the peak risk of exposure to tick-borne pathogens (Gage et al., 2008), it is difficult to estimate how strongly these changes will be expressed, since adequate, long-term data are missing. The reasons for this are multiple: (i) it is difficult to distinguish between climate change and climate variability, so that every climate change signal is superimposed on the background noise of climate variability (Kovats et al., 2001), (ii) the relationship between TBDs such as LD and climate change is difficult to determine due to diagnostic problems and limited reporting in various countries (Gray et al., 2009), and (iii) TBD systems are extremely complex, meaning that climatic factors are not the only factors responsible for changes in tick populations and TBD dynamics (Sumilo et al., 2007; Knap et al., 2009; Randolph, 2010a). This complexity makes a linear response to climate change unlikely and an exclusive focus on climate change might result in the neglect of social phenomena that may be more amenable to effective action aimed at reducing the incidence of disease (Randolph, 2008).

Again it is important that long-term data be collected from different areas because global warming is not uniform and changes can be more extreme depending on, for example, latitude, with higher northern latitudes expected to undergo more extreme warming (American Meterological Society, http://www.ametsoc.org/policy/2012climatechange.html, accessed 23 April 2013). An increase in temperature in certain areas, leading to a hotter and drier climate, might limit the population density of ticks and thus the risk of TBPs (Olwoch et al., 2008).

4.2.2. Mobility, travel and trade

Today, world citizens move 23 billion km/year in total, and it is expected that by 2050 that figure will have grown to 105 billion km/year (Schafer and Victor, 2000), resulting in an enhanced risk

of spreading vectors and pathogens throughout the world (Sutherst, 2004; Cunningham, 2005). The preconditions for successful invasions of ticks and TBDs are that the tick population is large enough and able to adapt to the new environmental conditions, and that susceptible hosts are present (Léger et al., 2013).

Reports on the introduction of infected ticks without hosts and the subsequent emergence of disease in the invaded area have not been found. It seems rather that the anthropogenic related movement of host animals over long distances leads to the introduction of ticks to new areas (Nicholson et al., 2010; Burridge, 2011). The massive translocation of livestock has already led to the introduction and geographical spread of ticks and their associated pathogens into new areas.*Amblyomma variegatum*, which is a vector of African tick bite fever (Raoult et al., 2001) and CCHF (Estrada-Peña and Jongejan, 1999) to humans has been introduced to and become established in several regions including the Caribbean, Madagascar and Yemen (Pegram et al., 1982; Barré et al., 1995). It is regarded as the second most invasive tick species on the planet, after *R.* (*B.*) *microplus* and the most important tick in Africa, as it is has the widest distribution with endemic occurrence in over 30 countries. The invasion of the Caribbean region began around the 19th century with the introduction of infested cattle from African countries to Guadeloupe and neighboring islands. Then in the 1950s the tick spread across wide parts of the Caribbean. This might be attributed to some extent to the increase in the numbers of cattle egret (*Bubulcus ibis*), a bird that commonly serves as a host for *A. variegatum* immature stages which could have facilitated dissemination of the tick (Barré et al., 1995; Deem, 1998; Léger et al., 2013). The reasons for the successful translocation of this tick include its ability to survive long periods without feeding, its adaptation to a wide variety of habitats and hosts, and the ability of engorged females to lay up to 20,000 eggs (Jongejan and Uilenberg, 2004; Léger et al., 2013). This pattern of spread is likely to continue not only for *A. variegatum* but also for several other African tick species as an increase in suitable habitat together with changes in climatic conditions are predicted, holding the potential for future dissemination of ticks and their associated pathogens (Cumming and Van Vuuren, 2006).

Another aspect of increasing mobility is travel health. International travellers represent a group potentially at high risk of disease acquisition wherever they enter endemic areas, because they tend to have limited knowledge about health risks in the destination area (Hamer and Connor, 2004) and are easily exposed to tick-infested habitats (Goddard, 1989). Tick-borne infections may be taken home where they can be misdiagnosed or not diagnosed at all by physicians who lack experience with non-endemic TBDs (Randolph, 2002; Bröker and Gniel, 2003).

5. Conclusions

One of the problems which we see at the moment is a tendency to relegate hypotheses to a status of low significance if data sets do not provide an immediate indication of their importance. We consider this to be true for both climate change, for which the current data may or may not be indicative of changes in tick distribution and abundance due to global warming, and to the role of biodiversity in reducing the incidence of TBD. It is remarkably easy to criticize limited data sets, and most of our data sets are limited, and it is extremely difficult to design really comprehensive field studies, and analyze them adequately, let alone find the funding to carry them out.

Another problem is that over one-third of ixodid tick species are known to feed on humans, with this value rising to above 50% for the genera *Rhipicephalus*, *Dermacentor* and *Hyalomma* (Guglielmone et al., in press), many of which can transmit pathogens. Most of our information on the host-tick-pathogen system comes from very few species, and these are dominated by *I. ricinus* and *I. scapularis*. The genus *Ixodes* (the only one in the Prostriata; all other ixodid tick genera belong to the Metastriata) (Nava et al., 2009), have certain ecological characteristics, for example mating off-host, which are not shared by members of the Metastriata. Thus, our concentration on this group may lead to a bias which does not reflect the complex dynamics of other host-tick-pathogen systems.

TBDs develop within a complex, dynamic system involving the characteristics of vectors, hosts and the abiotic and biotic environment. To fully understand this system both long-term, i.e. long enough to assess both natural and progressive annual variability, small and large-scale studies incorporating the factors influencing TBD dynamics are required. These studies must include interdisciplinary teams with expertise not only in tick ecology and the molecular determination of TBPs, but also in physical and human geography, meteorology, sociology, veterinary and human medicine, as well as public health management in addition to ecology. The very complexity of the system and its significance for human and animal health should allow it to become a meeting point for difference fields of expertise and a model for holistic studies.

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