Tick-borne pathogens, transmission rates and climate change

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1. ABSTRACT

Ticks are parasites that expend most of their life cycles off the host. Most important parts of the tick life cycle are directly dependent upon climate. There exist some concerns about the effects of the forecasted climate change on the geographical distribution of ticks. As tick life cycle dynamics would also be affected, the transmission of tick-borne pathogens could also be transformed by climate trends. Tick cycles are the result of complex interactions between climate, hosts populations, landscape characteristics, and the fine modulation of the populations of every partner involved, and not a simple, straightforward correlation between abundance and climate. The understanding of the climate niche used by different tick species may help in the search of clues towards a clarification of the expected effects of climate changes on the reported tick range shift. Populations of ticks occupying different portions of a wide geographical range may use different "portions" of the climate envelope, therefore resulting in misinterpretations from modeling results. Some advances can be foreseen in the complex task of modeling tick-host-pathogen interactions.

2. INTRODUCTION

As is the case with many other arthropods, ticks are very sensitive to climate. Ticks spend most of their life cycle in the environment, and all tick life cycle stages are dependent on a complex combination of climate variables. Host availability and vegetation significantly modulate the dynamics of tick populations. As with all animals, tick survival depends on reproduction, food and shelter. Tick recruitment is dependent on successful reproduction, which in turn requires sufficient adult tick densities, available blood meal sources, and egg survival. A blood meal is required during immature mobile life stages to support development into the next life stage, and for egg production by adult females. Though many animals can serve as hosts, there are several determinants of host suitability. For example, host availability in time and space is an important determinant of tick bionomics. Shelter and protection from environmental extremes are critical to tick survival. Questing and diapausing ticks are vulnerable to extremes of temperature and humidity. There are concerns about how predicted climate change may alter several critical features of host-parasite relationships involving ticks, in particular

the potential for invasion of new areas or alteration of patterns of pathogen transmission. This chapter will review current knowledge of the impacts of climate change on tick distribution and life cycles, and the dynamics of tick-borne diseases.

3. CLIMATE AND CLIMATE NICHE OF TICKS

### 3.1. The framework of climate and tick distribution

Fundamental to understanding how climate change could affect tick-transmitted pathogens is assessment of its effect on the geographical range of tick populations, and the colonization of new areas as a consequence of their increased suitability as tick habitat. This is a complex exercise because of the many variables involved in the regulation of successful invasion and establishment of "new" tick populations beyond their historical range. Furthermore, the geographical ranges of tick populations are not static, and will shift as a consequence of cyclical but as yet unstudied changes in climate, or as an outcome of human activities (including changes in vegetation, land use or host displacement). One of the common assumptions associated with climate warming is the inexorable extension of the range of disease-transmitting arthropods, including ticks. It is assumed that climate change will produce an expansion in the geographical range of "any" tick, and that species currently found in warmer environments will be introduced to areas beyond their current range, probably by migratory birds or uncontrolled animal importations. In this regard it has been demonstrated that migratory birds can act as carriers of immature stages of tick species of economic and human health importance (1). Although there is generally inadequate surveillance and reporting of changes in distribution of tick populations, there are some well-documented reports, reviewed later, of the slow but apparently continuous expansion of the historical frontiers of some tick species into areas where they were previously absent. Warmer temperatures have been suggested as the main drivers of these range changes. However, the potential influence of changing rainfall patterns has largely been ignored despite the fact that this may have a greater effect than temperature on the ability of populations to establish in new areas. Invasive events (the transportation of an exotic tick species into an area far from its native range) are also well documented and seem to be related to unrestricted domestic animal movements or over-abundance of certain wild hosts.

3.2. The concept of climate niche

Climate suitability for a tick population can be defined as the fitness of a set of climatic conditions for the existence of that population in a given region. However, many other factors operating at different levels restrict the effective dispersal and establishment of potential invaders. Thus, while the climate in a particular location may be suitable for a given tick species, the potential for dispersal there and the ability to establish a new viable population may be very low. We can evaluate the trend in climate for a given region, compare it with the optimal conditions for the survival of tick species, and derive an index of suitability for the tick in that region. Several factors restrict the

colonization of new areas by a tick species, including the movement of host populations and the presence of physical barriers to dispersal of hosts and their ticks. Therefore, when the suitability of a new area for a tick population is evaluated, the assessment must consider climate and vegetation. Most data on climate preferences of ticks have been empirically derived from descriptions of their environmental niche, as defined by the climate supporting native populations, and based on the assumption that they are homogeneously distributed in the native area. Macroclimate (large-scale weather systems) may delineate regional distribution and mesoclimate may demarcate an ecosystem (e.g. forest canopy influences on humidity, temperature and wind strength). However, microclimatic variables such as soil surface temperature and relative humidity (which are affected by such things as slope and aspect, snow cover, vegetation, litter layer, humus and underlying soils) may be crucial in determining the distribution pattern of specific niches for tick survival within an ecological community. Deterministic models are needed to evaluate the possibility of a propagule (perhaps an engorged female or engorged nymphs introduced via migratory birds) becoming established in a newly invaded area. Adequate deterministic models, both matrix structure-based (2) and process-based (3), have been developed for the black-legged tick (*Ixodes scapularis*), as well as for some other prominent tick species including *Rhipicephalus (Boophilus) microplus, R. (B.) annulatus, Dermacentor variabilis* and *Amblyomma americanum* (4-6). These models were developed to simulate the effects of intra-annual variations of temperature and humidity on the seasonality of different tick instars, and to investigate the potential limit of northward spread of *I. scapularis* imposed by the effects of temperature on tick survival. The models did not take into account the effects of habitat fragmentation, or host availability and movement at the scale necessary to evaluate these factors. A quantitative improvement has been achieved with development of a model for the cattle tick that is based on population processes, and includes habitat structure, and host availability and movement (7,8).

The quantification of species–environment relationships has long been a fundamental pursuit in ecology, and is the basic framework for understanding the fitness of existing climatic conditions for a population of a given tick species. Currently available digital environmental data encompass many variables that influence the macrodistribution of species, and sophisticated software now exist for predicting distributions and mapping species–environment relationships based on ecological niche models (9). The underlying principles are being increasingly used for mapping important environmental factors for ticks. Since the pioneering work in this area (10, 11), new methods and refinements have been included in current models. The basic concept underlying species occurrence modeling is the definition of the ecological niche (Figure 1): each species is found within specific ranges for environmental variables which support individual survival and reproduction (12). We refer here to climate instead of environmental or ecological space, because these studies were aimed at understanding
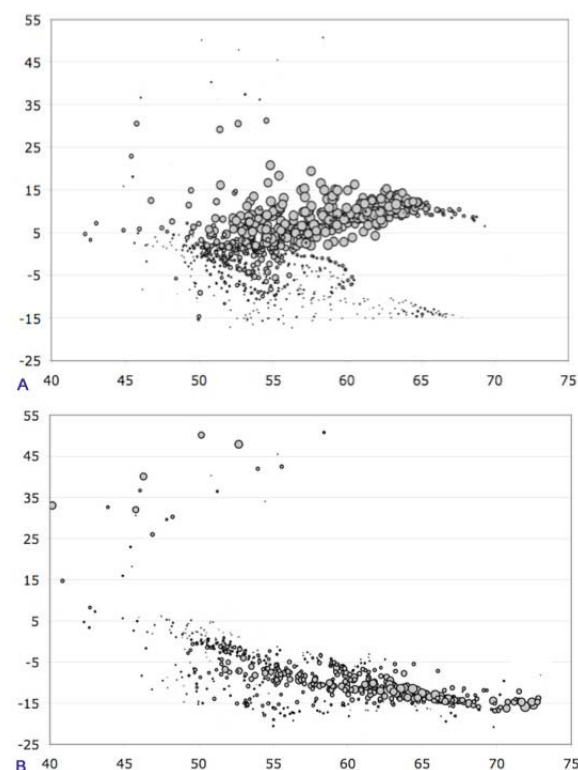
Figure 1. The concept of climate niche. Each tick species (or population) occupies a concrete position in the space of the climate. The figure shows the climate suitability for two African *Amblyomma* species, namely *A. variegatum* (A) and *A. hebraeum* (B) and the positions in the reduced space of climate after decomposition by principal component analysis. Rdry marks the intensity of the drought period (negative values mean for a longer and more intense drought period) and Rtot means for the total rainfall in the year. *A. hebraeum* prefer zones of the climate niche where the drought period is more intense. The diameter of the dots is proportional to the climate suitability in that given position of the climate space. Although this example shows only 2 principal components, the concept can be extended to "n" dimensions in the climate components. Unpublished data.

the relationship of ticks to climate, and ignored some basic aspects, such as vegetation patterns or host abundance, that are also involved in delineation of the "ecological" preferences of a tick species or population. Species occurrence can be predicted through inclusion of appropriate climate variables in what are commonly referred to as habitat suitability models (9): the relationships are generalized from a sample of correlations of species presence with specific values of environmental variables. This concept is being increasingly applied to predictive mapping and assessment of ecological determinants of disease vector distributions.

3.3. Tick populations and adaptations to local conditions

While it is well recognized that the climate niche space occupied by a species across its geographic range may vary for a variety of evolutionary and non-evolutionary reasons (13-16), this is rarely considered in current modeling approaches despite its obvious importance. When regional niche variations occur, a suitability model derived for a particular area may not apply to other areas, and a model derived from a large area may have comparatively weak local predictive power (17). A widely held assumption in traditional models of tick distribution is that responses of species to environmental gradients are unimodal and symmetrical. Thus, habitat suitability is predicted to decline from central (and ecologically optimal) areas of a species' range towards the periphery. In suboptimal conditions a species may compensate for physiological stress by a shift in niche position (18). For wide-ranging species, ecological conditions may vary considerably between different regions within the range.

Alternatively, populations at the range periphery may occupy habitat that is not found in the central parts of the range, resulting in no overlap in niche space between the two regions. Such patterns could result from differences between regions with respect to soil type, elevation, climate or other environmental factors. Even if all individuals of a species respond in the same way to environmental conditions, regional variation in the distribution of those conditions will lead to regional variation in responses. Thus, a map showing habitat suitability for a population occurring in central parts of a range may be very different from that for a population at the edge of the range. The occurrence of populations of a species that have significantly different climate requirements has been recognized within a complex metapopulation of *Boophilus* ticks in Africa and South America (19). This example demonstrates the need to account for regional variability in the response of species to climate gradients. In the Palaearctic, *Ixodes ricinus* is one of the most important vector species involved in transmitting pathogens to humans. Both Lyme borreliosis (LB) and tick-borne encephalitis (TBE) are transmitted by this tick in complex cycles that will be referred to later in this chapter. Therefore, there is great interest in mapping the potential distribution of *I. ricinus* and understanding its life cycle patterns (20). Mapping is directed at understanding the potential distribution area of the tick, based on climate features, and to forecast changes in its geographical range under several climate scenarios. As mentioned previously, these models are derived from the current known distribution of the species, using climate matching algorithms that compare this distribution with the climate existing in the whole area to be mapped. However, the existence of "demes" has been demonstrated for *I. ricinus* (21); demes are populations of closely related interbreeding organisms of the same species with differing response to the wide array of climate factors occurring across the geographical range of the species (Figure 2). The delineation of demes parallels results from a recent study of cuticular hydrocarbons, which can be useful markers for insect taxonomy. The study revealed at least 10 distinct *I. ricinus* groups with a pattern to their geographical
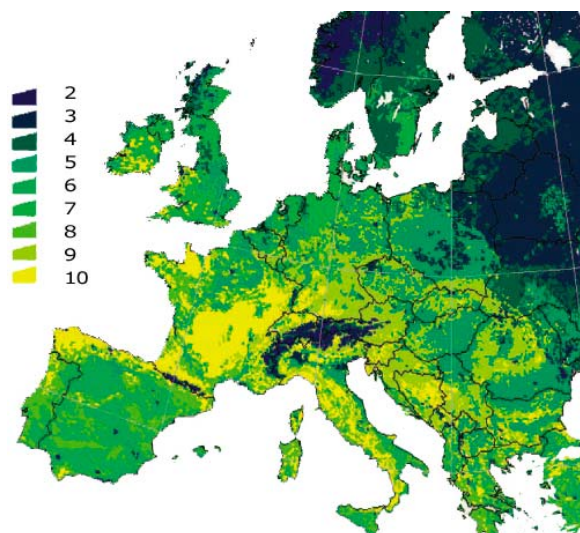
Figure 2. The ecological clusters as recognized over a portion of Europe. The image was obtained from a yearly series of monthly satellite images, capturing the Normalized Difference vegetation Index (NDVI) a measure of the photosynthetic activity of the vegetation. These images were subjected to a cluster analysis according to the monthly NDVI features, to obtain 10 categories (category 0 is water and not displayed in the picture). The records of *Ixodes ricinus* over that huge area were shown to be subjected to significantly different climate conditions, thus having regional adaptations to climate. This separation of vegetation-derived clusters and the *I. ricinus* populations recorded for these clusters are in close agreement with the phenotypic characteristics of the same populations (as detected by cuticular hydrocarbons chromatography) and by sequences of the 16S gene fragment. Reproduced from reference 21, with permission.

distribution (22), and is in general agreement with an unpublished 16S mitochondrial rDNA study of genetic variation in *I. ricinus* (23). The importance of these findings is that the ecological features correlated with the genetic and phenotypic clades in the whole tick metapopulation, with different populations having specific climatic requirements and unique genetic fingerprints. These populations have unique responses to the surrounding environment, and differ in potential for range expansion if transported to a new region beyond their historical range. This demonstrates why climate suitability models built to evaluate range expansion of ticks should not be performed with the whole set of available distributional data.

3.4. Predictions derived from climate matching models

Ixodes scapularis is the main vector in North America for the agents of LB (24), human babesiosis (25), and human granulocytic ehrlichiosis (26). An expansion of the tick's geographical distribution has been documented over the past several decades, due in part to intensified surveillance efforts (25, 27-29). The potential distribution of the tick has been mapped in several studies (30, 31) using climate suitability models derived from the complete

set of available records, and all show a clear trend of northern expansion of the tick beyond its current distribution range. These projections have already been confirmed by reports of new permanent populations of the tick in areas where it was previously absent (32). The process-based deterministic model already developed (3) also points to increasing climate suitability for the tick in the northern parts of its distribution range, including parts of south-eastern Canada. In a study of recent (1983–2000) climate changes in the USA, Estrada-Peña (33) used "complete-set" models to demonstrate that the trend towards warmer winter temperatures in parts of the current distribution area of *I. scapularis* is the main factor involved in the increased habitat suitability for that tick. The trend identified by the model has been correlated with reports based on field records (Figure 3). However, this study was based on relatively recent climatic events, and probably could have identified a secondary trend inside a longer climate cycle. An intensive study on the changes in climate suitability for *I. ricinus* in the western Palearctic (34) has been carried out using cluster-derived models based on the different populations recognized in the Palaearctic. The distribution records available for the different demes were used to build partial models (i.e. applied to regions of the whole distribution range) from which a complete map for the whole region was produced. The study used a long (1900–1999) series of climate data at coarse resolution (10 minutes of arc) to examine the trends in climate and to estimate sustained variations in climate suitability for *I. ricinus*. While some areas showed a deterministic (i.e. continuous) tendency towards increasing or decreasing suitability for the tick, others showed unambiguous cycles of climate suitability, termed areas of random walk. Populations of the tick in these areas may undergo periodical variations in their geographical range as consequence of cyclic changes in climate.

This analysis suggests that while a large area of Europe did not change in climate suitability for *I. ricinus* during the 100-year study period, suitability increased in specific geographically limited locations and decreased in others (Figure 4). These changes are not recent and are associated with yearly and summer rainfall patterns rather than with temperature. The reported increased abundance of *I. ricinus* in parts of Europe (35, 36) coincides geographically with the regions where a recent increase in HS has been detected, within zones having a marked random walk tendency. Thus, the observation of higher tick abundance in recent years may not be due to a permanent shift in tick populations, but rather because the long-term climate cycle, which varies on a wide timescale, has been in a phase that is favourable to tick survival. No single variable was consistently associated in the study period with changes in climate suitability across sites were random walk was detected. The absence of a single regulatory variable seems to be connected with the different climate niche experienced by the tick populations in their distribution area. Different portions of a tick climate niche vary in sensitivity to climate change (21). Thus, rainfall and temperature have different regulatory abilities according to the portion of the tick's climate envelope represented in a given area. This assertion is supported by the consistent
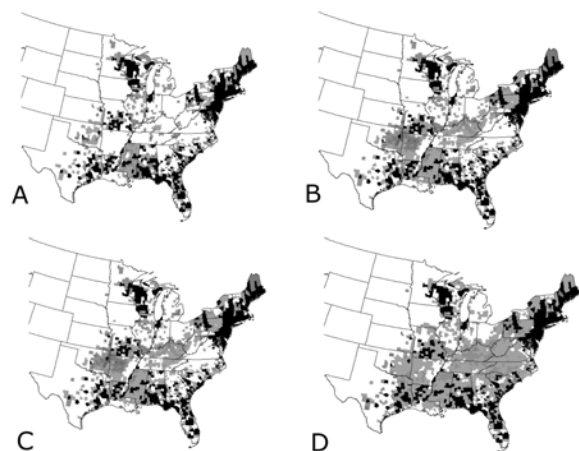
Figure 3. Changes in the climate suitability for the tick *Ixodes scapularis* in USA in the period 1983-2000. The sequence (A to D) shows the increasing suitability (areas of grey tones) for sites in wide areas in eastern USA. The main factor operating over these changes was a trend towards warmer winters. Reproduced from reference 33, with permission.

finding of a random walk area surrounding main regions exhibiting a deterministic trend, which seems to be related to the essence of the tick's environmental niche. The core area experiments buffered changes in climate, well within the range of the tick's climate envelope, while the surrounding portions of territory suffer a higher impact on the tick response.

As mentioned before, there is inherent complexity in evaluating the potential survival of invading propagules, even if only the climate features are considered. This is a consequence of the recognized ecological plasticity of tick species. We ignore if the recognized populations over the wide geographical range of a tick species are "spots" or "clouds of records" in the climate niche of the species, each adapted to a given set of climatic conditions. Therefore, these demes could be adapted to a set of local conditions, and lack the ability to quickly adapt to the conditions in other areas of their historical range already occupied by different demes (Figure 5). Alternatively, each population (or deme) might retain the complete ecological plasticity of the species, therefore adapting with the same malleability to a new set of environmental conditions. The second possibility is based on the theoretical assumption that the population already homogeneously occupies the complete set of available niches within a given species-specific range. The possibility of mutations enabling ticks to adapt to new climate gradients, and the speed with which this can occur, is unknown. A tick with a short life cycle (i.e. single-host ticks reproducing several times per year would adapt faster than a species, such as *I. ricinus,* where the complete life cycle takes about 3 years. Basic research is necessary to evaluate the responses of different demes to variable climate conditions, and to build accurate deterministic models applicable to the mapping of invasive probabilities. Resolving these features of basic tick biology may

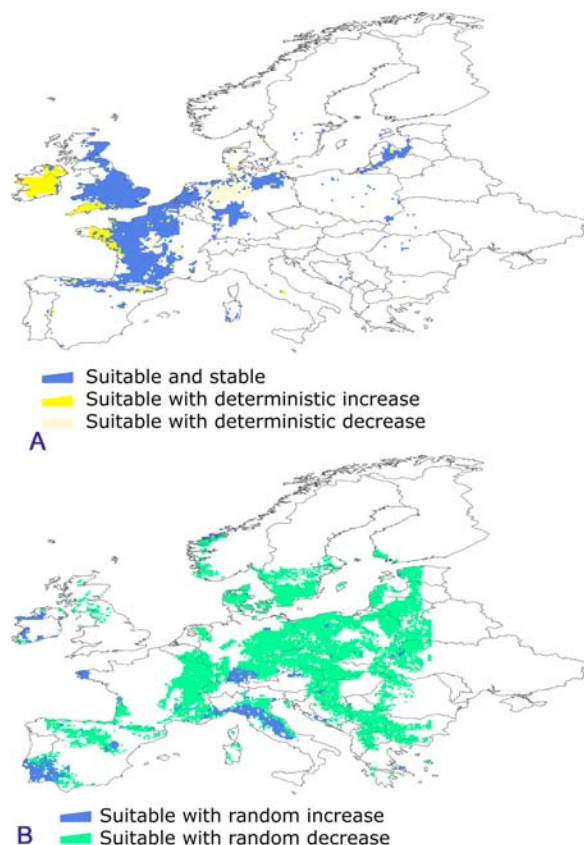drastically change the output of a modeling algorithm.

Giving these assumptions, it is of interest to compare the predictive performance of a deterministic model (based on tick life cycle processes) with evaluation of climate suitability obtained through actual records of the tick and its fitness to climate conditions. This comparison has already made for *R. (B.) microplus* (37) in southern America where the potential for southern spread of the tick was evaluated in the context of chemical control measures being relaxed. This study showed an adequate (but incomplete) agreement between the two types of model. It was also demonstrated that warmer winter temperatures provide an adequate context for expansion of tick populations into southern areas, which are currently too cold for tick survival. The combination of both models provided enhanced knowledge of the expected invasion range under different climatic conditions, as well as identifying the period of the year representing greatest risk of persistence of invading propagules (spring, in the studied region in southern Argentina).

In summary, even with the constraints noted above the models for those species already investigated (including *I. ricinus*, *I. scapularis* and *R. (B.) microplus*) predict a geographical shift of suitable conditions for survival and development of tick populations into higher altitudes and colder latitudes. However, caution is required in constructing models of this nature and interpreting the information derived from them, because of the need to take account of populations with different response to climate conditions, even within the same species. Despite this, results point to an expansion in the Mediterranean region of areas with suitable climate for ticks including *Rhipicephalus turanicus* and *Hyalomma marginatum marginatum*, both of which are species with importance in the transmission of human diseases including *Rickettsia* spp. or Crimean-Congo hemorrhagic fever (CCHF). As mentioned above, these models did not account for vegetation and host-derived effects, and only focused on the impact of climate on the expected geographical range. Consequently these tick species are expected to find sites with adequate climate towards northern latitudes, and fewer sites for survival in their southern ranges (38).

3.5. Reports about range shift in tick distribution
In addition to information obtained from modeling, there are reports of changes in the distribution of some ticks in several parts of their distribution ranges. For example, the northward expansion of the geographical range of *I. ricinus* in Sweden (39) in the period 1980–1990 has been related to milder winters and extended spring and autumn seasons (35). This phenomenon was also observed in Denmark (40) and Norway (41). In the Czech Republic, long-term field studies (36, 42) have revealed a shift in the altitudinal range of *I. ricinus*, and colonization of new habitats where these ticks where formerly absent. Engorged *I. ricinus* ticks had been introduced several times to altitudes exceeding their former vertical limit. Although part of the developmental cycle was occasionally completed, adequate climate conditions did not favor their survival and a stable local population was never established

Suitable and stable
Suitable with deterministic increase
Suitable with deterministic decrease

A

Suitable with random increase
Suitable with random decrease

B

Figure 4. An analysis of the long-term changes in climate suitability for the tick Ixodes ricinus in Europe (1900-2000). A temporally extensive gridded dataset was subjected to a temporal analysis to understand how climate has changed in 100 years and how this trend affected the climate suitability for the tick. Areas are divided into suitable and unsuitable (without colours in the figure). In the panel "A", the area marked as suitable and stable means for no changes in the suitability for the tick. Deterministic increase or decrease mean for a continued trend towards increasing or decreasing climate suitability. Panel B shows the areas where random walk trend has been observed. These areas are subjected to periodic cycles of climate, thus allowing cycles of increasing or decreasing climate suitability for the tick. It should be noted that areas where the tick has been reported as "more abundant" in the last 20 years (i.e. southern Scandinavia) are in fact part of a cyclic climate behaviour. Reproduced from reference 34, with permission.

(43, 44). Climate changes in the past two decades, particularly higher temperatures in spring and autumn, have provided a longer period for the development of ticks at higher altitudes (45), and thus contributed to the occurrence of populations in mountains. Regular reports of the presence of all active host-seeking stages, and tick occurrence on pets (34, 46), provide evidence for the existence of established local populations, and not just surviving individuals occasionally brought in with hosts. Similar invasive behavior has been reported for the tick *I. scapularis* in Canada (47). This tick has permanent

populations in northern USA, close to the Canada–USA border. From 1980–1990 the tick was sporadically recorded in Canada, probably as a result of the arrival of engorged immature stages on migratory birds. However, passive surveillance of broad areas of southern and south-eastern Canada revealed permanent and expanding populations of *I. scapularis*. Previous studies in the same area did not detect such populations before the year 2000. It has been argued that the increasingly warm winters may be improving the survival of ticks in that region. The tick *Dermacentor reticulatus* has also been spreading in areas of western Germany (48) and The Netherlands (49). The indigenous sub-Saharan African cattle tick *R. (B.) decoloratus* is being rapidly displaced by the Asian congeneric *R. (B.) microplus* in regions where the ticks co-occur (50). There is also evidence of rapid adaptation of populations of the latter tick to different hosts (e.g. goats) and to climate conditions different from those prevailing in areas native to the invading population (51).

Another well-documented expansion has been recorded for the tick *Amblyomma hebraeum* in Zimbabwe. *A. hebraeum* and *A. variegatum* are vectors of heartwater (*Ehrlichia ruminantium* infection) in Zimbabwe, and were believed to be confined to the low-lying regions of the south and the north-west of the country, respectively. The central plateau (highveld) of Zimbabwe separated the southern limits of *A. variegatum* from the northern limits of *A. hebraeum*, and neither species permanently established in agricultural areas of the highveld during the past century (52). However, country-wide surveys in 1975–1980, 1988–1991 and 1996 demonstrated that both species were established in western parts of the highveld plateau. Cattle dipping in the communal farming areas in the low-lying southern part of the country (southern lowveld) was disrupted between 1977 and 1980 because of the pre-independence war, and *A. hebraeum* and heartwater spread rapidly (52-54). By 1980 *A. hebraeum* had been recorded throughout the southern lowveld, and its distribution in central Zimbabwe had extended northwards onto and beyond the highveld plateau. At this time there was some overlap between the distributions of *A. hebraeum* and *A. variegatum*. Between 1981 and 1985, when intensive dipping was restored in the communal lands, *A. hebraeum* apparently disappeared from the highveld areas to which it had spread. However, *A. hebraeum* has subsequently re-established in the highveld. *A. variegatum* was already established in the northern lowland and there was no evidence of significant spread of this species. The spread of *A. hebraeum* has been attributed to the breakdown in government-provided dipping services in small-holder communal farming areas, as well as to movements in wild ungulates, which are alternative hosts for *Amblyomma* species (55). A study of long-term changes in climate in the different regions of the country, and how these may affect the ticks, showed that in the period 1970–2000 there was a trend towards deeper droughts in summer. These conditions were more suitable for *A. hebraeum* (unpublished data), and the tick thus invaded progressively drier areas. This factor, together with relatively cold temperature, is creating a barrier between these two sympatric species. *A. hebraeum* extends into areas which are becoming progressively drier
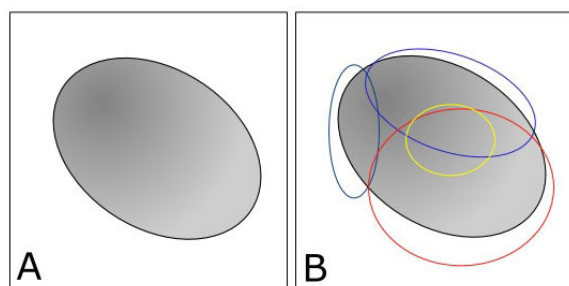
Figure 5. Several allopatric populations of the same tick species may occupy different portions of the climate niche. In A, the whole set of specimens of the population is occupying the complete climate niche (represented by the greyed oval) in a schematic representation of two climate variables (axes X and Y). In B, the same space in the climate niche is occupied by different allopatric populations (coloured ovals), colonizing different geographic areas and adapted to the prevailing regional conditions. These populations are well adapted to their regional climate conditions, but poorly adapted to survive if "transported" to a different portion of the climate niche of another population. This concept, already demonstrated for both *Ixodes ricinus, I. scapularis* and *Boophilus* species, may have deep implications in the development of habitat suitability models. As the modelling algorithms capture the behaviour of the whole set of records, predictions for wide areas may be biased because the local characteristics of adaptations of ach population.

in summer, while *A. variegatum* spreads into zones which are becoming progressively warmer but have a higher level of moisture, adequate for the survival of the species.

3.6. Distribution *versus* abundance: other effects of climate conditions on tick populations

The term "increased abundance" (or combinations or synonyms of these words) has been used to define one of the outcomes of climate warming on tick populations. Increased abundance is an expected consequence of warmer temperatures in winter and shorter annual cold periods, which limit development and increase mortality of tick stages, as noted earlier for the mountain regions of the southern Czech Republic. A long-term study of questing stages of *I. ricinus* in northern Spain (1992–2002) showed a clear increase in monthly abundance of all stages, no clear correlation with the climate variables recorded at the site, and weak but significant correlations with autumn–winter temperatures (56). Climate would have only had a secondary influence on these findings, as landscape fragmentation or other effects of human urbanization have the dominant influence on host abundance, and thus on the abundance of questing ticks. Habitat fragmentation has long been recognized as an important factor, together with climate, in influencing the abundance of the tick *I. scapularis* in the USA. The increasing fragmentation of formerly forested areas in the north-eastern USA, as a direct consequence of urbanization, is considered to play a pivotal role in the abundance of that species. This tick is commonly reported on humans and is more abundant in field surveys in very fragmented areas (57, 58). A spatially

explicit model covering a wide area in northern Spain (59) has shown how habitat fragmentation and landscape connectivity are related to the abundance of *I. ricinus*. Landscapes are heterogeneous mosaics of habitats and land uses, in which habitat quality for the tick and their hosts varies across the landscape. Habitat connectivity is a central theme in the maintenance of tick populations, and refers to the ability of organisms to access habitat, which affects colonization rates, persistence and density. As ticks can only be spread by their hosts, the movement of host populations across a landscape is a key factor in understanding tick density in areas where climate variables provide adequate habitat. Field surveys have demonstrated that habitat patches most visited by hosts are significantly and consistently correlated with high densities of questing *I. ricinus*. However, patches of habitat far from these "main paths" of host movement tend to have no or smaller tick populations, even if adequate environmental (climate) conditions are present (Figure 6). Thus, the spatial structure of the landscape and its connectivity are key factors in understanding the emergence of local tick populations. Patch availability and landscape fragmentation have a direct influence in the infectivity rates of tick populations, as will be reviewed later for LB and CCHF.

Related to the comments above, a landscape-derived model based on host habit and migratory aspects has been developed (60) to assess the dispersal potential of *I. scapularis*. The model involves a rectangular lattice, and investigates factors involved in host movements which are necessary to disseminate the tick population from infested to uninfested areas. However, the model does not explore climate suitability for the tick and is extremely sensitive to the many parameters involved. The study identified the need to obtain adequate data from field investigations of these parameters. As the authors suggested, the inclusion of all seasonal host movements (e.g. migration and juvenile dispersal) should increase the estimated rate of range expansion, because seasonal movements occur over longer distances than daily movements (61). Introducing spatial heterogeneity to the modeled landscape would make the model more realistic (62) and allow geographical barriers to *I. scapularis* spread (e.g. rivers and urban areas) to be identified. The length of the *I. scapularis* life cycle greatly influences the rate of expansion. If environmental conditions promote a shorter life cycle (such as in the southern United States) or longer than two years (as in Canada), the rate of expansion will change accordingly. The discussion above provides an overview of the many factors involved of the range shift of tick populations. The main point is that climate trends may underpin the expansion or retraction of the historical range of some tick species, and reports are beginning to confirm this for some important tick species. However, factors in addition to climate (including vegetation, hosts and landscape configuration) are also key variables affecting tick distribution. Furthermore, the results obtained from models may be biased by the use of data inadequate for extrapolating habitat suitability for a given species. As we continue to improve our knowledge of the distribution and ecological requirements of ticks, there is an urgent need to integrate these findings into a model explaining the effects of every variable involved in the regulation of tick populations.
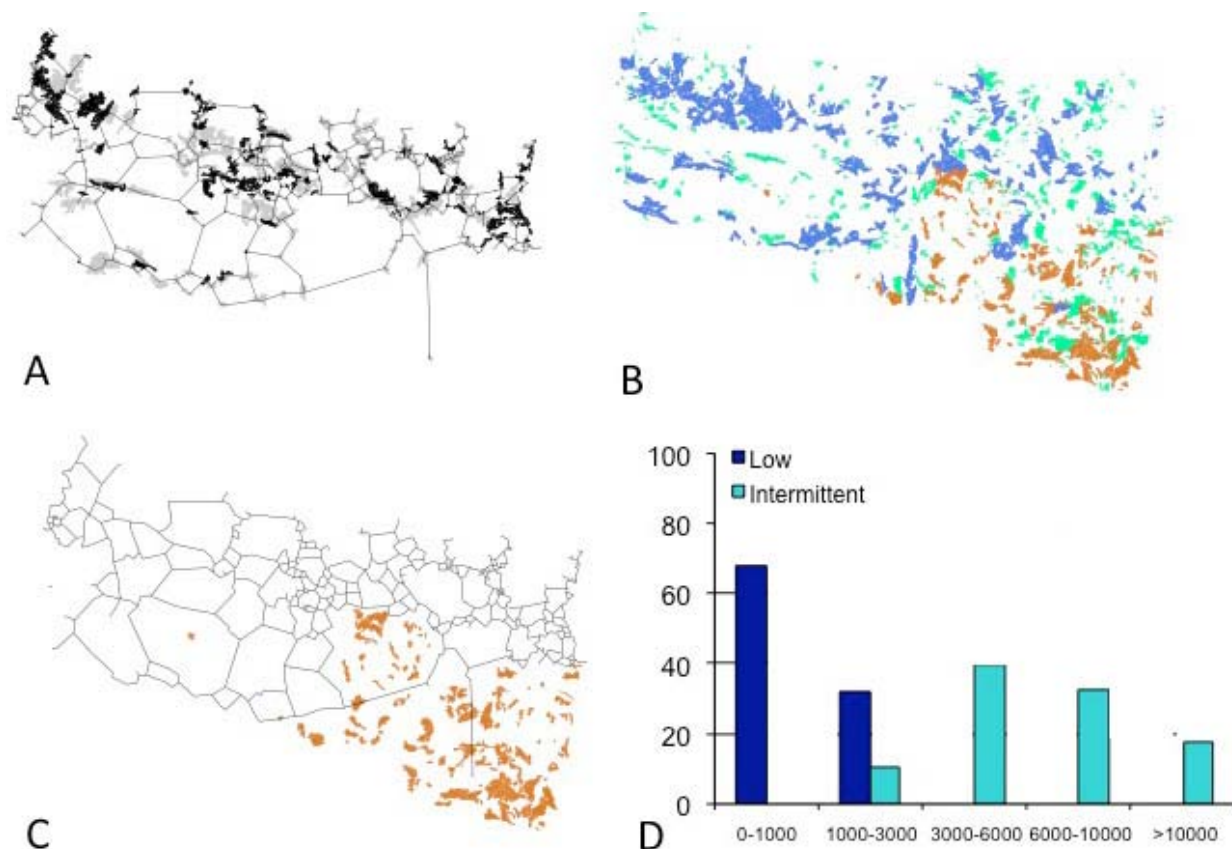
Figure 6. The figure shows the results of a field survey in northern Spain concerning the abundance of nymphal *Ixodes ricinus* according to the landscape characteristics and fragmentation in a long term suvey (1996-2000). In the panel A, patches where *I. ricinus* was abundant (black) and where it had medium abundance (grey) are displayed, together with the networks of interpatch connections. These links are the highest probability movements of the hosts between the patches. Panel B shows the patches were I. ricinus had permanent populations in low abundance (blue) and where *I. ricinus* was intermittently collected (green). Patches in red are the sites where climate and vegetation suitability was predicted to be adequate for the species, but where *I. ricinus* was never collected. Panel C shows that these patches are located far from the main links followed by the host in their interpatch movements. Chart in D shows the percent of the different patch types according to *I. ricinus* abundance and the distance to these interpatch links. Blue bars are the percent of patches where *I. ricinus* was abundant, and they are located at a maximum of 3,000 meters from a host link. Yellow bars are the percent of sites where *I. ricinus* was absent, even if the climate suitability was optimum. Distance to links was intermediate was always higher than 6,000 meters. These findings indicate that a simple climate model cannot explain the abundance of the ticks in the field, and that landscape configuration has a deep influence in the behaviour of the populations. Reproduced from reference 59, with permission.

4. THE TRANSMISSION OF PATEHOGENS: HARMONIZED CONTACTS BETWEEN HOSTS AND PATHOGENS.

4.1. Generalities

In temperate zones of the northern hemisphere, the vast majority of vector-borne diseases of humans are transmitted by ticks rather than insects. In both the USA and Europe, ticks of the genus *Ixodes* are involved in the transmission of human babesiosis, LB, human granulocytic ehrlichiosis or TBE. These diseases have been recognized as an "emergent" problem in the last 20–30 years, but explanations for the rise in reported cases seem to go far beyond the forecasted warmer climate. From discussion in the previous chapter of the abiotic or climate factors involved in the distribution of tick vectors, the reader will appreciate the complexity of the dynamics of tick-borne diseases and our efforts to understand the role of climate. A key factor is seasonal tick dynamics. Some species (or species under certain climate conditions) have a well-defined seasonal pattern of activity, markedly influenced by prevailing climatic conditions. To find a host, ticks climb to vantage points in the vegetation, but are particularly vulnerable to desiccation during this phase of their life cycle. They can rehydrate by descending to the humid base of the vegetation, but this costs energy and most species appear to time their host-seeking activity to avoid dry or cold periods of the year. Host-seeking activity in the majority of habitats is most intense in spring and early summer, with relatively little activity in mid summer. For *I. ricinus* a second, usually lower, peak of activity occurs in

autumn in some areas. This basic pattern is subject to considerable variation, even within areas, due to the influence of host availability and macro- and micro-climate effects (63).

4.2. Lyme borreliosis
 In contrast to the environmental determinants of tick distribution, tick-borne pathogen distribution appears to be determined solely by biotic factors (64). Host-related factors are the major determinants of pathogen transmission, and ultimately the geographic range of the pathogen. In the case of LB, besides the requirement for a suitable vector that will harbor the pathogen and infect naïve hosts, a suitable vertebrate reservoir host is necessary to maintain the spirochete. For example, an efficient tick host is not necessarily a suitable disease reservoir, as illustrated by the white-tailed deer in the case of LB in the USA (65), and by the zooprophylactic effect of western fence lizards (*Sceloporus occidentalis*) for the same disease in California (66). It has long been assumed that vector ticks can only acquire the pathogen from systemically infected vertebrates. However, it is now apparent that some pathogens can be transmitted by co-feeding, whereby short-term localized infections of the skin can serve as a source of pathogen acquisition by uninfected ticks feeding in the same area at the same time as, or shortly after, infected ticks. This mechanism has been shown to be of great importance in the transmission of TBE, in which viremia is low and short-lived; hosts which do not become viremic because of inherent or immunological resistance may still serve as a source of infection (67). Co-feeding transmission has also been demonstrated in *Borrelia burgdorferi* s.l. (68), but since many animals in typical LB habitats can be systemically infected by this pathogen, co-feeding transmission is probably of limited significance in its eco-epidemiology. In summary, synchronized host and vector encounters are required for completion of the Lyme disease spirochete life cycle, since horizontal transmission is the principal manner by which the spirochete is passed, with vertical transmission apparently playing only a negligible role (69).

 The epidemiology of LB is quite different in Europe and the USA, and even between the two areas of spirochete transmission in central-eastern and western USA (70). Different hosts occur in the wide distribution area of the disease, and all have different rates of amplification of the disease. Maintenance of the disease in natural foci depends on the ability of the infective agent to be passed into non-infected feeding ticks. Consequently, the host preferences of the tick population (or the availability of defined groups of hosts when ticks are active) in a given region are pivotal in determining the different infection rates in ticks, reported for various sites across the distribution range. Studies have been made of the ability of different hosts to support and infect immature ticks (71-73), and a comprehensive understanding of amplification factors for LB in Europe has also been developed (74). Therefore, the transmission and maintenance of LB spirochetes in the field is dependent upon a wide array of host-derived features that vary locally. These may significantly affect the infection rates of nymphs, the most important stage in the transmission of the disease to humans. How could forecasted climate change affect these locally different populations and

host associations? Warmer winters may increase the survival of ticks, as already demonstrated (3), but drier and warmer summers may have a major impact on the survival of these relatively desiccation-intolerant tick species. However, we currently lack a sufficiently detailed model that captures the effects of climate on changes in tick and host seasonal dynamics and abundance. This framework would undoubtedly improve our understanding of the transmission cycles of LB, as affected by climate.

 A third factor, landscape fragmentation, has been proposed in addition to tick and host abundances as an explanation for the increased rate of nymphs found infected with LB spirochetes in field studies. Landscape fragmentation has been identified as a central feature driving the abundance of hosts, and therefore of ticks feeding on them. In approximately the last 20 years there has been an increased rate of human LB infections reported in the USA. There is evidence that deforestation and elimination of deer during the 18th and 19th centuries in the USA disrupted conditions suitable for survival of *I. scapularis* and enzootic cycles of *B. burgdorferi* (75). These conditions were reestablished around 1930 by reforestation and reintroduction of deer, which was followed by the spread of *I. scapularis* from undisturbed refuges. With enzootic cycles already reestablished (the disease was discovered at the end of the 1970s) there was a rapid increase in reported cases, probably as a consequence of increased awareness and improvements in diagnostic methods. These cycles became more evident (or amplification of the infection was more successful) under conditions of high habitat fragmentation, typical of the urbanized forests of the north-eastern USA. Under these conditions hosts for adult ticks (typically deer) and competent reservoir hosts for the pathogenic agent (rodents, chipmunks, some birds) find adequate habitat. Therefore, high numbers of infectible larvae, derived from females feeding on deer, come in contact with high numbers of reservoir hosts. Furthermore, human activities are common in these highly fragmented areas, resulting in a high probability of contact between infected nymphs and people. Thus, the conditions increased the abundance of reservoir hosts and resulted in an over-abundance of ticks (because of biotic causes). Together with improved surveillance and diagnosis, this must surely have exaggerated the rate of epidemic emergence.

4.3. Climate and masting: are they markers of Lyme borreliosis rates?
 There have been attempts to find a direct and simple relationship between the LB rates over a wide geographical area and climate variables. These were aimed at being able to predict rates of human cases of LB from a series of "proxy" variables that could explain the behavior of the disease. In one study (76), significant correlations were found between the reported rates of LB in seven north-eastern states and the June moisture index two years earlier in the region. Less significant correlations were found with winter temperatures 1.5 years prior to disease detection. Keeping in mind the wide heterogeneity of ecological conditions in those states, the locally variable density of adequate reservoirs, and the wide range of urban densities (and therefore possibilities of "human contact" with infected ticks), these results reflect an averaged relationship

between some climate features and the mean number of ticks in a wide area. However, these results are not a local measure of the effects of climate on LB incidence. It has been suggested that variations in LB rates in the USA fluctuate according to changing weather conditions affecting tick survival, or fluctuating acorn production affecting the behavior and abundance of reservoir mammals (77, 78). Acorn production fluctuates greatly from year to year, with synchrony over spatial scales of the order of tens to hundreds of kilometers (79). Abundant acorns attract white-tailed deer, the primary host for adult *I. scapularis* (80), and also cause increased abundance of white-footed mice and eastern chipmunks (78). Both species are important hosts for larval ticks and are highly competent reservoirs of *B. burgdorferi*. A systematic study of the climatic and biotic variables presumed to be acting as drivers of LB incidence (81) did not find any spatial correlation between weather variables and LB rates in those states. Acorn production and mice densities were good predictors of LB incidence rates in some states, but their effects seemed to be diluted by other factors that predominate in non-oak-dominated landscapes. The study (81) was premised on a theory that links acorn production with LB rates at a coarse resolution (i.e. the scale of a state), ignoring the cycles of *B. burgdorferi* s.l. in nature. However, there is adequate evidence that these cycles are complex, and that a direct link between acorn production and LB rates is highly improbable at local scales (82). The main "hidden factor" in these theories is that mice are not the only reservoir for the disease, either in the USA or Europe. Many other hosts (squirrels, pheasants, birds) have been shown to be adequate reservoirs and amplifying factors. Therefore, the reported rates of LB reflect a very complex chain linking climate, landscape fragmentation, host availability and social changes (82).

4.4. Tick-borne encephalitis

The importance of harmonized host and vector encounters has been demonstrated for TBE foci in Europe, as co-feeding by immature I. ricinus has important implications for the present and possible future distribution of TBE (83, 84). Although LB and TBE are transmitted in Europe by the same vector (I. ricinus) and share some reservoir hosts, they show very different epidemiological patterns. Whereas LB spirochetes circulate wherever there are competent hosts and tick species, TBE is restricted to distinct foci within central Europe and the Baltic states, including the south-eastern rim of Scandinavia (85). Some epidemiological patterns suggest that the TBE virus circulates within a narrower window of opportunity (86) with a lower force of infection. Relative indices of the basic reproduction number are an order of magnitude lower for TBE than for LB (86), largely because of the shorter period during which the virus can be acquired from infected hosts by the ticks (a few days) compared to that for acquisition of the spirochetes (several months). Based on laboratory experiments (87), theoretical considerations (86) and analysis of field data (88), it appears that enzootic circulation of the TBE virus depends on the amplification of non-systemic infections between infected nymphs and large numbers of infective larvae co-feeding on rodents. Therefore, the maintenance of TBE foci relies on synchrony in an individual host between the feeding of the nymphs of one generation and the larvae of the next. Analysis of available data (89) shows that TBE foci occur only where infectible larvae are active when infected nymphs are feeding. Predictive maps of the geographically variable seasonal tick

dynamics are not yet available. The features supporting that kind of cycle were identified (84) using statistical correlations between the spatial pattern of TBE distribution and environmental conditions, as obtained from the Advanced Very High Resolution Radiometer at 8 km resolution. One of the remotely sensed variables identified as an important determinant of these foci was the NDVI, because it is a good descriptor of habitats for I. ricinus (90). The second variable, land surface temperature, appears to be a critical feature in the outline of TBE patterns. The rate at which mean monthly temperature decreases from August to October is higher in TBE foci in relation to the midsummer peak, than in areas free of the virus (89). This has been confirmed using high-resolution remotely sensed imagery in an area of northern Italy (91).

In the absence of a generic, deterministic model for I. ricinus across its geographical range, it has been suggested (89) that rapid cooling in autumn inhibits host-seeking activity of larvae that emerge from eggs laid during the summer, and that they are reactivated, together with the nymphs, by rapidly rising temperatures in spring. The basic conclusion from the experimental work is that TBE cycles are very fragile in nature, as they are highly dependent on coordination of larval and nymphal activity, as well as on patterns of activity of suitable hosts, which may be affected in different ways by changes in winter and spring temperatures. So how might climate change affect these cycles? Some studies (84) have compared the current distribution of TBE foci, as driven by the known multivariate factors, with future climate scenarios. Although these scenarios are of coarser resolution than the original satellite imagery used to capture the current distribution of these foci, some conclusions are possible. The progressively warmer and drier summers, together with warmer winters, appear to drive the distribution of the TBE foci into higher latitudes and higher altitude regions. Much of central Europe appears to be free of the virus (though not necessarily of the vector) and the foci of disease will concentrate around regions of the Baltic states. The prediction that the distribution of TBE may expand north and west of Stockholm is consistent with recent foci detected in south-west Sweden. Increased TBE incidence in Stockholm County since 1984 has been related to higher winter temperatures, which allow a prolonged tick activity season (92). However, there is no correlation between the high TBE incidence rates in the same area in 1956, 1958 and 1960 and similarly warmer winters (84).

4.5. Crimean-Congo hemorrhagic fever

Another interesting problem of a re-emerging zoonosis involves CCHF, which is a sometimes fatal viral infection described from parts of Africa, Asia, eastern Europe and the middle east (93). The virus belongs to the genus *Nairovirus* in the *Bunyaviridae* family, and causes a severe disease in humans with a reported mortality rate of 3–30% (94). The geographic range of CCHF virus is the most extensive among the medically important tick-borne viruses. Humans become infected through tick bites, by contact with a patient with CCHF during the acute phase of infection, or by contact with blood or tissues from viremic livestock. There has been a substantial increase in reports of CCHF over the past five years. The CCHF virus circulates in an enzootic tick–vertebrate–tick cycle, and there is no evidence that the virus causes disease in animals other than humans. CCHF viral infection has been broadly demonstrated among smaller wildlife species (hares and hedgehogs), which act as host for the immature stages of the

vector ticks (93). Antibodies against the virus have been detected in the sera of horses, donkeys, goats, cattle, sheep and pigs in various regions of Europe, Asia and Africa (95). Although no ground-feeding birds have shown detectable viremia, 71 birds may have a role in the transportation of CCHF virus-infected ticks among various countries (96).

Ticks of the genus Hyalomma, particularly H. marginatum, transmit the CCHF virus. The virus was isolated from adult Hyalomma ticks in the 1960s (93, 94), and viral isolates were also obtained from field-collected eggs and unfed immature stages of H. marginatum, providing evidence of transovarial and transstadial transmissions (95). H. marginatum is known as the Mediterranean Hyalomma, and it may be the main vector of the CCHF virus in Europe. The virus has also been isolated from Hyalomma anatolicum and other Hyalomma species. Changes in climatic conditions have been suggested to be one of the factors that has facilitated reproduction of the tick population, and consequently the increased incidence of tick-borne infectious disease. In the northern hemisphere, H. marginatum is usually activated by increasing temperature in the spring, particularly in April or May, and the immature stages are active in the summer between May and September. In general, CCHF outbreaks have developed against a background of favorable climatic factors and environmental changes supporting both the survival of large numbers of Hyalomma spp. ticks and the hosts of their immature and adult stages. In the former Soviet Union, environmental changes include wartime neglect of agricultural lands, introduction of susceptible military personnel or new settlers into an infected area, wide-scale collectivization of agriculture, changing pasture patterns, and conversion of floodplains to farmland. During World War II, after the occupation of the Crimea, normal agricultural activities were disrupted and the common sport of hunting European hares was abandoned. When Soviet troops reoccupied the hilly Crimean steppes in 1944, hares had become very abundant and neglected pastures were overgrown with weeds. This period corresponded with the first documented outbreak of CCHF in the modern era. Interestingly, a similar explanation has been suggested for the CCHF outbreak in Turkey (98), where hunting and pasturing had been locally abandoned between 1995 and 2001 because of terrorist activities in the region. In this period the number of small mammals (e.g. hares) and wild animals (e.g. boars) increased. After 2001, the fields became available again for hunting and pasturing, and cattle and sheep were exposed to virus-carrying ticks.

In a recent study of the eco-epidemiological conditions driving the ongoing epidemic of CCHF in Turkey (almost 2000 cases were recorded between 2002 and 2007), it was shown that the area of suitable habitat for H. marginatum marginatum roughly coincides with the distribution of the disease (99). However, dense clusters of reported disease are located in areas with high habitat suitability and high fragmentation, as detected by high-resolution satellite imagery. This could provide a clue to one of the factors driving these epidemics: clusters of disease tend to be concentrated in areas where increased landscape fragmentation facilitates increased contact between small mammals (reservoirs), the infected ticks, and humans involved in agricultural activities. Interestingly, while it has been demonstrated that different strains of the virus are circulating in areas of western Turkey (Thrace) and models show adequate climate suitability for the tick in that region, only a few human cases have been reported there (100). Studies

are under way to understand the ecological factors driving this puzzling pattern of infection. Analysis of the climate features over the central Anatolian plateau in Turkey (unpublished data) has revealed an increase in mean annual temperature of about 2°C between 1990 and 2001, but similar changes were also detected in different periods of the 20th century, as part of a climate cycle. However, the dramatic changes in the landscape between 1990 and 2000 in many parts of central Turkey were unparalleled before that time. While we cannot discard an effect of climate (especially warmer winters leading to decreased mortality of overwintering ticks), it seems that growing populations of reservoir mammals and the continuous fragmentation of habitat are behind the observed epidemic in Turkey.

4.6. Other tick-borne diseases

Other studies have modeled the tick-borne disease Theileriosis, or East Coast Fever (ECF), caused by the protozoan parasite Theileria parva. This is one of the most important livestock diseases in Africa (102, 103). The transmission and distribution of ECF depends on the tick Rhipicephalus appendiculatus (a three-host tick), which mainly parasitizes cattle, and the disease distribution is directly related to the distribution of the tick. ECF extends south from southern Sudan to eastern South Africa, and as far west as the Democratic Republic of Congo. Each year it kills 1.1 million cattle and causes economic losses of $168 million (101). Mortality is higher (up to 100%) in exotic cattle than in the indigenous Zebus, where the average mortality is estimated at 10%. Efforts have been made to understand the factors regulating the distribution of the disease (102), and a population model for the vector tick has been developed based on information derived from remote sensing (103). This model aimed to understand the basic dynamics of the tick population, and incorporated features for assessing reproduction rates (R0) of the disease under different conditions of mortality, development rates and diapausing conditions over the geographical range of the vector tick (104). Other efforts have concentrated on mapping the disease under different climate scenarios, based on changes in tick distribution (105). However, we should keep in mind that the distribution of the disease is not simply related to the suitability of climate for the vector tick, and that factors regulating the seasonal dynamics of the tick are behind a complex cycle of transmission (103, 104). The evidence is increasingly clear that tick population dynamics are driven primarily by environmental factors. Superimposed on this are biotic factors, diverse and specific interactions among ticks, hosts and the transmitted parasites (determining how many of the ticks are infected), and the infection prevalence in host populations. It is not surprising that simple correlative models based on climate suitability for ticks do not seem not to correlate with disease pressure.

5. SUMMARY AND PERSPECTIVE

The potential impacts of climate change on human health are significant, ranging from direct effects such as heat stress and flooding, to indirect influences including changes in disease transmission. Development agencies and policy makers tasked with implementing adaptive strategies recognize the need to plan for these impacts. The immediate requirement is to create multidisciplinary research teams bringing together skills in both climate and tick modeling. This will facilitate considerable information exchange, and closer collaboration will highlight current uncertainties and hopefully identify

routes to their reduction. We know that climate is only one aspect influencing the highly complex regulation of tick-transmitted diseases issues. However we are optimistic that models simulating climate–health relationships and addressing uncertainty will provide much needed estimates of the likely impacts of climate change on human tick-borne diseases.

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