Ecology, 90(4), 2009, pp. 906–912

Do rising temperatures matter?

MERCEDES PASCUAL[1,3] AND MENNO J. BOUMA[2]

[1]*Howard Hughes Medical Institute and Department of Ecology and Evolutionary Biology, University of Michigan, Ann Arbor, Michigan 49109-1048 USA*
[2]*Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, University of London, London WC1E 7HT United Kingdom*

The greatest advances of climatology are destined to lie in the border field of biology provided cooperative research becomes the trend in attacking future problems.

—H. E. Landsberg (1958)

Relationships between the environment and population dynamics in ecology have a long history of polarized debates usually involving two alternative and opposite explanations that exclude each other. One of the best known examples is found in the early question of what regulates populations and the role of extrinsic vs. intrinsic factors, opposing the importance of the environment (or density-independent factors) to that of feedbacks within the nonlinear dynamics of the population itself (or density-dependent factors). Since then, population ecology has recognized the importance of the interplay between external environmental forcing and intrinsic nonlinearities in determining population dynamics. With some delay, the same polarization appeared, and is still present, in debates on the role of climate in the dynamics of infectious diseases at different temporal scales, from interannual fluctuations to longer trends. Although opposite views serve to organize our thinking and the testing of hypotheses, taken to extremes such polarization is unproductive, and delays understanding. From this perspective, Lafferty's (2009) review is a welcome addition to the existing literature on the importance of considering climate in the context of other aspects of change (e.g., Lindblade et al. 2000, Chaves et al. 2008). However, Lafferty's description of the state of the science as a "crisis discipline, reminiscent of the early phases of conservation biology" is already outdated, applying for example to the earlier scenarios for the global resurgence of malaria. An earlier reaction to such a "crisis discipline" has contributed to a polarization of the field and it would be unfortunate if conclusions in this review, on the lack of a net effect of climate change on the geographic range of infectious diseases at large spatial scales, were mistakenly taken as further support for the view that climate does not matter.

Lafferty argues that climate driven range shifts are more likely than range expansions (with no net positive change) in vector-transmitted diseases such as malaria. We focus first on this point to emphasize that range shifts will matter and should be better understood, regardless of net effects at the large scales of continents or the globe. Importantly, assessments of net effects at too large a spatial scale miss fundamental considerations, as emphasized here with a focus on epidemic malaria in tropical regions. Furthermore, assessments based on current indices of climate suitability are problematic given the limitations of the current indices themselves. Similarly problematic are extrapolations from the history of malaria in Europe to epidemic regions that are climate sensitive.

At shorter temporal scales, the relevance of climate has been addressed with seasonal and interannual patterns. Whether and how climate variability drives seasonality and cycles of longer period is important for the mechanisms by which infectious diseases will respond to climate change, for example in the length and timing of the seasons and in the amplitude of phenomena such as the El Niño Southern Oscillation (ENSO). The second part of our commentary concerns Lafferty's review of interannual climate effects. We argue that the conclusions of the re-analysis of historical yellow fever and ENSO in the US do not extrapolate to yellow fever in general, and that more recent results on epidemic malaria in African highlands support a role of climate variability. With the case study of cholera on the evidence for a role of ENSO, we illustrate current approaches that consider climate drivers in the context of nonlinear disease dynamics.

The challenge of considering climate in the context of other aspects of change goes beyond socioeconomic factors and includes pathogen evolution. Importantly, however, this is not an argument against the importance of climate itself, as we illustrate with the open question of the possible synergy of climate and drug resistance.

CLIMATE CHANGE AND RANGE SHIFTS VS. EXPANSIONS

On a global scale, malaria loses its grip where population densities are low, and vector dynamics and

Manuscript received 17 April 2008; revised 22 July 2008; accepted 13 August 2008. Corresponding Editor: K. Wilson. For reprints of this Forum, see footnote 1, p. 901.
[3] E-mail: pascual@umich.edu

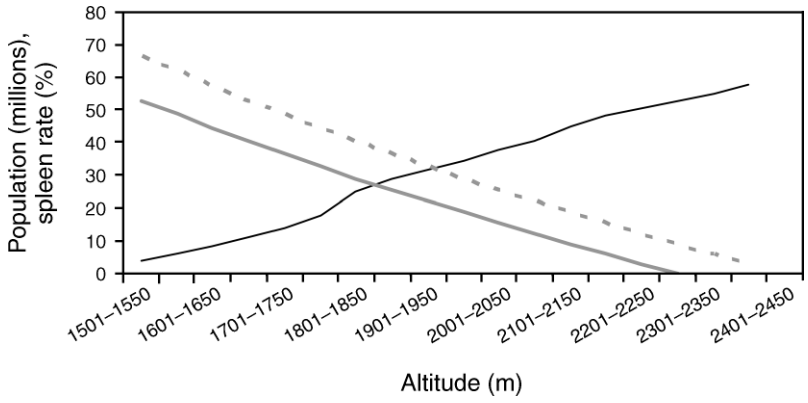

FIG. 1. Altitudinal gradient in population distribution and malaria endemicity in Ethiopia. The figure shows the cumulative population of Ethiopia (in millions, solid black line) for altitudes between 1500 and 2400 m (accounting for 75% of the total population of 77.1 million) and the regression line ($r^2 = 0.77$) for spleen rates (solid gray), the classic measure of malaria endemicity in the second half of the 20th century (Cox et al. 1999). A one-degree increase in ambient temperature (gray broken line) would shift the regression line 150 m, based on the local relation between increasing altitude and decreasing mean temperatures (157 m per °C [Tulu 1996]). On average, the Ethiopian highlands are inhabited by 6 million people for every 100 m in this altitude range. Using the population and malaria intensity for each altitude band, the malaria burden of temperature change can be estimated. When we conservatively restrict the estimate to half of the population (below 15 years, as adults are likely to have developed some degree of immunity), the increased intensity of transmission would amount for an extra 2.8 million children affected for a rise of 1°C. The territorial extension of malaria for this change would result in 410 000 people (adults and children) contracting malaria in an area with unprepared health services and little or no immunity. Global warming occurring as a gradual process could facilitate human adaptation to higher levels of transmission. Interannual variability in temperatures superimposed to a warming trend may obscure or interact with the effects of gradual change in dynamical ways we do not yet understand and could result in risk scenarios of similar magnitude to the one described here over much shorter time scales. Ethiopia's last epidemic in 2003 (Negash et al. 2005, Checchi et al. 2006) for which the official mortality figures have not been released, showed an explosive character in areas even above 2500 m. The estimated mortality for 2003 during the malaria season was between 45 000 and 114 000 people (United Nations 2004), a quarter of unofficial estimates.

pathogen development are climatologically restricted. In low-rainfall tropical regions, vector survival beyond the parasite's incubation time is critically reduced with low humidity and high temperatures and restricted breeding sites (Molineaux 1988). The most dramatic reduction of the distribution of malaria followed development, treatment, and vector control in higher latitude countries in the first half of the 20th century. The climate-sensitive latitudinal fringes of malaria (e.g., in Canada, Sweden, and Siberia) disappeared, to be replaced by climate-insensitive "control-fringes." However, in tropical malarious countries, temperature-sensitive highland fringes remain where lower temperatures reduce the generation time and biting frequency of vectors, as well as the development of the parasite in the vector. Fig. 1 illustrates such an altitudinal gradient (Cox et al. 1999), with malaria endemicity expressed as a function of altitude, similar to those in other East African highlands (Drakely et al. 2005). It is obvious that both climate variability and climate change can shift these gradients and that the human cost of increased temperatures would depend on both the altitudinal population distribution within countries with highlands and the absolute number of people in the fringe areas.

Lafferty (2009) proposes that range shifts are more likely than range expansions as the result of global warming, and provides a picture in which gains (high altitudes) and losses (arid regions) might ultimately balance each other with no net change. If the burden of malaria from the loss in desert regions were to cancel out the gains in high altitudes, the net effect of climate change would be negligible. This hypothesis is based, however, on the assumption that territorial surfaces, and more importantly human populations at risk, are similar at both ends of the distribution. This is clearly not the case for population density. In Africa and South America, the highlands are the most populous regions, and malaria itself is likely to have played a major role in this human altitudinal distribution, through migration, fecundity, lower child mortality, and economic prosperity. The low-malarious highland plains in East Africa also support the highest population densities in the continent (Fig. 2). Although the land surface of desert fringes may exceed that of highland fringes in Africa, Ethiopia's highland population alone more or less equals the total population of all malarious countries in Africa with desert fringes (Sub Sahara and Kalahari). Not only is the absolute number of people in African highlands considerably larger than that of dry-land areas, but the population density itself is an additional risk factor, increasing the likelihood of transmission.

The extension of agriculture in the world's dryer regions does not bode well for Lafferty's assumption that the malaria burden may ease in the warmer part of malaria's global distribution. Increasing population densities in semiarid areas are found where damming

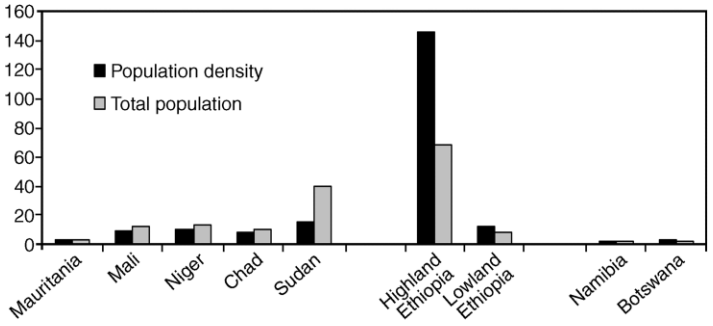

FIG. 2. Total population (millions of people) and population density (number of people/km^2) in Africa's malarious desert fringe countries compared to those in the highland fringe of Ethiopia. In these transition regions, the population abundance of the vector and the development of the pathogen are limited by temperature and/or rainfall. It is in these climate-sensitive regions that the potential for impacts of climate change is highest. Even if expansions into highlands were matched by retractions from deserts from the perspective of geographical areas, it is clear that the size of the populations affected will vary considerably.

of rivers and irrigation projects are initiated (Sissoko et al. 2004, Keiser et al. 2005). Unfortunately, additional water sources in arid areas extend, rather than contract, the geographic range of the vector, and as a result, that of malaria, with irrigation in tropical Africa usually making transmission perennial rather than seasonal, increasing transmission in unstable regions (Sissoko et al. 2004). Apparently only the irrigation associated with rice cultivation in Africa's semiarid areas, can reduce the malaria burden (Gaddal et al. 1985), providing less than optimal breeding sites and, most likely, economic prosperity. On the Indian subcontinent, the malaria epidemic belt has shifted to dryer regions with advancing irrigation. Whereas the semiarid Punjab was notorious for its malaria epidemics, particularly after irrigation in the late 19th and early 20th centuries, this pattern is now observed where irrigation permits subsistence in the more arid areas of Gujarat and Rajasthan bordering the Thar desert (Bouma and van der Kaay 1995, 1996). In these desert areas, the urban vector *Anopheles stephensi* appears to be the main culprit behind this changing pattern (Mathur et al. 1992), an observation that underscores the challenges for scenarios' building, in a world where vector shifts are possible and urban and peri-urban areas will increasingly grow and interface with more rural environments. Consideration of gross domestic product (GDP) alone, particularly at large scales that average across spatial heterogeneities and inequalities, will be insufficient.

Whereas conclusions on the reduction in malaria prevalence in desert fringes is premature and at best ambiguous, shifts in highlands are less questionable given the relation between altitude and malaria in malarious highlands (Fig. 1). In former British India, malaria has been studied and most meticulously recorded over 100 years. Here, extensive stretches of country between 1500 and 2000 m above sea level considered malaria free during the early 1900s are now reported as malarious (McMichael and Bouma 2000). The dramatic increase of *Plasmodium falciparum* in Pakistan's northern region in the 1980s has been associated with rising temperatures, far in excess of the mean annual temperature, during critical months (Bouma et al. 1996).

Spatial "suitability" indices for malaria have been used to show that malariogenic conditions have not improved since 1901 (Hay et al. 2002, Lafferty 2009). This attempt to define malaria's climate envelope is loosely defined and was originally devised to identify possible malaria transmission on a large spatial scale (Garnham 1948). This suitability index does little justice to the local vector bionomics, particularly in highland regions. In these regions, where strikingly low numbers of vectors are able to maintain malaria transmission, the seasonality of different vectors and the importance of specific windows in time when weather determines vector densities have been overlooked (Bouma 2003). Fig. 3 shows that for Madagascar there is no clear relationship between this index and the size of epidemics in different years, even though temperature itself in critical months is a good predictor of the interannual variability of the disease (Bouma 2003). Examination of similar limitations in other indices would be of interest. Fig. 3 illustrates the challenges of creating scenarios for vector-transmitted diseases at global scales. The temporal population dynamics of the disease, particularly the epidemic dynamics for "unstable" malaria, are not explicitly considered (and couldn't be reliably modeled and parameterized for such large extents); instead, static indices derived from complex mathematical models and/or statistical relationships pertaining to the vector and/or pathogen in relation to environmental variables, are used to map risk spatially. The question of how to take into account dynamical aspects of the response to variable environments in these indices, especially given the known nonlinearities in critical parameters of vector and pathogen as a function of temperature, is a fundamental one. We need efforts that combine risk maps and more detailed studies of local long-term dynamics of the disease in climate-sensitive regions. Better and more empirical data on the effects of temperature, rainfall, and humidity on the life history of vectors are urgently needed.

Interpretation of the results in maps for future scenarios does also defy simple categorization. The predictions of Tanser et al. (2003) are cited in Lafferty (2008) as an example of little change in latitudinal ranges. However, other aspects of change appear

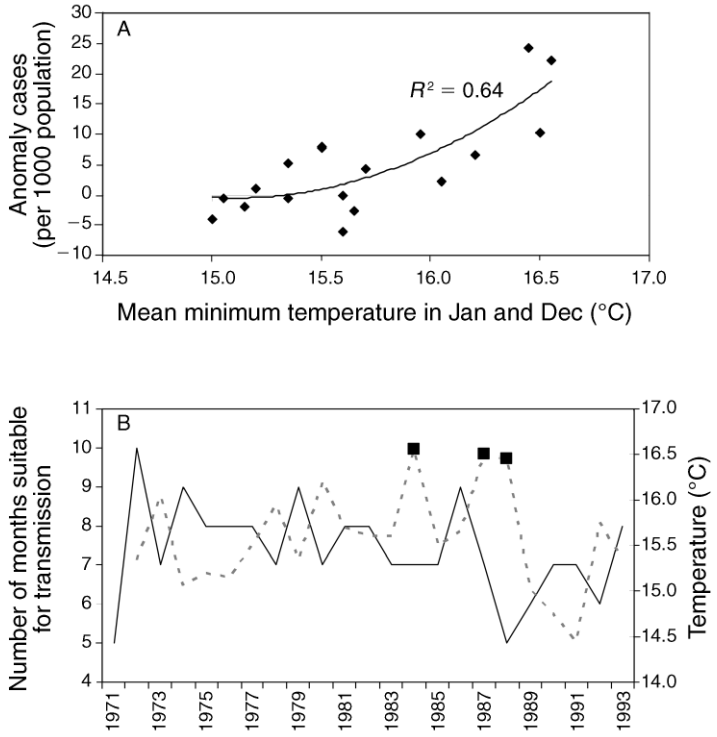

FIG. 3. Suitability index and interannual variability. The highlands in Madagascar witnessed a marked rise in malaria during the 1980s (Mouchet et al. 1998), at the same time as the rise observed in East African countries with extensive highlands. This rise followed disruptions in control efforts, and the rising trend may to some extend reflect malaria's recovery of its highland niche. However, malaria deviations (from the trend) have been explained with temperature alone (Bouma 2003) (panel A). Minimum temperatures in January and the preceding December show high correlations with the annual malaria burden between 1970 and 1989. Higher temperatures in these rainy months will affect the length of the transmission season and coincide with the highest densities of *Anopheles gambiae* (Fontenille et al. 1990), one of the vectors in Madagascar's highlands. "Garnham index," a coarse spatial determinant of malaria (the number of months [at least two consecutive] with mean temperature over 15°C, and rainfall over 152 mm [Garnham 1948]) has been used to show negligible changes in suitability since 1901 (Hay et al. 2002). However, in Madagascar's highlands, the correlation between malaria's interannual anomalies and Garnham's index is negative (–0.39). Panel B shows that the devastating epidemics in 1984 and 1987–1988 (black squares) would have occurred during the least suitable years for malaria transmission, had this index (solid line) been used for prediction. Contrary to the rising trend in minimum December–January minimum temperatures (broken lines), the trend between 1970 and 1988 of Garnham's index is negative, and not surprisingly, the correlation between both possible predictors is also negative (–0.32). The insensitivity of Garnham's index to changes in temperatures (e.g., –2°C to +2°C for all months) in these highlands makes this index unsuitable to explain interannual variability (the average of Garnham's index between 1970 and 1993 for the actual temperatures at Antenarivo yields 7.4 suitable months: –2°C, 7.3 months; –1°C, 7.3 months; +1°C, 7.5 months; +2°C, 7.5 months). This demonstrates the dangers of using crude spatial determinants of environmental suitability to infer aspects of temporal variability, including the effects of rising temperatures on the burden of disease.

significant in their projections. For example, Tanser et al. (2003) also included an overall potential increase of a 16–28% in person-months of exposure (assuming a constant population), a large proportion of which will occur in areas of existing transmission, and a 5–7% increase in altitudinal distributions in their 2100 projections. As we argued above for highland fringes, such percentages only become meaningful when referred to their human impact in terms of population size, and importantly, also susceptibility, since higher mortality and more epidemic behavior of the disease is expected in these regions where immunity is low. Calculations of net change at too large a spatial scale of aggregation will not only miss the relevant scales of human suffering, but also those relevant to control measures and economic costs of intervention.

Interannual Variability in Climate and Infectious Diseases

Cycles of period longer than one year can result from the nonlinear dynamics of infectious diseases in the absence of any forcing by interannual climate variability such as ENSO (e.g., Earn et al. 2000, Alonso et al. 2006). The possibility of these "intrinsic" cycles is one main reason why the presence alone of frequencies in disease time series that match those in climate data is not sufficient to infer a role of climate forcing (Rogers et al. 2002). Also, disease dynamics can interact with climate

forcing and blur or weaken linear correlations between the two. Change in the number of immune individuals is a key mechanism behind these interactions and the generation of intrinsic disease cycles at interannual scales.

The three-year cycles of epidemic malaria in Kenyan highlands (Hay et al. 2000) are often miscited as an example of intrinsic cycles in a vector-transmitted disease (Lafferty 2009). Hay et al. (2000) analyzed a monthly time series of hospitalized cases, as well as those for temperature and rainfall at a local station in Kericho, Kenya. The Fourier power spectrum of the cases shows a peak at a period of approximately three years consistent with the expectation of the natural frequency of oscillation of a Susceptible-Infected-Recovered (SIR) disease model with malaria parameters. However, this frequency was not evident in the Fourier power spectra of the concomitant environmental variables. In contrast, seasonality was pronounced in both rainfall and temperature; this makes it extremely difficult to examine the interannual variability present in these data, unless anomalies (deviations from the average seasonal cycle) are considered. Furthermore, the disease time series is highly non-stationary, with a pronounced trend and changes in the variability around this trend. A more recent analysis of the power spectrum using wavelets, a method especially well suited for non-stationary data, shows that rainfall time series for local stations do exhibit variability at the same characteristic scales than those in the disease dynamics (Pascual et al. 2008*b*). A cross-wavelet spectrum shows significant patterns of local association between rainfall and cases in the 1990s for cycles of approximately two and three years. A simple SIR time series model fitted to the data does not account for the three-year cycle, further supporting the extrinsic nature of this cycle. A longer four-year cycle in a neighboring tea estate does appear to involve disease dynamics (or the resonance of these dynamics with rainfall forcing at a lower period) but these findings remain limited by possible measurement errors in the data (Pascual et al. 2008*b*). It will be of interest to revisit these results using a model better suited to epidemic malaria than a weakly modified SIR framework. Rainfall has also been associated with malaria variability in desert fringes, for example in Bostwana, where it has been the basis for the development of an effective early-warning system (Thomson et al. 2006).

A number of quantitative approaches have been developed to disentangle the role of intrinsic and extrinsic factors in disease dynamics, by fitting mechanistic (or process-based) models to disease time series for partially observed systems (for which one has information only on the number of cases and not on the number of immune and non-immune individuals, e.g., Koelle and Pascual 2004, Koelle et al. 2005, Ionides et al. 2006, King et al. 2008). Studies of endemic cholera in Bangladesh have shown that the response of seasonal epidemics to El Niño events of similar magnitude can vary across years depending on the previous history of infection and therefore variation in the number of susceptible individuals (Koelle et al. 2005, Pascual et al. 2008*a*). Given these confounding interactions with disease dynamics and the high mortality of historical yellow fever, the inconclusive patterns of associations described by Lafferty (2009) for ENSO and this disease in the United States are not completely surprising.

More importantly, Lafferty's analysis of ENSO and yellow fever in U.S. cities provides at most some hints of climate forcing, but cannot be used to more generally refute an effect of weather on yellow fever dynamics in the proximity of enzootic reservoirs. This is because zoonoses such as yellow fever and plague have a very narrow niche in remote areas of rainforests and mountainous regions respectively. Studying the possible sensitivity to climate of these diseases in regions remote from enzoonotic foci, such as yellow fever epidemics in U.S. cities with accidental (urban) vectors and accidental human hosts is likely to yield inconclusive results.

Other Drivers of Change

Lafferty (2009) rightly emphasizes the importance of factors other than climate, such as land use, drug resistance, and socioeconomic conditions. Statistical analyses of retrospective patterns will be particularly challenging because of the difficulty in distinguishing the effects of concomitant trends. Because the timing of a trend in the rise of *P. falciparum* in Africa coincides with that of the spread of chloroquine resistance and rising temperatures since the 1980s, the role of temperature has been ambiguous (Shanks et al. 2005, Pascual et al. 2006). However, the increase of malaria in tropical highlands has not been limited to *P. falciparum* and chloroquine sensitive *P. vivax* has also increased in regions where both species co-occur such as in Ethiopia (Tulu 1996) and Pakistan (M. J. Bouma, *unpublished observations*). In the highlands of Madagascar, drug resistance was not considered a problem before the devastating malaria epidemic of 1987–1988, although the gradual buildup of cases during the 1980s was similar to that seen in the East African highlands (Loevinsohn 1994). As shown in Fig. 3A, malaria anomalies (deviations from the trend) are significantly associated with temperature. The ratio of highland to lowland cases of malaria follows the deviations, but also the trend of malaria in the 1980s, a phenomenon incompatible with drug resistance, assuming the development of resistance is not restricted to the highlands (Bouma 2003). Future research should investigate how to identify the importance of potentially concomitant drivers using infectious disease models; this will require data sets that include quantitative measurements of the drivers themselves, including drug resistance levels. Although trends in drug resistance and temperature are typically viewed as alternative hypotheses for malaria's exacerbation in African highlands, future efforts should consider the possibility of a synergy

between these factors in the larger context of pathogen evolution under changing environmental conditions.

Conclusions

The question of whether climate change is more likely to shift distributions than to generate range expansions in infectious diseases cannot be used to assess the importance of climate change effects on infectious disease dynamics. When the size of the populations affected is taken into account, projected shifts in the spatial distribution of epidemic malaria in tropical regions are not likely to be negligible. Interannual climate variability (ENSO, rainfall) has been shown to influence the size of outbreaks in a number of infectious diseases; recent modeling developments seek to identify the role of climate in the context of disease dynamics. Dynamical consequences of climate variability superimposed on longer trends are yet to be addressed. There are many urgent challenges to improve our understanding of climate–disease couplings, as well as our capacity to build informative scenarios for a warmer future. Serious limitations are the paucity of long records for the past and empirical data on the vectors and pathogens in relation to environmental variables. Challenging questions, not surprisingly, involve problems of scale, particularly in the way we incorporate our ecological understanding of temporal and spatiotemporal disease dynamics into meaningful quantities for interpreting and mapping spatial risk. Consideration of factors other than climate, including land-use, socioeconomic factors, drug resistance, the emerging HIV epidemic, and their synergistic effects with climate are also important.

Acknowledgments

We acknowledge the support of the Graham Environmental Sustainability Institute (GESI) at the University of Michigan, and the joint funding of NSF/NIH (Ecology of Infectious Diseases) and NOAA (Oceans and Health). M. Pascual is a HHMI investigator.

Literature Cited

Alonso, D., A. McKane, and M. Pascual. 2006. Stochastic amplification in epidemics. Journal of the Royal Society Interface 4(14):575–582.

Bouma, M. J. 2003. Climate change and tropical disease. Methodological problems and amendments to demonstrate effects of temperature on the epidemiology of malaria. A new perspective on the highland epidemics in Madagascar, 1972–89. Transactions of the Royal Society of Tropical Medicine and Hygiene 97:133–139.

Bouma, M. J., C. Dye, and H. J. van der Kaay. 1996. Falciparum malaria and climate change in the NWFP of Pakistan. American Journal of Tropical Medicine and Hygiene 55(2):131–137.

Bouma, M. J., and H. J. van der Kaay. 1995. Epidemic malaria in India's Thar desert. Lancet 346:1232–1233.

Bouma, M. J., and H. J. van der Kaay. 1996. The El Niño Southern Oscillation and the historic malaria epidemics on the Indian subcontinent and Sri Lanka: an early warning system for future epidemics? Tropical Medicine and International Health 1:86–96.

Chaves, L. F., J. M. Cohen, M. Pascual, and M. Wilson. 2008. Social exclusion modifies climate and deforestation impacts on a vector-borne disease. PLoS Neglected Tropical Diseases 2(2):e176.

Checchi, F., J. Cox, S. Balkan, A. Tamrat, G. Priotto, K. P. Alberti, D. Zurovac, and J. P. Guthmann. 2006. Malaria epidemics and interventions, Kenya, Burundi, Southern Sudan, and Ethiopia, 1999–2004. Emerging Infectious Diseases 10:1477–1485.

Cox, J., M. Craig, D. Le Sueur, and B. Sharp. 1999. Mapping malaria risk in the highlands of Africa. Mapping Malaria Risk in Africa/Epidemiology of Highland Malaria in Africa Project (MARA/HIMAL) technical report. South African Medical Research Council, Durban, South Africa.

Drakely, C., I. Carneiro, H. Reyburn, R. Malima, J. P. A. Lusingu, J. Cox, T. G. Theander, W. M. M. M. Nkya, M. M. Lemnge, and E. M. Riley. 2005. Altitude-dependent and -independent variations in *P. falciparum* prevalence in the northern Tanzania. Journal of Infectious Diseases 91:1589–1598.

Earn, D. J. D., P. Rohani, B. M. Bolker, and B. T. Grenfell. 2000. A simple model for dynamical transitions in epidemics. Science 287:667–670.

Fontenille, D., J. P. Lepers, G. H. Campbell, I. Rakotoarivony, M. Coluzzi, and P. Coulanges. 1990. Les vecteur du paludisme et leur role dans la transmission, a manarintsoa sur les hauts plateux de Madagascar de 1988 a 1990. Arch Instit Pasteur Madagascar 57:335–368.

Gaddal, A. A., A. A. Haridi, F. T. Hassan, and H. Hussein. 1985. Malaria control in the Gezira-Managil irrigated scheme of the Sudan. Journal of Tropical Medicine and Hygiene 88: 153–159.

Garnham, P. C. C. 1948. The incidence of malaria at high altitudes. Journal of the National Malaria Society 7:275–284.

Hay, S. I., J. Cox, D. J. Rogers, S. E. Randolph, D. I. Stern, and G. D. Shanks. 2002. Climate change and the resurgence of malaria in the East African Highlands. Nature 415:105–106.

Hay, S. I., M. F. Myers, D. S. Burke, D. W. Vaughn, T. Endy, N. Ananda, G. D. Shanks, R. W. Snow, and D. J. Rogers. 2000. Etiology of interepidemic periods of mosquito-borne disease. Proceedings of the National Academy of Sciences (USA) 97:9335–9339.

Ionides, E., C. Breto, and A. A. King. 2006. Inference for nonlinear dynamical systems. Proceedings of the National Academy of Sciences (USA) 103:18438–18443.

Keiser, J., M. C. De Castro, M. F. Maltese, R. Bos, M. Tanner, B. H. Singer, and J. Utzinger. 2005. Effect of irrigation and large dams on the burden of malaria on a global and regional scale. American Journal Tropical Medicine and Hygiene 72: 392–406.

King, A. A., E. L. Ionides, M. Pascual, and M. J. Bouma. 2008. Inapparent infections hold the key to cholera dynamics. Nature 454:877–880.

Koelle, K., and M. Pascual. 2004. Disentangling extrinsic from intrinsic factors in disease dynamics: a nonlinear time series approach with an application to cholera. American Naturalist 163(6):901–913.

Koelle, K., X. Rodo, M. Pascual, M. Yunus, and G. Mostafa. 2005. Refractory periods to climate forcing in cholera dynamics. Nature 436(4):696–700.

Lafferty, K. D. 2009. The ecology of climate change and infectious diseases. Ecology 90:888–900.

Landsberg, H. E. 1958. Trends in climatology: The investigation of climate is moving from a descriptive science to a science grounded in physics. Science 128:749–757.

Lindblade, K. A., E. D. Walker, A. W. Onapa, J. Katungu, and M. L. Wilson. 2000. Land use change alters malaria transmission parameters by modifying temperature in a highland area of Uganda. Tropical Medicine and International Health 5(4):263–74.

Loevinsohn, M. E. 1994. Climatic warming and increased malaria incidence in Rwanda. Lancet 343:714–718.

Mathur, K. K., G. Harpalani, N. L. Kalra, G. G. K. Murthy, and M. V. V. L. Narasimham. 1992. Epidemic of malaria in Barmer district (Thar desert) of Rajasthan during 1990. Indian Journal of Malariology 2:1–10.

McMichael, A., and M. J. Bouma. 2000. Global change, invasive species and human health. Pages 191–210 *in* H. Mooney and R. Hobbs, editors. The impact of global change on invasive species. Island Press, Covelo, California, USA.

Molineaux, L. 1988. The epidemiology of human malaria as an explanation of its distribution, including some implications for its control. Pages 913–998 *in* W. H. Wernsdorfer and I. McGregor, editors. Malaria. Churchill Livingstone, Edinburgh, UK.

Mouchet, J., S. Manguin, J. Sircoulon, S. Laventure, O. Faye, A. W. Onapa, P. Carnevale, J. Julvez, and D. Fontanille. 1998. Evolution of malaria in the last 40 years: impact of climate and human factors. Journal of the American Mosquito Association 14:121–130.

Negash, K., A. Kebede, A. Medhin, D. Argaw, O. Babaniyi, J. O. Guintran, and C. Delacollette. 2005. Malaria epidemics in the highlands of Ethiopia. East African Medical Journal 82:186–192.

Pascual, M., J. Ahumada, L. F. Chaves, X. Rodó, and M. Bouma. 2006. Malaria resurgence in East African Highlands: temperature trends revisited. Proceedings of the National Academy of Sciences (USA) 103:5829–5834.

Pascual, M., L. F. Chaves, X. Rodo, B. Cash, and M. Yunus. 2008*a*. Predictability of endemic cholera: the role of climate variability and disease dynamics. Climate Research 36:131–140.

Pascual, M., B. Gazelles, M. J. Bouma, L. F. Chaves, and K. Koelle. 2008*b*. Shifting patterns: malaria dynamics and rainfall variability in an East African Highland. Proceedings of the Royal Society Series B 275:123–132.

Rogers, D. J., S. E. Randolph, R. W. Snow, and S. I. Hay. 2002. Satellite imagery in the study and forecast of malaria. Nature 415:710–715.

Shanks, G. D., S. I. Hay, J. A. Omumbo, and R. W. Snow. 2005. Malaria in Kenya's western highlands. Emerging Infectious Diseases 11:1425–1432.

Sissoko, M. S., A. Dicko, O. J. Briët, M. Sissoko, I. Sagara, H. D. Keita, M. Sogoba, C. Rogier, Y. T. Touré, and O. K. Doumbo. 2004. Malaria incidence in relation to rice cultivation in the irrigated Sahel of Mali. Acta Tropica 89: 161–170.

Tanser, F. C., B. Sharp, and D. le Sueur. 2003. Potential effect of climate change on malaria transmission in Africa. Lancet 362:1792–1798.

Thomson, M. C., F. J. Doblas-Reyes, S. J. Mason, R. Hagedorn, S. J. Connor, T. Phindela, A. P. Morse, and T. N. Palmer. 2006. Malaria early warnings based on seasonal climate forecasts from multi-model ensembles. Nature 439(2):576–579.

Tulu, A. N. 1996. Determinants of malaria transmission in the highlands of Ethiopia: impact of global warming on morbidity and mortality ascribed to malaria. Dissertation. London School of Hygiene and Tropical Medicine, London, UK.

United Nations. 2004. Focus on Ethiopia. UN Country team Ethiopia. August 2004. United Nations, New York, New York, USA.

Ecology, 90(4), 2009, pp. 912–920

FORUM

Climate change and wildlife diseases: When does the host matter the most?

DREW HARVELL,[1,7] SONIA ALTIZER,[2] ISABELLA M. CATTADORI,[3,4] LAURA HARRINGTON,[5] AND ERNESTO WEIL[6]

[1]*Department of Ecology and Evolutionary Biology, Cornell University, Ithaca, New York 14853 USA*
[2]*Odum School of Ecology, University of Georgia, Athens, Georgia 30602 USA*
[3]*Division of Animal Production and Public Health, Faculty of Veterinary Medicine, University of Glasgow, Glasgow G61 1QH United Kingdom*
[4]*Center for Infectious Disease Dynamics, Department of Biology, The Pennsylvania State University, University Park, Pennsylvania 16802 USA*
[5]*Department of Entomology, Cornell University, Ithaca, New York 14853 USA*
[6]*Department of Marine Sciences, University of Puerto Rico, P.O. Box 9013, Mayagüez, Puerto Rico 00681-9013 USA*

INTRODUCTION

The paper by Lafferty (2009) injects careful detail and new science into the question of how climate warming will affect the prevalence and distribution of vector-borne diseases of humans. This has been an area of intense controversy, in part because of implications for human health and disease prevention strategies. Six years ago, one hypothesis about climate change and infectious diseases suggested that increased temperature and rainfall could facilitate the emergence and persistence of many infectious microorganisms, i.e., a warmer world would be a sicker world (Harvell et al. 2002). Of all the infectious diseases, it seemed likely that human vector-borne diseases would respond most promptly to localized warming events. Specifically, in temperate climates, we might expect the range and activity of

Manuscript received 1 April 2008; revised 4 June 2008; accepted 16 June 2008; final version received 6 August 2008. Corresponding Editor: K. Wilson. For reprints of this Forum, see footnote 1, p. 901.

[7] E-mail: cdh5@cornell.edu

mosquitoes and the pathogens they vector, such as malaria and dengue, to increase with warmer temperatures (Martens 1999; but see Rogers and Randolph 2000). From a later vantage point in 2009, the evidence outlined by Lafferty considers new complexities and uses long-term data sets to re-evaluate previous predictions. Surprisingly, insect-vectored diseases resoundingly do not show a net expansion in range or increase in prevalence, based on evidence and predictions from GIS analyses and mathematical modeling studies. Lafferty (2009) lays out three explanations: (1) anthropogenic activities directly influence the distributions of vectors and infectious disease in ways unrelated to climate, (2) vectors and pathogens are limited by thermal maxima, so that temperature changes lead to shifts rather than expansions in distribution, and (3) other factors such as host acquired immunity and vector or parasite life history traits are linked to habitat suitability in addition to climate.

As highlighted throughout Lafferty's paper, the complexity of malaria ecology (as well as that of other mosquito-borne infections) requires that models adequately consider the effects of climate on vector population biology, biting activity and vector–parasite interactions, each of which can have a significant impact on the final predictions (Garrett-Jones 1964, Styer et al. 2007, Harrington et al. 2008). Human malaria is, in fact, caused by four biologically distinct species of *Plasmodium*. Each species has characteristic rates of development within the human host and invertebrate vector, intricate relationships with the immune systems of both host and vector, and biological compatibility with certain species of mosquito. Not all vectors are the same, just as the course of malaria pathology is not the same in all human hosts. Additionally, the impact of factors such as partial immunity and multiple infections are difficult to estimate. Therefore, the alarming predictions of malaria returning to temperate regions should be critically assessed.

One reason why the threat of malaria returning to Europe and North America is not as dire as some would predict is because humans are the only vertebrate reservoir for infection, and large numbers of infected people would be required to sustain a malaria outbreak in England and many other countries where malaria has been eradicated. Competent mosquito vectors still thrive in England, other European countries and also in the United States, but the quality of health care and standards of living have changed tremendously in these countries since malaria was considered endemic. Indeed, the potential for positive feedback between human poverty and the threat of an expansion of vector borne diseases was highlighted by Lafferty in his review, with particular reference to the difficulty in teasing apart interactions between anthropogenic environmental changes, drug resistance, lack of health care, and vector control. Given our limited scientific knowledge, Lafferty (2009) has presented a balanced overview, demonstrating little evidence for net range expansions and increases in human cases based on climate warming alone. Instead, a clearer relationship between poverty, lack of effective control strategies and malaria infections represents a more certain cause of future increases in incidence of human cases of malaria.

Lafferty's focus on vector-borne human infectious diseases provides a useful test case against which to compare our expectations for the effect of global changes on pathogens affecting wildlife populations. New questions that are raised include: do simple predictions that many infections will increase with climate warming hold up where pathogens and vectors are not controlled by humans? What happens when both host and pathogen are sensitive to temperature changes? If climate–disease relationships are not observed for some pathogens, why and when is the modulating effect of climatic variables on the interaction between hosts and infectious diseases lost? In this perspective we detail a few examples of wildlife-pathogen interactions in both marine and terrestrial animal systems that emphasize how host biology can be crucially important for climate-disease relationships. Specifically, we argue that (1) correlations between climate warming and pathogen outbreaks have contributed to dramatic declines or extinctions in several groups of ectothermic hosts, (2) animal migrations and range shifts can be affected by climate change and this can potentially increase or decrease disease transmission, and (3) host acquired immunity can alter the expected direct effect of climate on disease dynamics.

Pathogen Expansions and Emergence in Ectothermic Hosts

Interactions between climate warming and pathogen outbreaks have caused serious declines or extinctions in several groups of ectothermic hosts. In terrestrial ecosystems, entire communities of amphibians have been driven to the edge of extinction and beyond owing to chytridiomycosis outbreaks, with the timing of die-offs linked with warmer temperatures. Amphibians on the whole are extremely threatened, with nearly half of all species declining in their range of distribution (Stuart et al. 2004). Infectious diseases have caused some of the most rapid and severe declines, in some cases wiping out entire communities in a matter of months (Lips et al. 2006). A correlational analysis on the amphibian community in Costa Rica provided support for warmer years favoring the growth of the pathogenic fungus *Batrachochytrium dendrobatidis* at high altitudes (Pounds et al. 2006). Specifically, it has been suggested that climate warming shifted nighttime temperature minima towards the pathogen's growth optimum, and simultaneously prevented daytime maxima from exceeding the pathogen's thermal limits through increased cloud cover. This hypothesis helps to explain the die-offs of numerous species of harlequin frogs in Central and South America following warm years, and the spread of

the pathogenic fungus into amphibian populations at mid-to-high elevations. However, the strength of this climate-disease association was recently questioned by Lips et al. (2008); specifically, a reanalysis of mortality data suggested that multiple introductions of *B. dendrobatidis*, coupled with its spatial spread along mountain ranges, better explained the timing of harlequin frog die-offs (Lips et al. 2008). It is important to note that warmer temperatures have also been linked with the occurrence of chytrid-related disease in montane regions in Spain (Bosch et al. 2007), and that the effects of climate, disease and other factors causing amphibian declines are not mutually exclusive and could interact in ecologically significant ways.

In the ocean, several species of California abalones have experienced major population declines caused by a combination of warming water and infectious disease. Elevated seawater temperatures have been shown to play a key role driving both transmission of the rickettsial agent and development of associated clinical disease (withering syndrome, WS) in red abalone, *Haliotis rufescens*, one of the five California abalones that were commercially fished prior to closure of the fishery nearly a decade ago (Moore et al. 2000, Braid et al. 2005, Vilchis et al. 2005). Similarly, black abalone (*H. cracherodii*) has been almost extirpated from southern California by its temperature-dependent susceptibility to WFS (Altstatt et al. 1996, Moore et al. 2000). On the Atlantic coast, infections of oysters (*Crassostrea virginica*), by the protozoan parasite *Perkinsus marinus* represent the best documented case of a marine parasite range expansion driven by climate warming. This parasite expanded from its range in the southeast up through Maryland to a new 500 km northeastern range, coincident with winter warming in the 1990s (Cook et al. 1998). The 1990–1991 expansion into the northeast has continued in coincidence with the anomalously warm temperatures recorded in the last decade (Ford and Smolowitz 2007). Epizootics of *P. marinus* are impressively seasonal at all locations, with prevalence peaking in late summer and dying back in winter (Ford and Smolowitz 2007). However, careful studies highlight the potential for multiple factors to be involved in warming-associated range expansion (Ford and Smolowitz 2007). For example, there is evidence that the level of aggressiveness and transmission of *P. marinus* has increased throughout its range, and hence recent epizootics are more quickly established in new areas. This raises the now familiar question of whether the new range expansion is caused by change in temperature directly, or by evolutionary changes in properties of the host or pathogen. The evolutionary hypothesis was recently rejected by experimental studies which showed that *P. marinus* had not differentiated genetically in northern oyster populations that had experienced more recent increases in disease; the parsimonious conclusion is that warming winter temperatures alone have allowed the northward parasite range expansion (Ford and Chintala 2006, Ford and Smalowitz 2007).

Coral reefs represent an entire marine ecosystem that is threatened by the encroachment of temperature-sensitive disease outbreaks; indeed, coral reefs are the ecosystem the most impacted by small increases in temperature causing bleaching and mortality and facilitating disease outbreaks (Hoegh-Guldberg et al. 2007). For example, 2005 was the warmest summer/fall season recorded for the eastern Caribbean in 100 years. At its peak in late October, the warm temperature anomaly that developed reached 14 degree-heating weeks (i.e., temperatures of 1°C above the typical seasonal maximum for 14 successive weeks; Wilkinson and Souter 2008). In the Virgin Islands, the primary reef building coral species bleached during this warming event, eventually recovered its pigments, but then developed lethal white plague disease (Miller et al. 2006). As a result, coral cover was reduced by 50% in this one event alone. Again in the Virgin Islands, a disease of the federally listed endangered coral species *Acropora palmata* also increased during the 2005 temperature anomaly event (Muller et al. 2008).

In many reef areas of the Caribbean, Caribbean yellow band disease (CYBD) prevalence and virulence increased significantly from the late 1990s to the mid 2000s, and this is now the most damaging bacterial disease that affects all four coral species of the genus *Montastraea*, the most important reef-building species for this area (Fig. 1A; Bruckner and Bruckner 2006, Weil et al. 2006, Croquer and Weil 2009, Weil and Croquer 2009). Disease prevalence in *Montastraea* populations has markedly increased over the last eight years and significantly covaried ($r^2 = 0.787$, $P \leq 0.01$) with the increase in the annual mean sea water temperature from 1999 to 2007 (Fig. 1A). Likewise, the within-colony dynamics of the disease (based on visual disease signs and lesion growth rates) have changed dramatically in the last eight years. In fact, the seasonal pattern of high growth rates of lesions in summer and significantly lower growth rates or complete disappearance in winter has now been replaced by a significant increase in the growth rate of the lesions throughout the year, and no sign of disease decline (Fig. 1B). A significant positive relationship was observed between the lesion growth rate and mean water temperatures ($r^2 = 0.54$, $P \leq 0.05$), providing evidence that water temperature affects the development of CYBD on colonies of the star coral *Montastraea faveolata* (Fig. 1B). Winter average water temperatures used to drop below 25.5°C in the area, however, following the summer of 2002, the average winter temperatures have not dropped below 26.5°C, and a steady increase in the mean winter temperatures has been recorded throughout the last nine years. Warmer winters seem to favor CYBD growth and pathogenicity, which now remain high even during the winter seasons,

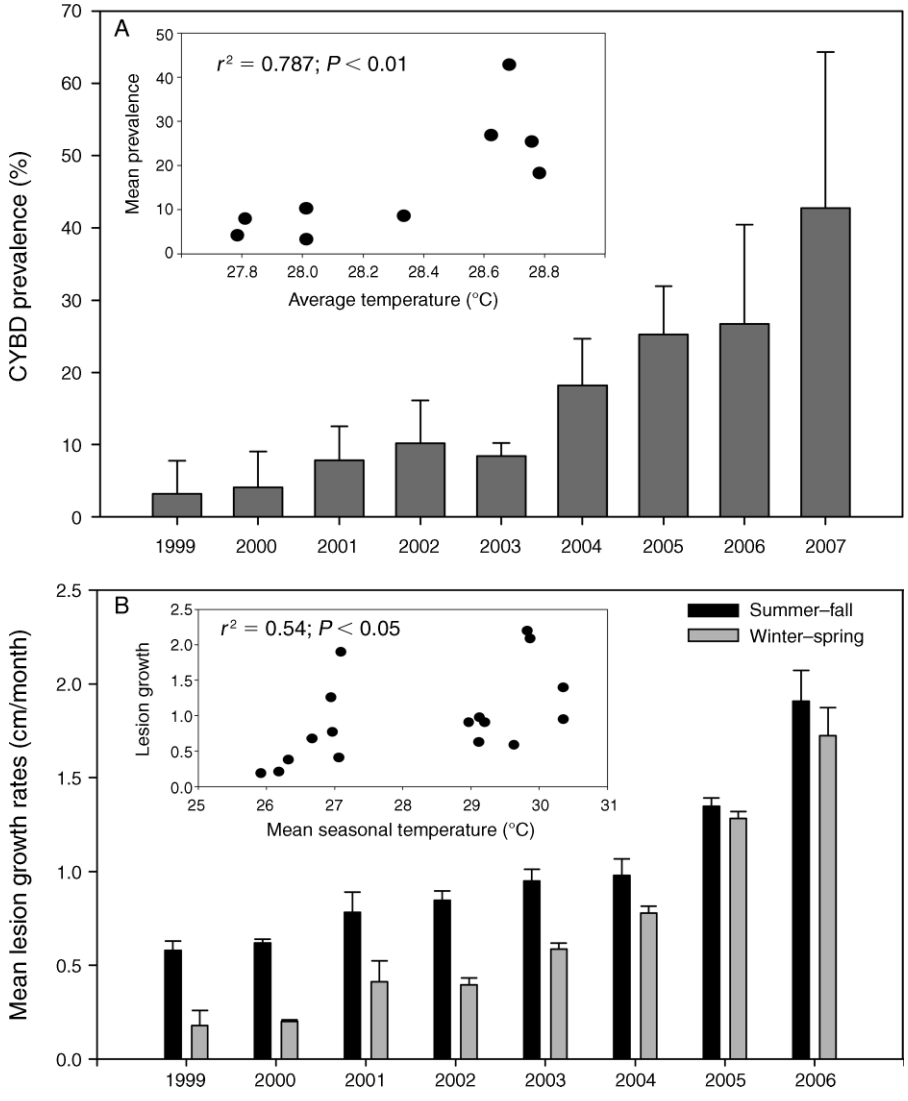

FIG. 1. Temporal changes in Caribbean yellow band disease (CYBD). (A) Increase in CYBD prevalence in the Caribbean coral genus *Montastraea* in reefs off the southwest coast of Puerto Rico from 1999 to 2007. The inset shows the positive and significant correlation between the yearly increase in mean prevalence and the average yearly surface water temperature. (B) Seasonal variability in CYBD lesion growth rates measured in over 100 tagged colonies of *Montastraea faveolata* in La Parguera, Puerto Rico from 1999 to 2006. The inset shows the significant positive covariation between the linear lesion growth rates and the average seasonal surface seawater temperature for the same period. Error bars show +SE.

causing epidemic levels of disease in populations of the *Montastraea* species in many reefs across the Caribbean.

The mechanisms of climate sensitivity for many different coral syndromes are not fully understood (Harvell et al. 2007). In the few cases where a coral pathogen was cultured, experiments showed a positive relationship between temperature and pathogen growth rate (Harvell et al. 2007). One prevailing hypothesis is that many new coral pathogens are opportunists that become more virulent (grow faster or become more infectious) at warmer temperatures. Because warmer temperatures can also directly immune compromise the hosts, this combined impact of virulent pathogens and immuno-compromised hosts could underlie many disease outbreaks (Harvell et al. 2007). Although an appealing hypothesis, in the case where immunity and environment were studied in gorgonian corals using short term laboratory experiments and data from sustained field monitoring, results showed that enzymes and cellular immunity were actually activated (and not suppressed) by both pathogen inoculation and temperature increase (Ward et al. 2006, Mydlarz et al. 2008). This observation raises questions concerning whether some clades of cnidarians like gorgonians corals show more immune resilience in the face of warming than others, like scleractinian corals.

As in most ecosystems, the question remains open about which is the more important driver of changing

pathogen distributions: increasing pathogen growth, transmission and virulence with temperature, or changes in host immunity (Ellner et al. 2007). The tension between a direct positive effect of temperature on host defenses, combined with the potential for temperature stress to compromise host immunity, has been often highlighted in ectothermic hosts. For example, a recent study by Raffel et al. (2006) on red-spotted newts showed that between-season (longer-term) environmental temperature was positively correlated with the numbers of circulating lymphocytes and eosinophils in the individuals. Moreover, within-season effects and responses of newts to climate variability showed that these animals could be more susceptible to infectious diseases during autumn or following fluctuations in temperature. As pointed out by Fisher (2007), these considerations are important for predicting (1) how well amphibians and other ectotherms can mount an immune response against infectious agents outside of their typical climate envelope, (2) how temperature affects different types of host defenses (which in turn respond to different types of infectious diseases), and (3) the role of climate variability, in addition to average changes in temperature, on host susceptibility.

Animal Movements, Host Range Shifts, and Infectious Diseases

Another mechanism relevant to the emergence or outbreaks of infectious diseases is the effect of climate change on the movements of animal populations to enhance their exposure to infectious diseases. Migratory species can be particularly sensitive to climate change (Collingham and Huntley 2000, Hickling et al. 2006) and some migratory species have already responded to altered thermal regimes by shifting their ranges of distribution and migration routes (Parmesan and Yohe 2003, Perry et al. 2005). In other cases, climate warming could cause a gradual break down in the migration itself by making environmental conditions in breeding grounds more favorable for the year-round survival of host populations (i.e., replacing migratory populations with year-round resident populations; Lusseau et al. 2004, Bradshaw and Holzapfel 2007). Migrations can confer multiple benefits by allowing hosts to escape the continual build-up of pathogens in the environment (Loehle 1995, Altizer et al. 2004) or by weeding infected animals out of the population during strenuous migratory journeys (e.g., Gylfe et al. 2000, Bradley and Altizer 2005). Several host–parasite systems offer evidence that seasonal host migrations reduce parasite prevalence, including studies of warble flies affecting reindeer (Folstad et al. 1991) and nematodes affecting fall armyworm moths (Simmons and Rogers 1991).

A case study of monarch butterflies and the protozoan parasite *Ophyrocystis elektroscirrha* provides support for both the role of migration in lowering parasite prevalence (Altizer et al. 2000) and the vulnerability of migration to climate warming (Oberhauser and Peterson 2003). Globally, all monarch populations examined to date are parasitized by *O. elektroscirrha*; prevalence is highest in monarchs from tropical locations that breed year-round (i.e., nonmigratory populations) and lowest in the population in eastern North America that migrates the longest distances annually. Climate warming, combined with increased planting of tropical milkweed species that do not die back seasonally, has enabled the persistence of small winter breeding populations in the southeastern United States in recent years. These nonmigratory populations are likely to suffer from heavy parasite burdens and can also harbor more virulent parasite strains (i.e., strains that replicate faster and cause greater harm to hosts; De Roode et al. 2008). Thus, reductions in migratory tendancies among animals that breed in traditionally seasonal temperate regions could favor the transmission of infectious diseases and negatively impact wildlife populations.

Altered migration routes could also result in migratory animals encountering and transferring pathogens to previously unexposed host populations, or becoming exposed themselves to novel infectious diseases. More generally, many terrestrial species are expected to undergo range shifts to higher elevations or latitudes as a result of climate warming, a phenomenon already observed for some taxonomic groups (Hickling et al. 2006). A largely overlooked phenomenon is the degree to which these range shifts could bring novel groups of species into contact and facilitate cross-species transmission of infectious disease (e.g., Morgan et al. 2004, Brooker et al. 2007). Pathogens introduced into previously unexposed host populations can spread quickly, cause high case fatality rates and lead to stunning reductions in host abundance. For example, two major outbreaks of phocine distemper virus among harbor seals in the North Sea are thought to have been triggered by viral introduction from harp seals migrating far outside of their range (Osterhaus and Vedder 1988, Jensen et al. 2002). Although the hypothesis is that aberrant harp seal migrations were probably caused by over-fishing rather than by climate change, future introductions of novel pathogens are likely to occur as animal movement routes and geographic ranges shift in response to climate warming.

Acquired Immunity and Climate-Disease Synergisms

Host immunity can play a major role in driving large scale and long term disease emergence and persistence. For parasites with direct life cycles that are not regulated by an effective immune response, we expect climate warming to increase the force of infection (the rate at which a host gets infected), leading to an increase in the prevalence and/or intensity of infection in adult hosts. On the other hand, for parasites that are regulated by inducible and lasting host defenses, climate warming could still increase the force of infection and parasite intensity in younger hosts, but older individuals will be more efficient at clearing the infection because of a faster

activation of the immune response (Cattadori et al. 2005*a*, Hudson et al. 2006). Therefore, if host–parasite interactions are immune-modulated, we expect that climate changes will be less powerful in driving disease dynamics, and the direct effect of climate on host–parasite interactions will be less apparent.

Climate change, immunity, and the pattern of infection of two common gastrointestinal nematodes (*Graphidium strigosum* and *Trichostrongilus retortaeformis*) have been investigated in a population of European rabbits (*Oryctolagus cuniculus*) in Scotland. Parasite intensity has changed in the rabbit population over 26 years, but in different ways for each of the two parasite species: *T. retortaeformis* showed large multi-annual variations but no long term trend, whereas *G. strigosum* increased more than two-fold over the same time period (Hudson et al. 2006). These patterns were consistent among hosts of different age classes, suggesting that changes in parasite intensity were not caused by a variation in the age structure of the host population over the years. Previous studies suggested that *T. retortaeformis*, but not *G. strigosum*, elicits a strong acquired immune response (Cattadori et al. 2005*a*, 2007, 2008, Cornell et al. 2008). Adult rabbits are able to clear almost completely *T. retortaeformis* infections, whereas no obvious regulation seems to occur in *G. strigosum*, and parasite intensity increases exponentially with host age.

Both parasite species have a free-living stage spent on the pasture, and the warm and moist environment of the grass micro-climate has a fundamental role in the survival, development, and behavior of the parasites (Crofton 1948*a*, *b*, Anderson 2000). Climatic data from the rabbit study showed an increase of 1°C in the mean air temperature and a weak positive trend in rainfall between 1980 and 2002 (Hudson et al. 2006; I. M. Cattadori, *unpublished data*). These data sets were also characterized by large multi-annual variations (coefficient of variation [CV]: 4% and 16%, respectively). An analysis of the relationship between climatic variables and parasite intensity revealed a significant and positive association between *G. strigosum* intensity and mean air temperature ($P = 0.004$, Fig. 2) but no association with total rainfall ($P = 0.241$). As expected, no relationships between climatic variables and *T. retortaeformis* were observed ($P = 0.860$ and $P = 0.174$, for mean air temperature and total rainfall, respectively, Fig. 2). These findings suggest that *G. strigosum*, which elicits no apparent immune response in its host, has been affected by temperature warming, and this probably caused the increase in parasite intensity in the adult rabbit population over two decades. Although *T. retortaeformis* free living stages are exposed to similar environmental conditions, the damping effect of host immunity has probably prevented this parasite from showing clear associations with climate records.

This example of climate change influencing a host–nematode interaction is not an exception. The intensity of infection of the gastrointestinal nematode *Trichostrongylus tenuis* has increased in its common host, the Red Grouse (*Lagopus lagopus scoticus*), over the last 30 years in England (Hudson et al. 2006). *T. tenuis* has a direct life cycle with a free living stage, parasite intensity is mainly regulated by birth–death demographic processes, and acquired immunity does not appear to play a relevant role in clearing host infections (Hudson and Dobson 1997, Hudson et al. 2006). Interestingly, the long term pattern of infection of this nematode very much resembles *G. strigosum*, such that intensity has consistently increased over the last three decades (Hudson et al. 2006). A detailed look at this pattern revealed that mean rainfall between April and July has slowly increased in the Red Grouse in English moorlands since 1979 and a very weak but significant positive relationship has been observed between *T. tenuis* intensity and April–July rainfall ($P < 0.024$). The Red Grouse breed mainly between April and July, and during this time of the year the parasite has the most detrimental effects on host reproduction and annual growth rate (Hudson et al. 1992). April to July mean rainfall also exhibited large multi-annual fluctuations since 1979 (CV: 29.5%). A large scale study on the effect of climate fluctuations and nematode transmission on spatial synchrony among Red Grouse populations

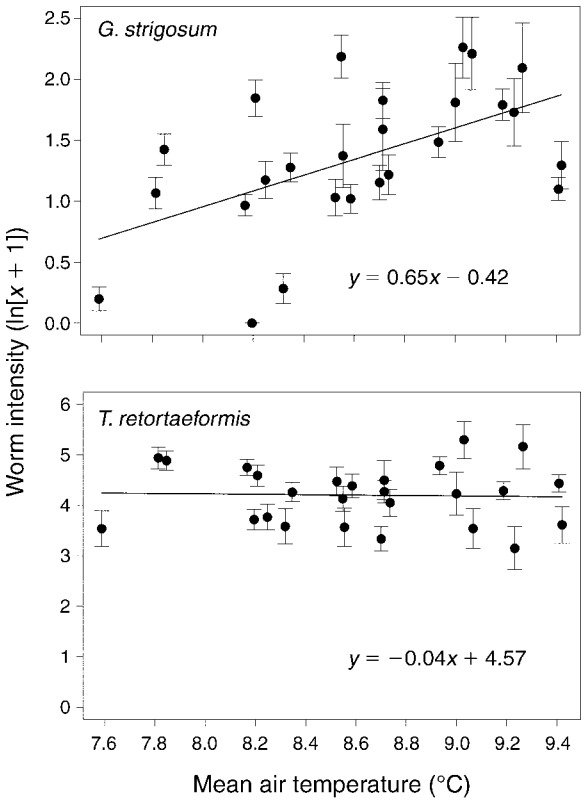

FIG. 2. Relationship between the mean intensity for two parasite species of the European rabbit and mean air temperature between 1977 and 2002 in Scotland (UK). Standard errors of the mean annual parasite intensity are reported.

revealed that unexpected climatic events could cause dramatic and synchronous crashes or peaks in Red Grouse abundance. These stochastic climate anomalies were suggested to have a major effect on the transmission of *T. tenuis* infective stages during the host breeding period, and consequently caused large scale synchrony in the dynamics of Red Grouse populations (Cattadori et al. 2005*b*).

Summary and Conclusions

In conclusion, Lafferty (2009) is a strong summary of climate change effects on mosquito-transmitted human infectious diseases. The goal of our commentary was to highlight examples from wildlife diseases that span many types of animal hosts and for which human management has not yet affected our ability to detect climate drivers. Importantly, introduced diseases are driving some amphibian and coral hosts to extinction; evidence of climate-linked disease epidemics in amphibians has been recently questioned, but for corals, the evidence linking disease prevalence and severity with warmer temperatures is stronger. We also point out that the migrations of animals are recognized as being especially sensitive to climate warming, and changes in host migratory patterns will likely have important consequences for infectious disease in ways that have not yet been fully explored. Finally, as with malaria, parasites affecting vertebrate animals can be driven by host immunity, and this can dampen the effect of climate change on disease dynamics. Some invertebrate hosts, particularly in marine ecosystems, appear to lack this buffering effect and are currently experiencing strong declines by infectious and opportunistic diseases. Collectively, examples discussed here suggest that ecologists need to consider how host biology, including movement behavior and acquired immunity, can mediate the impacts of global change on parasite/pathogen dynamics and disease severity. At present, many of these mechanisms are poorly known. Immune-mediated changes in host susceptibility and resistance as well as climate-related changes in parasite transmission may alter the interaction between wildlife hosts and their communities of parasites (Cattadori et al. 2007). Therefore, it is important to identify how climate changes modulate, both directly and indirectly, host–parasite interaction and disease persistence.

Acknowledgments

D. Harvell was supported by NSF OCE-0326705; S. Altizer by NSF DEB-0643831; I. M. Cattadori by the Royal Society of London (UK) and NSF DEB-0716885; L. Harrington by Gates Grand Challenge; and E. Weil by the Caribbean Environmental Programme (UNEP), CARICOMP, NOAA-CRES (NA170p2919), GEF-World-Bank Coral Reef Targeted Research and Capacity Building program, and the Department of Marine Sciences, UPRM. Thanks to Carolyn Friedman for helpful comments.

Literature Cited

Altizer, S. M., K. Oberhauser, and L. P. Brower. 2000. Associations between host migration and the prevalence of a protozoan parasite in natural populations of adult monarch butterflies. Ecological Entomology 25:125–139.

Altizer, S. M., K. O. Oberhauser, and K. A. Geurts. 2004. Transmission of the protozoan parasite, *Ophryocystis elektroscirrha*, in monarch butterfly populations. Pages 213–218 *in* K. Oberhauser and M. Solensky, editors. The monarch butterfly: biology and conservation. Cornell University Press, Ithaca, New York, USA.

Altstatt, J. M., R. F. Ambrose, J. M. Engle, P. L. Haaker, K. D. Lafferty, and P. T. Raimondi. 1996. Recent declines of black abalone *Haliotis cracherodii* on the mainland coast of central California. Marine Ecology Progress Series 142:185–192.

Anderson, R. C. 2000. Nematode parasites of vertebrates: their development and transmission. Oxford University Press, CABI Publishing, Wallingford, UK.

Bosch, J., L. M. Carrascal, L. Duran, S. Walker, and M. C. Fisher. 2007. Climate change and outbreaks of amphibian chytridiomycosis in a montane area of Central Spain; is there a link? Proceedings of the Royal Society Series B 274:253–260.

Bradley, C., and S. Altizer. 2005. Parasites hinder monarch butterfly flight ability: implications for disease spread in migratory hosts. Ecology Letters 8:290–300.

Bradshaw, W. E., and C. M. Holzapfel. 2007. Evolution of animal photoperiodism. Annual Review of Ecology, Evolution and Systematics 38:1–25.

Braid, B. A., R. P. Hedrick, R. S. Tjeerdema, and C. S. Friedman. 2005. Health and survival of red abalone, *Haliotis rufescens*, under varying temperature, food supply and exposure to the agent of withering syndrome. Journal of Invertebrate Pathology 89:219–231.

Brooker, R. W., J. M. T. Travis, E. J. Clark, and C. Dytham. 2007. Modelling species' range shifts in a changing climate: the impacts of biotic interactions, dispersal distance and the rate of climate change. Journal of Theoretical Biology 245: 59–65.

Bruckner, A. W., and R. Bruckner. 2006. Consequences of YBS on *Montastraea annularis* (species complex) populations on remote reefs off Mona Island, Puerto Rico. Diseases of Aquatic Organisms 69:67–73.

Cattadori, I. M., R. Albert, and B. Boag. 2007. Variation in host susceptibility and infectiousness generated by co-infection: the myxoma-*Trichostrongylus retortaeformis* case in wild rabbits. Journal of the Royal Society Interface 4:831–840.

Cattadori, I. M., B. Boag, O. N. Bjørnstad, S. Cornell, and P. J. Hudson. 2005*a*. Immuno-epidemiology and peak shift in a seasonal host-nematode system. Proceeding of the Royal Society B 272:1163–1169.

Cattadori, I. M., B. Boag, and P. J. Hudson. 2008. Parasite co-infection and interaction as drivers of host heterogeneity. Journal of International Parasitology 38:371–380.

Cattadori, I. M., D. T. Haydon, and P. J. Hudson. 2005*b*. Parasites and climate synchronize red grouse populations. Nature 433:737–741.

Collingham, Y. C., and B. Huntley. 2000. Impacts of habitat fragmentation and patch size upon migration rates. Ecological Applications 10:131–144.

Cook, T., M. Folli, J. Klinck, S. Ford, and J. Miller. 1998. The relationship between increasing sea surface temperature and the northward spread of *Perkinsus marinus* (Dermo) disease epizootics in oysters. Estuarine Coastal Shelf Science 40:587–597.

Cornell, S., O. N. Bjørnstad, I. M. Cattadori, B. Boag, and P. J. Hudson. 2008. Seasonality, cohort-dependence and the development of immunity in a natural host–nematode system. Proceedings of the Royal Society B 275:473–591.

Crofton, H. D. 1948*a*. The ecology of immature phases of Trichostrongyle nematodes: I. The vertical distribution of

infective larvae of *Trichostrongylus retortaeformis* in relation to their habitat. Parasitology 39:17–25.

Crofton, H. D. 1948*b*. The ecology of immature phases of Trichostrongyle nematodes: II. The effect of climatic factors on the availability of the infective larvae of *Trichostrongylus retortaeformis* to the host. Parasitology 39:26–38.

Croquer, A., and E. Weil. 2009. Local and geographic variability in distribution and prevalence of coral and octocord diseases in the Caribbean II: genera-level analyses. Diseases of Aquatic Organisms, *in press*.

De Roode, J. C., A. Yates, and S. Altizer. 2008. Virulence–transmission tradeoffs and population divergence in virulence in a naturally occurring butterfly parasite. Proceedings of the National Academy of Sciences (USA) 105:7489–7494.

Ellner, S., L. E. Jones, L. Mydlarz, and D. Harvell. 2007. Within host disease ecology in the sea fan *Gorgonia ventalina*: modeling the spatial immunodynamics of a coral–pathogen interaction. American Naturalist 170:1–21.

Folstad, I., F. I. Nilssen, A. C. Halvorsen, and O. Andersen. 1991. Parasite avoidance: the cause of post-calving migrations in *Rangifer*? Canadian Journal of Zoology 69:2423–2429.

Ford, S. E., and M. M. Chintala. 2006. Northward expansion of a marine parasite: testing the role of cold adaptation. Journal of Experimental Marine Biology and Ecology 339: 226–235.

Ford, S. E., and R. Smolowitz. 2007. Infection dynamics of an oyster parasite in its newly expanded range. Marine Biology 151:119–133.

Garrett-Jones, C. 1964. Prognosis for the interruption of malaria transmission through assessment of a mosquito's vectorial capacity. Nature 204:1173–1175.

Gylfe, A., S. Bergstrom, and J. Lundstrom. 2000. Reactivation of *Borrelia* infection in birds. Nature 403:724–725.

Harrington, L. C., F. Vermeylen, J. J. Jones, S. Kitthawee, R. Sithiprasasna, J. D. Edman, and T. W. Scott. 2008. Age-dependent survival of the dengue vector, *Ae. aegypti*, demonstrated by simultaneous release and recapture of different age cohorts. Journal of Medical Entomology 45: 307–313.

Harvell, C. D., E. Jordan-Dahlgren, S. Merkel, L. Raymundo, E. Rosenberg, G. Smith, E. Weil, and B. Willis. 2007. Coral disease, environmental drivers and the balance between coral and microbial associates. Oceanography 20:58–81.

Harvell, C. D., C. E. Mitchell, J. R. Ward, S. Altizer, A. P. Dobson, R. S. Ostfeld, and M. D. Samuel. 2002. Climate warming and disease risks for terrestrial and marine biota. Science 296:2158–2162.

Hickling, R., D. R. Roy, J. K. Hill, R. Foz, and C. D. Thomas. 2006. The distributions of a wide range of taxonomic groups are expanding polewards. Global Change Biology 12:450–455.

Hoegh-Guldberg, O., et al. 2007. The carbon crisis: coral reefs under rapid climate change and ocean acidification. Science 318:1737.

Hudson, P. J., I. M. Cattadori, B. Boag, and A. P. Dobson. 2006. Climate disruption and parasite–host dynamics: patterns and processes associated with warming and the frequency of extreme climatic events. Journal of Helminthology 80:1–9.

Hudson, P. J., and A. P. Dobson. 1997. Transmission dynamics and host–parasite interactions of *Trichostrongylus tenuis* in Red Grouse (*Lagopus lagopus scoticus*). Journal of Parasitology 83:194–202.

Jensen, T., M. van de Bildt, H. H. Dietz, T. H. Andersen, A. S. Hammer, T. Kuiken, and A. Osterhaus. 2002. Another phocine distemper outbreak in Europe. Science 297:209.

Lafferty, K. D. 2009. The ecology of climate change and infectious diseases. Ecology 90:888–900.

Lips, K. R., F. Brem, R. Brenes, J. D. Reeve, R. A. Alford, J. Voyles, C. Carey, L. Livo, A. P. Pessier, and J. P. Collins. 2006. Emerging infectious disease and the loss of biodiversity in a Neotropical amphibian community. Proceedings of the National Academy of Sciences (USA) 103:3165–3170.

Lips, K. R., J. Diffendorfer, J. R. Mendelson, and M. W. Sears. 2008. Riding the wave: reconciling the roles of disease and climate change in amphibian declines. PLoS Biology 6(3):e72.

Loehle, C. 1995. Social barriers to pathogen transmission in wild animal populations. Ecology 76:326–335.

Lusseau, D., R. Williams, B. Wilson, K. Grellier, T. R. Barton, P. S. Hammond, and P. M. Thompson. 2004. Parallel influence of climate on the behaviour of Pacific killer whales and Atlantic bottlenose dolphins. Ecology Letters 7:1068–1076.

Martens, P. 1999. Climate change impacts on vector-borne disease transmission in Europe. Pages 45–54 *in* A. Haines and A. J. McMichael, editors. Climate change and human health. Royal Society, London, UK.

Miller, J., R. Waara, E. Muller, and C. Rogers. 2006. Coral bleaching and disease combine to cause extensive mortality on corals reefs in US Virgin Islands. Coral Reefs 25:418.

Moore, J. D., T. T. Robbins, and C. S. Friedman. 2000. Withering syndrome in farmed red abalone *Haliotis rufescens*: thermal induction and association with a gastrointestinal Rickettsiales-like prokaryote. Journal of Aquatic Animal Health 12:26–34.

Morgan, E. R., E. J. Milner-Gulland, P. R. Torgerson, and G. F. Medley. 2004. Ruminating on complexity: macroparasites of wildlife and livestock. Trends in Ecology and Evolution 19:181–188.

Muller, E. M., C. S. Rogers, A. S. Spitzack, and R. van Woesik. 2008. Bleaching increases likelihood of disease on *Acropora palmata* (Lamarck) in Hawksnest Bay, St. John, U.S. Virgin Islands. Coral Reefs 27:191–195.

Mydlarz, L., S. Holthouse, E. Peters, and D. Harvell. 2008. Cellular responses in sea fan corals: granular amoebocytes react to pathogen and climate stress. PLos One 3:1811.

Oberhauser, K., and A. T. Peterson. 2003. Modeling current and future potential wintering distributions of eastern North American monarch butterflies. Proceedings of the National Academy of Sciences (USA) 100:14063–14068.

Osterhaus, A. D. M. E., and E. J. Vedder. 1988. Identification of a virus causing recent seal deaths. Nature 335:20.

Parmesan, C., and G. Yohe. 2003. A globally coherent fingerprint of climate change impacts across natural systems. Nature 42:37–42.

Perry, A. L., P. J. Low, J. R. Ellis, and J. D. Reynolds. 2005. Climate change and distribution shifts in marine fishes. Science 308:1912–1915.

Pounds, J. A., et al. 2006. Widespread amphibian extinctions from epidemic disease driven by global warming. Nature 439: 161–167.

Raffel, T. R., J. R. Rohr, J. M. Kiesecker, and P. J. Hudson. 2006. Negative effects of changing temperature on amphibian immunity under field conditions. Functional Ecology 20:819–828.

Rogers, D. J., and S. E. Randolph. 2000. Fragile transmission cycles of tick-borne encephalitis virus may be disrupted by predicted climate change. Proceedings of the Royal Society B 267:1741–1744.

Simmons, A. M., and C. E. Rogers. 1991. Dispersal and seasonal occurrence of *Noctuidonema guyanense*, an ectoparasitic nematode of adult fall armyworm (Lepidoptera, Noctuidae), in the United States. Journal of Entomological Science 26:136–148.

Styer, L. M., J. R. Carey, J. L. Wang, and T. W. Scott. 2007. Mosquitoes do senesce: departure from the paradigm of constant mortality. American Journal of Tropical Medicine and Hygiene 76:111–117.

Vilchis, L. I., M. J. Tegner, J. D. Moore, C. S. Friedman, K. L. Riser, T. T. Robbins, and P. K. Dayton. 2005. Ocean warming effects on growth, reproduction and survivorship of southern California abalone. Ecological Applications 15:469–480.
Ward, J. R., K. Kim, and C. D. Harvell. 2006. Temperature affects coral disease resistance and pathogen growth. Marine Ecology Progress Series 329:115–121.
Weil, E., and A. Croquer. 2009. Local and geographic variability in distribution and prevalence of coral and octocoral diseases in the Caribbean I: community-level analyses. Diseases of Aquatic Organisms, *in press*.
Weil, E., G. W. Smith, and D. L. Gil-Agudelo. 2006. Status and progress in coral reef disease research. Diseases of Aquatic Organisms 69:1–7.
Wilkinson, C., and D. Souter. 2008. Status of Caribbean coral reefs after bleaching and hurricanes in 2005. Global Coral Reef Monitoring Network and Reef and Rainforest Research Centre, Townsville, Australia.

Ecology, 90(4), 2009, pp. 920–927

FORUM

Climate variability, global change, immunity, and the dynamics of infectious diseases

ANDY DOBSON[1]

Ecology and Evolutionary Biology, Guyot Hall, Princeton University, Princeton, New Jersey 08544 USA

Global climate change will have a diversity of impacts on ecological systems. The paper by Lafferty (Lafferty 2009) provides a number of important insights into the ways in which climate change will modify the dynamics of infectious diseases. Here I will focus on three aspects that pick up on his theme that any simple links between climate change and rates of disease transmission will be complicated by the web of ecological interactions within which host–parasite relationships are intimately embedded (Lafferty et al. 2006). Much of the history of mathematical modeling of infectious diseases has focused upon systems where a single pathogen infects a single host species; this approach has provided critical insights into the dynamics of many human pathogens and vital insights into how increased efficiency can be achieved in their control (Anderson and May 1991, Smith et al. 2005). These approaches now need to be extended to consider systems where transmission is dependent upon climate variability and also upon systems with multiple host species and potentially multiple pathogens (Dobson 2004). This will be particularly important if climate warming allows vector-transmitted pathogens to spread from the species rich tropics, into the temperate and Mediterranean countries where reduced host diversity will focus vector activity and potentially increase the proportion of bites that go to humans and domestic livestock. Ironically, the complexities of studying infectious disease dynamics in the tropics will be confounded by a diversity of other interacting variables (insecticide resistance, host species diversity, land conversion and the emergence of new pathogens such as HIV); thus I will conclude with a plea to also study host–pathogen systems in the Arctic where there are less confounding variables and a stronger signal of climate change. The lessons learned in these less diverse systems will be crucial in interpreting the more complex patterns we will certainly see in the tropics.

Manuscript received 22 April 2008; revised 2 September 2008; accepted 8 September 2008; final version received 2 October 2008. Corresponding Editor: K. Wilson. For reprints of this Forum, see footnote 1, p. 901.

[1] E-mail: Dobson@princeton.edu

Global change and climate variability

A variety of different approaches have been used to examine the relationship between climate and disease; they can be broadly grouped into two different approaches: static dynamics and time-series approaches. Static approaches focus on global climate change and use expressions for R_0 (basic reproductive number), or "entomological potential" to examine how potential changes in climate will modify the potential range of specific human pathogens. Most interest here has focused on malaria and other vector transmitted diseases as there is a considerable body of empirical work that has quantified the temperature dependence of pathogen development in the poikilothermic insect and tick species that act as vectors. While there is naturally an emphasis on expansion of the pathogen into new areas, this will always be a relatively weak prediction of these models as it assumes the vectors and pathogen can readily disperse into areas where the climate has become favorable. In contrast, much stronger predictions can be made about the reduction in malaria incidence, and other insect-vectored pathogens, that will occur in areas that are no longer viable for transmission (Dobson and Carper 1992). While I partly agree with Kevin Lafferty that some of the costs of potential infectious disease expansion will be balanced by pathogen extinctions in

other areas, I feel it is important to note that the impact of malaria will be considerably higher as it expands into areas where people have had limited prior exposure and therefore have not acquired immunity to infection. This will be particularly important if the spread is into areas of higher population density where people have chosen to live to avoid malaria, while pathogen extinction is restricted to areas of low human-population density. Similarly, the loss of pathogens from an area is not necessarily beneficial to all parties; for example, the loss of sleeping sickness from significant areas of sub-Saharan Africa would lead to massive expansion of agriculture onto soils that may be too poor to sustain anything other than the current populations of wild artiodactyls that are resistant to trypanosomiasis (Rogers and Randolph 1988). The loss of these wild game species could lead to a significant reduction in tourism potential and a resultant loss of foreign currency income for countries such as Tanzania, Kenya, and Botswana.

Malaria and other tropical pathogens have proved disturbingly resistant to the development of vaccines that have been so powerful in the control of the directly transmitted viral infections of childhood (Anderson and May 1985, Grenfell and Bolker 1998). This is primarily because immunity to malaria, cholera, and other tropical diseases is transient and may require significant rates of re-exposure for hosts to mount a level of immunity that prevents disease. The transient nature of immunity may be further complicated by the strain diversity of pathogens that requires hosts to develop immunity to each strain of the pathogen present in a region (Gupta et al. 1994). This, in turn, is further confounded by the ability of pathogens such as malaria and the trypanosomes to sequentially change their surface structure and transiently escape recognition by the host's immune system (Frank 1999, Turner 1999).

Climate variability has been examined for malaria and a number of other human pathogens, most notably cholera, using time-series approaches (Pascual et al. 2000, Rodo et al. 2002, Koelle et al. 2005). When these approaches have been applied they provide detailed and important insights into how climate variability modifies disease dynamics. Unfortunately, the detailed long-term time-series required to parameterize the models are only available for a limited number of pathogens and for a very limited number of geographical locations. This alone is a sad testimony to the research priorities of tropical medicine over the last 25 years; most of the molecular level mechanisms upon which we have focused limited funding and capacity building have provided almost no insights into the dynamics of tropical diseases at the population level. This has considerably handicapped attempts to control these pathogens and it could be argued that ignoring the potential risk of evolution of insecticide and drug resistance, has ultimately made the task of controlling tropical pathogens much harder.

Seasonal dynamics and immunity

Initially let us simplify the problem by considering the dynamic interaction between host immunity and transmission in a system where there is a strong interaction between climate and force of infection. This will be the central feature of any human pathogen whose range could potentially be modified by global climate change. The dynamics of pathogens with intermediate levels of immunity can be examined using the standard SEIR dynamics framework. Here, I have modified the standard model and assume that transmission rate, β_t, varies with a seasonal cycle, and the magnitude of variation is sufficient to reduce transmission below outbreak levels for some part of the year ($R_0 < 1$), while causing out breaks at one other part of the year ($R_0 > 1$). The model can be described by the following set of coupled differential equations:

$$dS/dt = \mu(N - S) + \sigma R - \beta_0[1 + \beta_1 \cos(2\pi t)]SI/N \quad (1)$$

$$dE/dt = \beta_0[1 + \beta_1 \cos(2\pi t)]SI/N - (\mu + \varsigma)E \quad (2)$$

$$dI/dt = \varsigma E - (\mu + \delta)I \quad (3)$$

$$dR/dt = \delta I - (\mu + \sigma)R. \quad (4)$$

Here, the birth and death rates of the host are assumed at some constant rate, μ (=1/70), the duration of immunity if given by $1/\sigma$, the background rate of transmission, β_0 is modified by a sinusoidal annual cycle of magnitude, β_1. Exposed hosts take a period of $1/\varsigma$, to become infectious, they the recover after a period of time $1/\delta$; here I assume that the exposed and infectious periods last a week.

The properties of similar models have been well described for measles where seasonal forcing due to variation in rates of school attendance have been shown to amplify the intrinsic propensity of the system to cycle (Grenfell et al. 1994, Earn et al. 2000). More recent studies of measles in West Africa have shown that seasonal forcing due to climate driven variation in social behavior can create even more complex measles epidemic behavior (Ferrari et al. 2008). However, immunity to measles is effectively life-long, so rate of loss of immunity, σ, is essentially negligible ($<1/70$). This is not the case for many tropical diseases, such as malaria and cholera, so let us explore the dynamics of this seasonally forced system when immunity is more transient.

The more detailed interaction between transmission and immunity observed for cholera (Koelle et al. 2005) can be generalized for a broad range of levels of host immunity. Here I explore the very general case where immunity ranges from a month to 70 years. When the immunity of recovered individuals lasts nearly as long as host life expectancy, then "herd immunity" develops at the population level, particularly when transmission is high, as is the case for measles. The phenomenon is

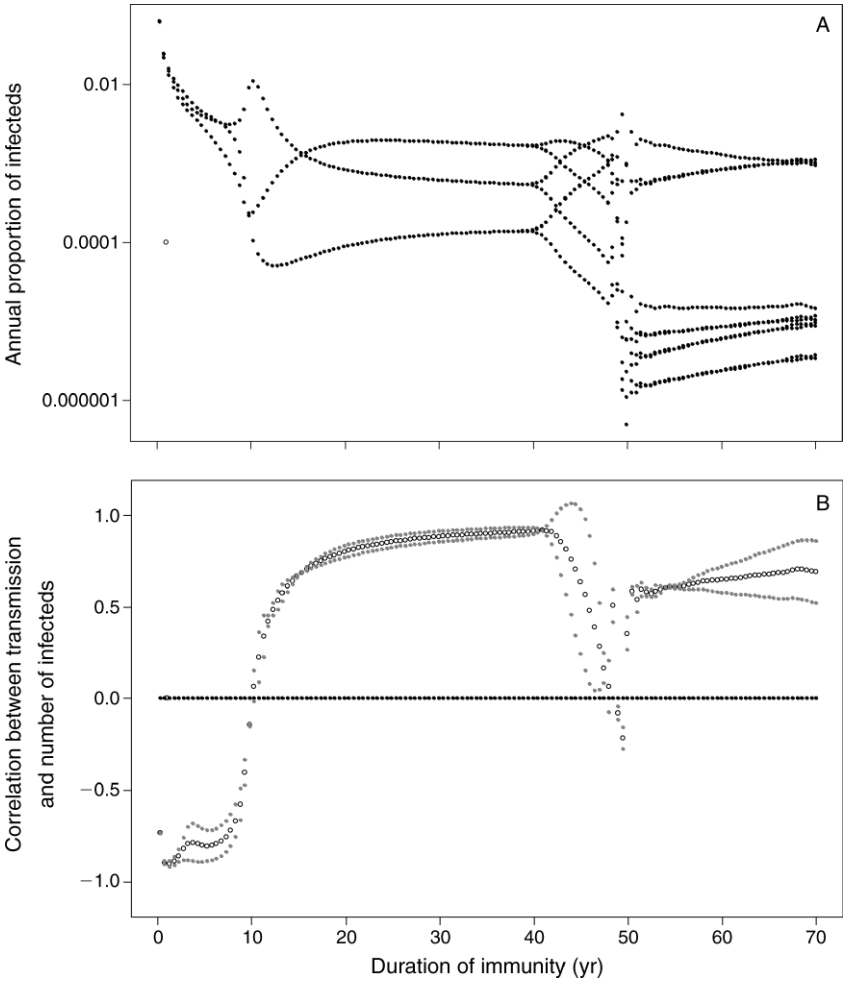

FIG. 1. The relationship between duration of immunity and the proportion of hosts infected for a simple seasonal SEIR epidemic model with transmission set as a simple sine function that varies annually in a way that corresponds to annual climate-driven variations in insect vector abundance, or to the volume of water in which cholera is transmitted. We have assumed constant host population size of around one million hosts and endemic infection, and that transmission is always sufficient to cause an outbreak (basic reproductive number $R_0 > 1$), but that the intensity of transmission varies throughout the year, with mean transmission such that $R_0 = 1.1$, with a maximum of 2.0. The initial proportion of susceptible hosts in the simulation is 0.06 of the hosts, there are also 0.939 recovered and resistant hosts, and 0.001 infectious individuals. Panel A illustrates the relationship between duration of immunity and the proportion of infected individuals in the population from time 90 to 100 years of the simulation (transients die out after 20 years). Panel B illustrates the correlations between the climate signal and the number of infected hosts at a subsequent time interval equal to the incubation period, the solid gray dots illustrate the bootstrapped 95% confidence intervals for the correlation coefficient. In both panels, the x-axis illustrates the duration of host immunity in hosts that have recovered from infection; this varies on a time scale from less than a week to full lifetime immunity. As the duration of immunity increases, the number of infected hosts exhibits more complex cycles, and the correlation between transmission and infected hosts switches between negative and positive with each phase transition of the dynamics model.

termed "herd immunity" as a significant proportion of hosts become immune and the pathogen's rate of transmission is constrained by low numbers of susceptible hosts (Fine 1993). In contrast, levels of herd immunity are considerably lower when duration of immunity is relatively short, or when birth rates are high. The model I have used is based on those of Grenfell et al. (1994), it assumes a human population of around a million people, initially divided into proportions of 0.939 recovered and resistant hosts, 0.06 susceptible hosts and 0.001 infectious individuals. The simple seasonal forced SEIR model is run for 100 years; after discarding the initial ninety years of transient data, I plot a bifurcation diagram of the transient dynamics of the proportion of infected hosts at different durations of immunity. When immunity is short (<1 year) the model exhibits the annual cycles of transmission that drive it. However, when immunity is more persistent the dynamics of the model pass through a number of phase transitions that exhibit more complex multi-year cycles and then chaotic dynamics (Fig. 1). Although numbers of infected hosts fall to low numbers in the troughs, the

size of the host population is sufficiently large to prevent extinction.

This interaction between seasonal forcing and the systems intrinsic tendency to cycle makes it very hard to detect any simple relationship between the observed number of infected hosts and the seasonal signal that forces the annual variation in transmission rate. This is most easily seen by plotting the correlation between the intensity of transmission and the observed number of infected hosts (in the next time interval, one exposure period) over the last 10 years of data. A significant positive correlation between the force of infection and number of newly infected hosts only occurs at intermediate durations of immunity; instead, the correlation switches between negative (when immunity is less than ten years), to positive (as immunity is more prolonged); this transition tends to occur each time the dynamic behavior of the system passes through a major phase shift. This suggests that it will be very hard to detect a strong and unambiguous signal between observed cases and transmission rates for the broad range of pathogens that exhibit relatively short durations of immunity. The magnitude of these resonance effects will differ between different pathogens and for the same pathogen in endemic versus epidemic circumstances. Unfortunately, many of the human pathogens that we are most concerned about from a climate change perspective (cholera, malaria) tend to exhibit short to intermediate durations of immunity and these will give rise to more complex epidemic dynamics. This imposes severe limits on the interpretation of analyses based only upon correlations between climate variability and disease outbreaks (Lobitz et al. 2000). For similar reasons, it is naïve, or disingenuous, to suppose that the three to five year cycles observed in time series for malaria or other vector-transmitted pathogens purely reflect the underlying intrinsic dynamics of host-parasite dynamics, rather than any interaction between climate and intrinsic dynamics (Hay et al. 2000). In order to interpret the dynamics of climate sensitive diseases such as cholera and malaria, we instead need to adopt time series approaches that fit models that explicitly include both immunity and climate variability (Little et al. 1996, Rodo et al. 2002, Koelle et al. 2005).

A second major advantage of these "mixed-models," that track both force of infection and levels of immunity in the host population, is that they will provide deeper insights into the mechanisms that drive transmission rates. Ultimately, this will be central to the development of viable mathematical and statistical models that can be used for making forecasts of when (and where) disease outbreaks are likely to occur. At present the epidemiological models are constrained by the paucity of time-series data, while the climate models, although rich in data, are computationally constrained by the time and spatial scale over which they can make predictions. These constraints are different for the temperate, than for the tropical zones. In the tropics we can often make mid-term (six-month) forecasts for key climate variables such as rainfall over broad regions as they are highly dependent on sea-surface warming events (Charney and Shukla 1981). In contrast, short-term (less than one week) forecasts are much less predictable for the tropics than they are for the temperate zones where the movement of weather fronts across the continents is now well characterized. Ironically, it is much harder to make mid-term predictions for the temperate zone, so this may make mid-term (six-month) disease outbreak prediction harder as the climate warms and tropical pathogens spread into these regions. This is important as mid-term predictions will be most useful for upgrading and focusing public health systems to deal with potential outbreaks.

The potential resonance of climate variability with herd immunity is likely to play a much smaller role in the dynamics of pathogens that utilize small mammals and birds as reservoir hosts (such as Hanta virus, plague, leptospirosis and West Nile virus). Here, the birth and death rates of the host populations operate at a sufficiently rapid level that immune hosts die and are replaced by young naïve hosts at relatively rapid rates. Thus, it is unlikely that any significant level of herd immunity will build up (although herd-immunity may be important at transient seasonal time scales for pathogens such as West Nile virus, as is observed in the House-Finch–mycobacterium system [Hosseini et al. 2004]). Instead, the dynamics of host–pathogen systems with short-lived mammalian and avian reservoirs are probably much more strongly influenced by climate driven host birth rates and seasonal aggregation for migration, than they are by levels of herd immunity. In these systems climate conditions that modify fecundity or social behavior will lead to changes in density and aggregation that will create conditions under which transmission crosses the thresholds that promote disease outbreaks.

The dynamics of many climate-sensitive pathogens will also be strongly coupled to the community of hosts that are used by the pathogen; this will be particularly important in the case of vector borne diseases whose development is often temperature dependent, but where transmission is also dependent upon the vector biting a viable host for the pathogen. As the pathogen's choice of host may only be a subset of the species chosen by the vector, this creates the potential for the vector to make mistakes and "waste bites" in communities with a diversity of host species. This phenomenon has been called the "dilution effect"; and is defined as the reduction in rates of pathogen transmission that may occur when "dead-end" hosts absorb transmission events (Hudson et al. 1995, Schmidt and Ostfeld 2001, LoGuidice et al. 2003, Dobson et al. 2006, Keesing et al. 2006).

Basic reproductive number for a vector transmitted pathogen with n host species

The potential for an outbreak of a vector transmitted pathogen such as West Nile virus or Lyme disease will

be determined by R_0, the basic reproductive ratio (number) of the pathogen (Anderson and May 1982, Diekmann et al. 1990). The methods developed by Diekmann et al. (Diekmann et al. 1990) can readily be used to derive a general expression for R_0 for a vector transmitted pathogen within a community with n host species (Hasibeder and Dye 1988, Dobson and Foufopoulos 2001). Consider the case for a vector-transmitted pathogen with two host species that occur at abundance C and B, each of these hosts is bitten at a rate determined by the background rate of mosquito biting β, and its relative abundance in the community (e.g., for C, relative abundance $= C/[C + B]$; notice that if each individual of species C is a times more attractive than an individual of species B, then the relative abundance that determines the proportion of bites received by C is $aC/[aC + B]$). We also assume that each host species has a relative efficiency as a host for the pathogen is determined by $1/(\alpha + d + \delta)$, where α is the pathogen induced host mortality, d is the background host mortality rate, and δ is the rate at which the host recovers from infection. We designate this aggregate parameter c for species C and b for species B. When this figure has a small value the host does not sustain infection with the pathogen for a long period of time and either dies or quickly recovers. We also assume a mosquito population density of M and that mosquitoes live for a period of $1/\mu$ years.

We can then write a simple matrix expression for the "next generation" of infections whenever an infected host is introduced into the population:

$$\mathbf{M} = \begin{bmatrix} 0 & \dfrac{M\beta B}{\mu(B + aC)} & \dfrac{M\beta aB}{\mu(B + aC)} \\ \dfrac{b\beta B}{(B + aC)} & 0 & 0 \\ \dfrac{ca\beta C}{(B + aC)} & 0 & 0 \end{bmatrix}. \quad (5)$$

The basic reproductive number for the pathogen is then given by the dominant eigenvalue of this matrix:

$$R_0 = \frac{\beta^2 M}{\mu(B + ac)} \sqrt{(bB^2 + ca^2C^2)}. \quad (6)$$

This can readily be shown to generalize for n species of hosts to

$$R_0 = \frac{\beta^2 M}{\mu \sum_{i=1}^{n} a_i A_i} \sqrt{\left[\sum_{i=1}^{n} v_i (a_i A_i)^2\right]}. \quad (7)$$

Here, a_i is the relative attraction of species i to mosquitoes, A_i is the abundance of species i, and v_i is species i's viability as a host ($1/[\alpha_i + d_i + \delta_i]$). Before using this expression to examine the factors which contribute to the dilution effect it is important to use it to illustrate the key difference between tick- and mosquito (insect)-vectored systems: in the mosquito case, vector abundance will be independent of host abundance as the carrying capacity for mosquitoes is dependent upon rainfall and the rate at which the bodies of water used as breeding sites appear and then evaporate. In contrast, tick abundance is intimately dependent upon the abundance of some of the hosts that are also hosts to the pathogen. Thus increases in host abundance should lead to increases in vector abundance in tick-vectored systems, but not in insect vectored systems.

The impact of host species diversity on R_0 for hypothetical tick- and insect-vectored systems are illustrated in Fig. 2. Two effects are important to notice here. First, increases in vector abundance always lead to increases in R_0; so if climate change allows vector populations to reproduce more rapidly, then this will increase the local impact of vector transmitted pathogens. Secondly, and more subtlety, increased potential host species diversity produces a consistent dilution effect that reduces the magnitude of R_0 at any vector abundance, however, the magnitude of this "dilution effect" is much less pronounced in the tick-transmitted system than they are in the insect-transmitted system (Randolph 1998). This occurs because increased host diversity (and abundance) tends to increase the vector abundance in the tick systems, but not in the mosquito-vectored systems. We would thus expect to see stronger dilution effects as host density and diversity increases in insect-vectored systems, and more subtle changes in tick-vectored systems. There is an irony here, as the most widely cited examples of "dilution effects" are for tick-transmitted systems (Ostfeld and Keesing 2000, LoGuidice et al. 2003); plainly we need to look for them more energetically in mosquito-vectored systems. In general, for vector-transmitted pathogens, increases in host species diversity always reduces R_0, except when the species that are added are both more abundant and more viable hosts for the pathogen. The strongest dilution effects occur when host species are added to the system that are both more abundant (settle to a higher carrying capacity) and less viable as hosts for the pathogen.

Latitudinal diversity and buffering of disease outbreaks

This relatively simple modeling exercise has important implications for climate change and the transmission of vectored pathogens such as malaria, West Nile virus, blue tongue virus, and leishmaniasis (Chaves et al. 2007). When these pathogens are restricted to tropical locations, their impact may be significantly buffered by the high levels of species diversity in these regions. If climate warming permits vector-transmitted pathogens to expand out of the tropics into Mediterranean and temperate regions, then the reduced levels of species diversity in these regions will cause the disease impact to fall hardest on the susceptible species that are most attractive to the vectors. This may well be humans and their domestic livestock. It is hard to think of a stronger utilitarian reason for conserving biodiversity; its diversity and abundance may play a major role in buffering

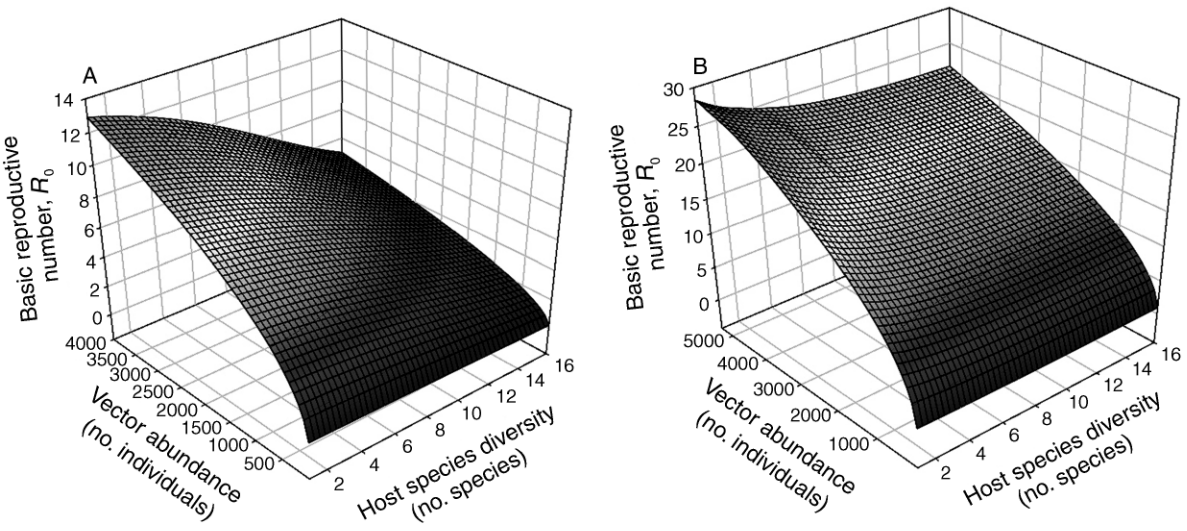

FIG. 2. The relationship between host-species diversity, vector abundance, and the basic reproductive number (R_0) of a pathogen for hypothetical (A) mosquito-borne and (B) tick-borne pathogens. In these figures, I have made a minimal number of assumptions by setting as many parameters as possible to unity; thus each host species is equally good at amplifying the tick population. Adding host species with lower viability for ticks will thus create a stronger "dilution effect." The other parameters used for each species i are biting rate, $\beta_i = 1$ for mosquitoes and $\beta_i = 0.5$ for ticks; attraction of each host to the vector, $a_i = 1$; viability of each host species, $v_i = 1$; and mortality rate of ticks, $\mu = 12$, and mortality rate of mosquitoes, $\mu = 24$.

humans and their food from the attention of the vectors of pathogens and infectious disease.

The decrease of biodiversity as we move from the equator to the arctic is matched by an opposing gradient of increased climate change at the poles. Ecologists need to take much greater advantage of this by examining the impact of significant climate change on the less diverse parasite-host communities that occur in the high Arctic and northern temperate regions (Kutz et al. 2005). In many ways these systems resemble the simpler one host, one parasite models on which so much epidemiological theory has been constructed. The patterns that we can already observe (and quantify) as Arctic systems respond to climate change will be significantly easier to interpret than those that occur in response to lower degrees of warming in the significantly more diverse host communities of the tropics. The patterns we are beginning to see in the Arctic provide an important template and "null expectation" for what may eventually happen in the tropics.

Patterns currently observed in the Arctic

Climate change is already well advanced in the Arctic and this is beginning to have quantifiable effects on the dynamics of parasite systems (Kutz et al. 2005). The patterns observed here provide important insights into what is likely to occur in regions with higher species diversity. Studies of nematode parasites of caribou and musk ox have shown they complete their life cycles much more quickly in the warming Arctic; while it used to take three to four years for Protostrongylid nematodes to complete their life cycles, they can now achieve this in a single year, this produces much higher worm burdens in hosts that lead to significant levels of morbidity and mortality (Kutz et al. 2005). The increased transmission rates of endemic pathogens are matched by a second insult; warming of the high arctic regions has allowed species such as elk and white-tailed deer to expand their range northwards into areas that overlap with the southern part of the range of musk ox and caribou. This leads to the introduction of novel pathogens to which the caribou and musk ox have no natural resistance (Dobson et al. 2003, Kutz et al. 2005); so more northerly species experience a double insult, their endemic parasites complete their life cycles at a faster rate and novel pathogens are introduced by species expanding their ranges from the south. Similar effects are likely to be seen as species ranges change in temperate and neotropical regions, but the higher hosts and pathogen diversity of these regions will make it much harder to dissect out the interactions between "climate-modified endemic pathogens" and "emergent pathogens" that are shared by expanding populations of potential competing host species.

A major additional caveat to this (and almost everything else described above) is that land-use change in the Tropics is occurring at rates that may well exceed those predicted for global climate change (Jetz et al. 2007). Both aspects of global change will have a huge impact on host-parasite relationships, but in many tropical areas, natural systems will likely be completely disrupted by habitat conversion, before climate change makes a significant impact. In other areas, climate change and land use change will interact in ways that obfuscate straightforward interpretations of the role of climate. This is partly why there is such controversy

about the role that climate change has played in modifying the incidence of malaria in the East African highlands (see Pascual and Bouma 2009). Ultimately, the observed increase in malaria cases represent a complex interaction between climate change, human population expansion, the evolution of drug resistance, and the rapid expansion of the AIDS epidemic. Teasing out the relative importance of each requires careful analyses of nonstationary time-series data where long term trends in global change, and annual seasonal variation in external forcing, interact with the intrinsic tendency of epidemic systems to cycle; this can produce very complex dynamics that defy simple statistical analysis. In each of these areas, there is a significant need for more theoretical work and considerably more empirical work. Increased funding is desperately needed to increase our understanding of infectious disease dynamics; there is also a major need for capacity building in this area.

Acknowledgments

I am most grateful to Ben Cash, Pete Hudson, Parviez Hosseini, Jim Kinter, Mercedes Pascual, and Xavier Rodo for discussions that formed the basis of this paper. I thank Ottar Bjornstad for the original measles R code used at the Cornell Ecology of Infectious Disease workshop; this morphed into that used for Fig. 1. All of my research is supported by the NIH/NSF Ecology of Infectious Disease Program grants.

Literature Cited

Anderson, R. M., and R. M. May. 1982. Coevolution of hosts and parasites. Parasitology 85:411–426.

Anderson, R. M., and R. M. May. 1985. Vaccination and herd immunity to infectious diseases. Nature 318:323–329.

Anderson, R. M., and R. M. May. 1991. Infectious diseases of humans: dynamics and control. Oxford University Press, Oxford, UK.

Charney, J. G., and J. Shukla. 1981. Predictability of monsoons. Pages 99–109 *in* J. Lighthill and R. P. Pearce, editors. Monsoon dynamics. Cambridge University Press, Cambridge, UK.

Chaves, L. F., M. J. Hernandez, A. P. Dobson, and M. Pascual. 2007. Sources and sinks: revisiting the criteria for identifying reservoirs for American cutaneous leishmaniasis. Trends in Parasitology 23:57–68.

Diekmann, O., J. A. P. Heesterbeek, and J. A. J. Metz. 1990. On the definition and the computation of the basic reproduction ratio R_0 in models for infectious-diseases in heterogeneous populations. Journal of Mathematical Biology 28:365–382.

Dobson, A. P. 2004. Population dynamics of pathogens with multiple hosts. American Naturalist 164:S64–S78.

Dobson, A. P., and R. J. Carper. 1992. Global warming and potential changes in host–parasite and disease vector relationships. Pages 201–217 *in* R. Peters and T. Lovejoy, editors. Global warming and biodiversity. Yale University Press, New Haven, Connecticut, USA.

Dobson, A. P., I. Cattadori, R. D. Holt, R. S. Ostfeld, F. Keesing, K. Krichbaum, J. R. Rohr, S. E. Perkins, and P. J. Hudson. 2006. Sacred cows and sympathetic squirrels: the importance of biological diversity to human health. PLoS Medicine 3:e231.

Dobson, A. P., and J. Foufopoulos. 2001. Emerging infectious pathogens of wildlife. Philosophical Transactions of the Royal Society of London B 356:1001–1012.

Dobson, A. P., S. Kutz, M. Pascual, and R. Winfree. 2003. Pathogens and parasites in a changing world. Pages 33–38 *in* L. H. T. Lovejoy, editor. Climate change and biodiversity: synergistic impacts. Yale University Press, New Haven, Connecticut, USA.

Earn, D. J. D., P. Rohani, B. M. Bolker, and B. T. Grenfell. 2000. A simple model for complex dynamical transitions in epidemics. Science 287:667–670.

Ferrari, M. J., R. F. Grais, N. Bharti, A. J. K. Conlan, O. N. Bjornstad, L. J. Wolfson, P. J. Guerin, A. Djibo, and B. T. Grenfell. 2008. The dynamics of measles in sub-Saharan Africa. Nature 451:679–684.

Fine, P. E. M. 1993. Herd immunity: history, theory, practice. Epidemiologic Reviews 15:265–302.

Frank, S. A. 1999. A model for the sequential dominance of antigenic variants in African trypanosome infections. Proceedings of the Royal Society B 266:1397.

Grenfell, B. T., and B. M. Bolker. 1998. Cities and villages: infection hierarchies in a measles metapopulation. Ecology Letters 1:63–70.

Grenfell, B. T., A. Kleczkowski, S. P. Ellner, and B. M. Bolker. 1994. Measles as a case study in nonlinear forecasting and chaos. Philosophical Transactions of the Royal Society London A 348:515–530.

Gupta, S., A. V. S. Hill, D. Kwietkowski, A. M. Greenwood, B. M. Greenwood, and K. P. Day. 1994. Parasite virulence and disease patterns in *Plasmodium falciparum* malaria. Proceedings of the National Academy of Sciences (USA) 91:3715–3719.

Hasibeder, G., and C. Dye. 1988. Population dynamics of mosquito-borne disease: persistence in a completely heterogenous environment. Theoretical Population Biology 33:31–53.

Hay, S. H., M. F. Myers, D. S. Burke, D. W. Vaughn, T. Endy, N. Ananda, G. D. Shanks, R. W. Snow, and D. J. Rogers. 2000. Etiology of interepidemic periods of mosquito-borne disease. Proceedings of the National Academy of Sciences (USA) 97:9335–9339.

Hosseini, P. R., A. A. Dhondt, and A. P. Dobson. 2004. Seasonality and wildlife disease: how seasonal birth, aggregation and variation in immunity affect the dynamics of *Mycoplasma gallisepticum* in House Finches. Proceedings of the Royal Society B 271:2569–2577.

Hudson, P. J., R. Norman, M. K. Laurenson, D. Newborn, M. Gaunt, L. Jones, H. Reid, E. Gould, R. Bowers, and A. Dobson. 1995. Persistence and transmission of tick-borne viruses: *Ixodes ricinus* and louping-ill virus in Red Grouse populations. Parasitology 111:S49–S58.

Jetz, W., D. Wilcove, and A. P. Dobson. 2007. Projected impacts of climate and land-use change on the global diversity of birds. PLOS Biology 5(6):e157.

Keesing, F., R. D. Holt, and R. S. Ostfeld. 2006. Effects of species diversity on disease risk. Ecology Letters 9:485–498.

Koelle, K., X. Rodo, M. Pascual, M. Yunus, and G. Mostafa. 2005. Refractory periods and climate forcing in cholera dynamics. Nature 436:696–700.

Kutz, S. J., E. P. Hoberg, L. Polley, and E. J. Jenkins. 2005. Global warming is changing the dynamics of Arctic host–parasite systems. Proceedings of the Royal Society B 272: 2571–2576.

Lafferty, K. D. 2009. The ecology of climate change and infectious diseases. Ecology 90:888–900.

Lafferty, K. D., A. P. Dobson, and A. M. Kuris. 2006. Parasites dominate food web links. Proceedings of the National Academy of Sciences (USA) 103:11211–11216.

Little, S., S. Ellner, M. Pascual, M. Neubert, D. Kaplan, T. Sauer, H. Caswell, and A. Solow. 1996. Detecting nonlinear dynamics in spatio-temporal systems, examples from ecological models. Physica D 96:321–333.

Lobitz, B., L. Beck, A. Huq, B. Wood, G. Fuchs, A. S. G. Faruque, and R. Colwell. 2000. Climate and infectious

disease: use of remote sensing for detection of *Vibrio cholerae* by indirect measurement. Proceedings of the National Academy of Sciences (USA) 97:1438–1443.

LoGuidice, K., R. S. Ostfeld, K. A. Schmidt, and F. Keesing. 2003. The ecology of infectious disease: effects of host diversity and community composition on Lyme disease risk. Proceedings of the National Academy of Sciences (USA) 100: 567–571.

Ostfeld, R. S., and F. Keesing. 2000. Biodiversity and disease risk: the case of Lyme disease. Conservation Biology 14:722–728.

Pascual, M., and M. J. Bouma. 2009. Do rising temperatures matter? Ecology 90:906–912.

Pascual, M., X. Rodo, S. P. Ellner, R. Colwell, and M. J. Bouma. 2000. Cholera dynamics and El Nino-Southern Oscillation. Science 289:1766–1769.

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

Rodo, X., M. A. Pascual, G. Fuchs, and A. S. G. Faruque. 2002. ENSO and cholera: a nonstationary link related to climate change. Proceedings of the National Academy of Sciences (USA) 99:12901–12906.

Rogers, D. J., and S. E. Randolph. 1988. Tsetse flies in Africa: bane or boon? Conservation Biology 2:57–65.

Schmidt, K. A., and R. S. Ostfeld. 2001. Biodiversity and the dilution effect in disease ecology. Ecology 82:609–619.

Smith, K. F., A. P. Dobson, F. E. McKenzie, L. A. Real, D. L. Smith, and M. L. Wilson. 2005. Ecological theory to enhance infectious disease control and public health policy. Frontiers in Ecology 3:29–37.

Turner, C. M. 1999. Antigenic variation in *Trypanosoma brucei* infections: an holistic view. Journal of Cell Science 112:3187–3192.

Ecology, 90(4), 2009, pp. 927–931

Perspectives on climate change impacts on infectious diseases

Sarah E. Randolph[1]

Department of Zoology, University of Oxford, South Parks Road, Oxford OX1 3PS United Kingdom

Introduction

Evidence suggests that climate change is causing shifts in some species distributions. Given the recorded, let alone unrecorded, comings and goings of countless species over the past 450 million years, why should we care? Organisms of all sorts have always redistributed themselves around the globe according to changing abiotic and biotic constraints, with the vast majority failing to survive. It is estimated that less (surely far less) than 0.1% of all species that ever existed are extant today. The reason we care, of course, is that one of those extant species is *Homo sapiens* and some of the shifting species are pathogens and pests that threaten our species directly or indirectly.

Kevin Lafferty brings some much-needed perspective to the rising panic over the supposed impacts of human-induced climate change on the distribution and incidence of infectious diseases (Lafferty 2009). Any infectious disease that responds to environmental conditions, both directly and indirectly, may be affected by climate change. These include a wide range of zoonotic mammalian viruses (e.g., the Hantaviruses, Nipah, Ebola, and many more), cholera and other water-borne agents, and even infections that are exacerbated by physical or mental stress through reduced nutrition or immunity. The potential ramifications are endless. Lafferty (2009), however, justifiably focuses principally on vector-borne diseases (VBDs). Because they are particularly sensitive to changing environmental conditions through the impact of temperature, moisture, and land cover on the demographics of the arthropod vectors, they are viewed as the canary in the mine, acting as an alert to focus our attention on likely threats. Implicit in almost all the literature on this subject is an assumption that environmental change is more likely to strengthen the transmission potential and expand the range, rather than to disrupt the delicate balance between pathogen, vector and host upon which these systems depend. VBDs, however, are no different from other components of global biodiversity that is predicted to be on the verge of catastrophic collapse, the sixth mass extinction (Wilson 1992, Lawton and May 1995). The arthropods that serve pathogens are as vulnerable as those that deliver the anthropocentrically designated "ecosystem services" (Foley et al. 2005).

The Origins and Perpetuation of Alarmism

Two seductive mind-sets have taken hold among scientists and lay people alike. First it is tacitly assumed, and even explicitly stated, that climate change will result only in a worsening of the situation, with expansion of VBDs into higher latitudes and increased incidence. Secondly, past events of this sort are commonly believed

Manuscript received 12 March 2008; revised 21 May 2008; accepted 29 May 2008. Corresponding Editor: K. Wilson. For reprints of this Forum, see footnote 1, p. 901.

[1] E-mail: sarah.randolph@zoo.ox.ac.uk

to be due to climate change to date, adding fuel to the fire of predicted impending doom. These ideas have become widespread and entrenched in both the scientific and popular literature since the repeated publication of a set of visually arresting maps in the late 1990s showing a disproportionate increase in the risk of malaria, for example, in the high northern latitudes (Martens et al. 1995, Martens 1998, Epstein 2000). These were explicitly interpreted as indicating that such infections are likely to spread northward from the tropics as temperatures rise through global warming. As Lafferty emphasizes, however, the biological, process-driven models upon which they were based did not include the generally adverse effects of increased moisture stress alongside higher temperatures. Nor did (can) they incorporate the many socioeconomic forces that have shaped the current distribution of malaria and will continue to do so; i.e., climate is not the only determinant of risk. Furthermore, they were incompletely parameterized, not least in their omission of information on the responses of vector populations to climate change. This necessitated maps of relative change in transmission potential in the assumed absence of any change in vector abundance, rather than maps of absolutely sufficient transmission potential. Pointing out these fundamental methodological flaws, and offering predictions (derived from alternative statistical, pattern-matching methods) of far more restrained shifts in malaria mostly around the edges of the current range (Rogers and Randolph 2000), has done little to shake the pervasive mindsets. Any invasion into new areas, for whatever reason, will expose naïve local populations, potentially causing severe disease that must not be ignored, but this is not on the same global scale as originally mapped by Martens.

These analyses fall squarely within the discipline of ecology. Lafferty's credentials as an ecologist give his measured assessment of this controversy considerable validity. Curiously, virtually none of the authors of these early predictions of VBD emergence, nor their spokespersons (McMichael et al. 1996, Haines and McMichael 1999, Kovats et al. 1999), had any prior expertise in primary research on the ecology of VBDs. Despite a more cautionary tone being adopted subsequently (Kovats et al. 2001), the original simple message was readily embraced by nonscientist commentators, and nowadays many who perpetuate these warnings are experts in the fields of virology, clinical pathology, economics, engineering, climatology, hydrology, and so on, but not ecology, yet feel qualified to write about the impacts of climate change on human health in general and VBDs in particular. Perfectly good papers in these disciplines are commonly embellished by final hand-waving paragraphs warning of unwelcome effects of climate change on pathogen distributions (Gould and Solomon 2008). There is little doubt that reference to climate change sells copy, with some editors doing little to quench the alarmist fires (Stott 2001) however shaky the original analyses (Lindgren and Gustafson 2001, Randolph 2001). Yet anything worth writing requires a proper understanding of the network of extrinsic and intrinsic forces driving the ecology (transmission processes) and epidemiology (observed patterns) of infectious diseases.

The studies reviewed by Lafferty (2009) provide clear evidence that intuitive assertions based on the undeniable sensitivity of VBDs to climate, and therefore climate change, are not a reliable basis for either explaining the past or predicting the future. The mercurial epidemiology of each VBD is the system-specific product of complex, commonly nonlinear, interactions between many disparate environmental factors. These include not only climate but also other abiotic conditions (e.g., land cover) and the physical structure of the environment (e.g., water sources), and furthermore biotic factors such as host abundance and diversity. In general, these will determine the transmission potential of each pathogen, and thus the risk posed to humans. In addition, socioeconomic factors drive human living conditions and behavior that determine the degree of exposure to that risk, and nutritional status and concomitant immunity that determine resistance to infection, so that incidence in the human population may increase or decrease without any change in the strength of the biological transmission cycles. Conversely, any increase in risk may be dealt with more or less easily by adopting avoidance or protective measures. At higher latitudes, such measures are likely to be much more effective against tropical diseases than in the tropics, partly because the force of transmission will be lower along the leading edge of expansion, where the system is up against its environmental limits, and partly because the generally higher standards of living make these measures more achievable. If the purpose of predictions about the future is to guide policy and therefore governmental spending (Huntingford et al. 2007), exaggerated simplistic rhetoric about the universality and uniformity of the impact of climate change on infectious disease risk is morally indefensible if it distracts public health agencies from more effective ameliorative action targeted at the real causes.

Evidence from the Past

Another perspective commonly overlooked is the intrinsic nature of predictions about the future; they are un-testable and therefore, by definition, nonscientific. Instead, many studies have correctly focused on the facts of the past to test hypotheses about likely events in the future. Historical perspectives on malaria in Europe and many other parts of the world clearly indicate the impact of agricultural and public health practices on the waxing and waning of malaria over several centuries (Reiter 2000, 2001, Reiter et al. 2004). Much compelling evidence now exists against the principal role of climate change in driving the more recent emergence of several important VBDs and in favor of other causal factors (Lafferty 2009). A particularly strong line of evidence is

the apparent absence of signals in climate records that match the epidemiological patterns. However strong the argument that climate change could exacerbate transmission potential, if appropriate changes have not occurred they cannot be the cause. This seems to apply to the resurgence of malaria at certain well-documented sites in the East African highlands during the 1980s and 1990s, which was not matched by contemporary trends in temperature, rainfall, vapor pressure, or the number of months suitable for malaria transmission for the same sites (Hay et al. 2002*a*). (Although a subsequent analysis did detect a significant upward trend in temperature [Pascual et al. 2006], claiming superior methods based on longer time series, but outside the period of malaria increase, the temperature records are visibly different over the period in common—compare Hay et al.'s Fig. 2a with Pascual et al.'s Fig. 1a—indicating different data sources.) While the variability of malaria incidence increased, particularly for cycles of one and three years periodicity (i.e., both seasonal and interannual cycles), contemporary temperature and rainfall records show no equivalent change (Rogers et al. 2002). Similarly, the periodicity in incidence of this and another mosquito-borne disease, dengue hemorrhagic fever in Bangkok, is best explained by intrinsic population dynamics, probably driven by host immunity, rather than climate (Hay et al. 2000).

Conversely, clear changes in climate have been documented in many places, but they are not always spatially or temporally appropriate to explain the epidemiological patterns. Across most parts of Europe where tick-borne encephalitis (TBE) virus circulates, temperatures have increased, but not gradually as always portrayed by smoothed curves. Rather, there was a step increase in temperatures in 1989, with no trends either before (back to 1970) or after (Šumilo et al. 2007). This sharp discontinuity can be compared with equally sharp discontinuities in recorded TBE incidence. In Sweden, TBE increased abruptly from 1984, but not, as claimed Lindgren and Gustafson (2001), dependent on an increase in the number of warm spring days, and in fact *before* the rise in mean spring temperatures in 1989 (Randolph 2001). A second step increase in TBE occurred from 2000, without any obvious matching climate signal, but by then cases had appeared in a number of new foci in southern Sweden (Falt et al. 2006), in places predicted to be climatically suitable according to satellite data for 1982–1993 (Randolph 2000). In the three Baltic States, on the other hand, major upsurges in each national mean TBE incidence in 1993 did indeed *follow* the rise in spring temperatures that might have favored TBE virus circulation. Changes in temperature and precipitation, however, were far too uniform across the Baltics to explain the variability in degree (2- to 700-fold) and timing (1990–1998) of the TBE upsurge at finer spatial scales (Šumilo et al. 2007), which appears instead to be the product of a network of environmental and socioeconomic factors, supposedly each operating differentially in time and space (Šumilo et al. 2008*b*).

These studies illustrate the universal problem of basing conclusions on superficial correlations in time between "emergence" of a variety of VBDs and changes in climate that have, after all, formed the ubiquitous backdrop to all events of the past few decades. Multiple assumptions of causal mechanisms are not always supported by fully informed analyses in sufficient spatiotemporal detail. A variety of alternative causes could equally well account for disease emergence, including drug resistance, declining health service provision, reduced vector control, increased wildlife host abundance, and changes in a range of human behavior relevant to exposure to risk (Hay et al. 2002*b*, Patz and Olson 2006). Epidemics of tick-borne Crimean-Congo Hemorrhagic Fever virus in 1944–1945 in Crimea and since 2002 in Turkey, for example, have been attributed to disruption of agricultural activities during military conflicts, allowing habitat change and unusually high densities of transmission hosts such as hares (Hoogstraal 1979, Estrada-Peña et al. 2007). With peace restored, on return to their fields, local people were exposed to increased densities of infected ticks. Furthermore, these same factors could equally well cause the observed declines in incidence of some VBDs, as trends may be rapidly reversed either by chance or through correctly targeted action. For example, the decline in pediatric malaria between 1999 and 2007 at three sites along the Kenyan coast has been tentatively attributed to the increased distribution of insecticide-treated bed nets and/or increased use of alternative antimalarial drugs (Okiro et al. 2007). In eastern Europe, just as visits to tick-infested forests for increased harvest of wild food in response to unemployment, poverty, and new market opportunities apparently helped drive the upsurge in TBE in the 1990s, this same factor may have been instrumental in the sharp decline in TBE in Latvia after 1998. The degree of decline varied spatially depending on previous incidence, suggesting human responses to perceived risk, partly in the form of incidence-dependent increases in vaccination, but also less frequent visits to forests (SKDS 2001, Šumilo et al. 2008*a*).

Contingencies

The upsurge of tick-borne diseases within preexisting endemic regions in central and eastern Europe thus appears to be an unforeseen consequence of the fall of the iron curtain and the end of the cold war, a sort of political global warming. The emergence of VBDs in lands far removed from endemic regions is more commonly recognized as being contingent on economic, commercial, or social events. The most general of these concerns global movements of people and trade goods, happily no longer one and the same. The introduction of the mosquito *Aedes aegypti* to the Americas within water containers on board slave ships from Africa was repeated four centuries later by the dispersal of the

Asian tiger mosquito, *A. albopictus*, from Japan to the United States within water trapped in used car tires (Hawley et al. 1987, Reiter and Sprenger 1987). This still continues today, augmented by trade in other water-carrying goods such as the Asian Lucky Bamboo plants, allowing this mosquito species to have established itself in almost all New World countries, a dozen European countries, parts of West Africa and the Middle East. This has nothing to do with climate change. Many parts of the world are linked by similar climates, potentially hospitable to a range of exotic pests, but remaining isolated until land or seas barriers are breached by chance through a sufficient volume of plane or shipping traffic (Tatem et al. 2006). Global maps of matching climates, linked to sources of pests and high-flow traffic routes, could allow risk to be assessed more systematically (Tatem et al. 2006), but it is doubtful whether such chance events as the introduction of West Nile virus into New York in 1999, most probably by air from Israel (Lanciotti et al. 1999), or of the BTV-8 strain of bluetongue virus into the Netherlands in 2006 from South Africa (Saegerman et al. 2008) could have been fully foreseen and guarded against. In both cases, the viruses found not only a hospitable climate, but a rich supply of competent resident vectors.

A Final Perspective

There are, of course, many other interactions between pathogens, their hosts and the environment that determine the dynamic global patterns of infectious diseases (Lafferty 2009). The complexity within each disease system emphasizes that any expectation of a simple consistent response to climate change, i.e., a universal worsening of the situation, is ill founded. Hitherto, there is no single infectious disease whose increased incidence over recent decades can be reliably attributed to climate change. The often-repeated statistic, that climate change is currently causing approximately 150 000 extra deaths per annum, may be stamped with the authority of the World Health Organization (Campbell-Lendrum et al. 2003), but is, in the opinion of many practicing disease ecologists, inestimable. Furthermore, large as this number is in terms of bereavements, it represents only ~0.15% of all-cause deaths (as a first approximation, assuming a global population of 6.7×10^9 and mean life expectancy of 67 years). Other, more avoidable, causes of premature deaths from infectious diseases deserve more attention than climate change.

There already exist tools to help predict the impact of interacting political, cultural, socioeconomic, environmental, and biological factors on the dynamics of infectious diseases within endemic and newly invaded regions. Geographical information systems (GIS) are not constrained by traditional disciplinary boundaries. They are simply computerized systems for archiving, inter-relating, analysing and displaying any sort of spatially explicit data, which, in skilful hands, can be programmed to explore the full range of multi-factorial causes of changing epidemiology. The same climate surfaces used to predict changing structural environmental conditions and human practices may also be used to drive full biological, process-based models of vector population dynamics and pathogen transmission potential (once they exist). Predictions of changing risk may then be matched to predictions of changing exposure to risk. With current emphases on both cross-disciplinary and "translational" research, and the birth of complex system studies (with which ecologists have long been familiar), now is surely the time to bring epidemiologists, population and climate modelers, GIS practitioners, sociologists, economists, and policy and management practitioners together to tackle this most complex of all complex systems, the changing threat of infectious diseases in a perpetually dynamic world.

Acknowledgments

The author is partially supported by the EU grant GOCE-2003-010284 EDEN; this paper is catalogued by the EDEN Steering Committee as EDEN0090. The contents are the sole responsibility of the author and do not necessarily reflect the views of the European Commission.

Literature Cited

Campbell-Lendrum, D., A. Pruss-Ustun, and C. Corvalan. 2003. How much disease could climate change cause? Pages 133–158 *in* A. J. McMichael, D. Campbell-Lendrum, C. Corvalan, K. L. Ebi, A. K. Githeko, J. S. Scheraga, and A. Woodward, editors. Climate change and health: risks and responses. World Health Organization, Geneva, Switzerland.

Epstein, P. R. 2000. Is global warming harmful to health? Scientific American 283:50–57.

Estrada-Peña, A., Z. Zatansever, A. Gargill, M. Aktas, R. Uzun, O. Ergonul, and F. Jongejan. 2007. Modeling the spatial distribution of Crimean-Congo Haemorrhagic fever outbreak in Turkey. Vector-Borne and Zoonotic Diseases 7: 667–678.

Falt, J., A. Lundgren, R. Alsterlund, B. Carlsson, I. Eliasson, M. Haglund, A. Lundkvist, S. Vene, and B. Settergren. 2006. Tick-borne encephalitis (TBE) in Skåne, southern Sweden: a new TBE endemic region? Scandinavian Journal of Infectious Diseases 38:800–804.

Foley, J. A., et al. 2005. Global consequences of land use. Science 309:570–574.

Gould, E. A., and T. Solomon. 2008. Pathogenic flaviviruses. Lancet 371:500–509.

Haines, A., and A. J. McMichael, editors. 1999. Climate change and human health. Royal Society, London, UK.

Hawley, W. A., P. Reiter, R. S. Copeland, C. B. Pumpuni, and G. B. Craig. 1987. *Aedes albopictus* in North America: probable introduction in used tires from northern Asia. Science 236:1114–1115.

Hay, S. I., J. Cox, D. J. Rogers, S. E. Randolph, D. G. Shanks, S. Stern, M. Myers, and R. W. Snow. 2002*a*. Climate change and the resurgence of malaria in the East African highlands. Nature 415:905–909.

Hay, S. I., M. F. Myers, D. S. Burke, D. W. Vaughn, T. Endy, N. Ananda, G. D. Shanks, R. W. Snow, and D. J. Rogers. 2000. Etiology of interepidemic periods of mosquito-borne disease. Proceedings of the National Academy of Sciences (USA) 97:9335–9339.

Hay, S. I., D. J. Rogers, S. E. Randolph, D. I. Stern, J. Cox, G. D. Shanks, and R. W. Snow. 2002*b*. Hot topic or hot air? Climate change and malaria resurgence in African highlands. Trends in Parasitology 18:530–534.

Hoogstraal, H. 1979. The epidemiology of tick borne Crimean-Congo hemorrhagic fever in Asia, Europe and Africa. Journal of Medical Entomology 15:307–417.

Huntingford, C., D. Heming, J. H. C. Gash, N. Gedney, and P. A. Nuttall. 2007. Impact of climate change on health: what is required of climate modellers? Transactions of the Royal Society of Tropical Medicine and Hygiene 101:97–103.

Kovats, R. S., D. Campbell-Lendrum, A. J. McMichael, A. Woodward, and J. S. H. Cox. 2001. Early effects of climate change: do they include changes in vector-borne disease? Philosophical Transactions of the Royal Society of London B 356:1057–1068.

Kovats, R. S., A. Haines, R. Stanwell-Smith, P. Martens, and R. Bertollini. 1999. Climate change and human health in Europe. British Medical Journal 318:1682–1685.

Lafferty, K. D. 2009. The ecology of climate change and infectious diseases. Ecology 90:888–900.

Lanciotti, R. S., et al. 1999. Origin of the West Nile virus responsible for an outbreak of encephalitis in the northeastern United States. Science 286:2333–2337.

Lawton, J. H., and R. M. May. 1995. Extinction rates. Oxford University Press, Oxford, UK.

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

Martens, P. 1998. Health and climate change: modelling the impacts of global warming and ozone depletion. Earthscan, London, UK.

Martens, P., L. W. Niessen, J. Rotmans, T. H. Jetten, and A. J. McMichael. 1995. Potential impact of global climate change on malaria risk. Environmental Health Perspectives 103:458–464.

McMichael, A. J., A. Haines, R. Slooff, and S. Kovats, editors. 1996. Climate change and human health. World Health Organization, Geneva, Switzerland.

Okiro, E. A., S. I. Hay, P. W. Gikandi, S. K. Sharif, A. M. Noor, N. Peshu, K. Marsh, and R. W. Snow. 2007. The decline in paediatric malaria admissions on the coast of Kenya. Malaria Journal 6:151.

Pascual, M., J. A. Ahumada, L. F. Chaves, X. Rodo, and M. Bouma. 2006. Malaria resurgence in the East African highlands: temperature trends revisited. Proceedings of the National Academy of Sciences (USA) 103:5829–5834.

Patz, J., and S. H. Olson. 2006. Malaria risk and temperature: influences from global climate change and local land use practices. Proceedings of the National Academy of Sciences (USA) 103:5635–5636.

Randolph, S. E. 2000. Ticks and tick-borne disease systems in space and from space. Advances in Parasitology 47:217–243.

Randolph, S. E. 2001. Tick-borne encephalitis in Europe. Lancet 358:1731–1732.

Reiter, P. 2000. From Shakespeare to Defoe: malaria in England in the little ice age. Emerging Infectious Diseases 6:1–11.

Reiter, P. 2001. Climate change and mosquito-borne disease. Environmental Health Perspectives 109:141–161.

Reiter, P., and D. Sprenger. 1987. The used tire trade: a mechanism for the worldwide dispersal of container breeding mosquitoes. Journal of the American Mosquito Control Association 3:494–501.

Reiter, P., C. J. Thomas, P. M. Atkinson, S. I. Hay, S. E. Randolph, D. J. Rogers, D. G. Shanks, R. W. Snow, and A. Spielman. 2004. Global warming and malaria: a call for accuracy. Lancet Infectious Diseases 4:323–324.

Rogers, D. J., and S. E. Randolph. 2000. The global spread of malaria in a future, warmer world. Science 289:1763–1766.

Rogers, D. J., S. E. Randolph, R. W. Snow, and S. I. Hay. 2002. Satellite imagery in the study and forecast of malaria. Nature 415:710–715.

Saegerman, C., D. Berkvens, and P. S. Mellor. 2008. Bluetongue epidemiology in the European Union. Emerging Infectious Diseases 14:539–544.

SKDS. 2001. Investigation into the factors hindering immunisations of the population against diphtheria and tick-borne encephalitis. [In Latvian.] National Public Health Agency SKDS, Riga, Latvia.

Stott, P. 2001. Climate change: the new bioterroism. Editorial. Lancet 358:1657.

Šumilo, D., L. Asokliene, T. Avsic-Zupanc, A. Bormane, V. Vasilenko, I. Lucenko, I. Golovljova, and S. E. Randolph. 2008*a*. Behavioural responses to perceived risk of tick-borne encephalitis: vaccination and avoidance in the Baltics and Slovenia. Vaccine 26:2580–2588.

Šumilo, D., L. Asokliene, A. Bormane, V. Vasilenko, I. Golovljova, and S. E. Randolph. 2007. Climate change cannot explain the upsurge of tick-borne encephalitis in the Baltics. PLoS ONE 2:e500.

Šumilo, D., A. Bormane, L. Asokliene, V. Vasilenko, I. Golovljova, T. Avsic-Zupanc, Z. Hubalek, and S. E. Randolph. 2008*b*. Socio-economic factors in the differential upsurge of tick-borne encephalitis in Central and Eastern Europe. Reviews in Medical Virology 18:81–95.

Tatem, A. J., S. I. Hay, and D. J. Rogers. 2006. Global traffic and disease vector dispersal. Proceedings of the National Academy of Sciences (USA) 103:6242–6247.

Wilson, E. O. 1992. The diversity of life. Harvard University Press, Cambridge, Massachusetts, USA.