

The Ecology of Climate Change and Infectious Diseases

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# CONCEPTS & SYNTHESIS

EMPHASIZING NEW IDEAS TO STIMULATE RESEARCH IN ECOLOGY

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## The ecology of climate change and infectious diseases

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**Abstract.** The projected global increase in the distribution and prevalence of infectious diseases with climate change suggests a pending societal crisis. The subject is increasingly attracting the attention of health professionals and climate-change scientists, particularly with respect to malaria and other vector-transmitted human diseases. The result has been the emergence of a crisis discipline, reminiscent of the early phases of conservation biology. Latitudinal, altitudinal, seasonal, and interannual associations between climate and disease along with historical and experimental evidence suggest that climate, along with many other factors, can affect infectious diseases in a nonlinear fashion. However, although the globe is significantly warmer than it was a century ago, there is little evidence that climate change has already favored infectious diseases. While initial projections suggested dramatic future increases in the geographic range of infectious diseases, recent models predict range shifts in disease distributions, with little net increase in area. Many factors can affect infectious disease, and some may overshadow the effects of climate.

**Key words:** *climate; ENSO; global warming; malaria; vector; yellow fever.*

### INTRODUCTION

In balmy medieval times, exports from English vintners economically threatened competing French wineries (Pfister 1988). Although English wine country seems a quaint historical oddity, a recent headline cheered: “Global Warming Spawns Wine in U.K.: Changing Climate Brings New Crops to the Land of Rain and Clouds!” Different grape varieties have specific physical requirements and a string of warm summers in southern England has again cracked open the climate window to produce a drinkable Chardonnay, Pinot Noir, and Pinot Meunier.

Is there a catch? Like grapes, mosquitoes and the infectious diseases they transmit like it warm. The warm period that favored medieval English vintners was also malarious. For instance, Chaucer’s (1385) *Canterbury Tales* tells of bouts of deadly fever, indicating endemic malaria. It is easy, then, to imagine how climate change might return infectious diseases like malaria to England. The British Chief Medical Officer predicts that by 2050 the climate of England will again be suitable for endemic malaria (Department of Health 2002). And not just

England: the conventional wisdom is that global climate change will result in an expansion of tropical diseases, particularly vector-transmitted diseases, throughout temperate areas (Epstein 2000). Examples include schistosomiasis (bilharzia or snail fever), onchocerciasis (river blindness), dengue fever, lymphatic filariasis (elephantiasis), African trypanosomiasis (sleeping sickness), leishmaniasis, American trypanosomiasis (Chagas disease), yellow fever, and many less common mosquito and tick-transmitted diseases of humans. Obviously, nonhuman hosts are also subject to infectious diseases, and the concern about climate change and disease extends to agriculture, conservation biology, and fisheries.

The extent and generality of the prediction that climate change will increase infectious disease is an important topic for ecologists to consider. I start this review by introducing how temperature drives important biological processes. I then consider how climate might affect spatial (latitude and altitude) and temporal (seasonal, interannual, historical) patterns in disease. Given that the climate has warmed during the last century, I ask whether current warming has affected infectious disease. Finally, I review models that project how climate change might affect infectious diseases in the future. I conclude that while climate has affected and will continue to affect habitat suitability for infectious diseases, climate change seems more likely to shift than to expand the geographic

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ranges of infectious diseases. Furthermore, many other factors affect the distribution of infectious disease, dampening the proposed role of climate. Finally, in parallel with predictions for biodiversity loss, shifts in climate suitability might actually reduce the geographic distribution of some infectious diseases.

#### THERMAL PHYSIOLOGY

Warm temperatures speed up biochemical reactions (catabolism and anabolism) that expend energy, permitting increased activity, growth, development, and reproduction. However, faster metabolism comes at a cost because it requires higher food consumption rates to maintain a positive energy balance. This can decrease survivorship as temperature increases, particularly for non-feeding free-living stages (e.g., eggs, cysts, larvae; King and Monis 2007). For instance, the survival of *Cryptosporidium parvum* cysts declines with prolonged exposure to warm temperatures because increased metabolism drains the energy reserves of cysts (Fayer et al. 1998). For these reasons, the relationship between temperature and an organism's performance (e.g., growth, fitness, lifespan, reproductive output) should follow a convex function. Climate varies on multiple time scales (daily, seasonally, annually, and longer) and to buffer against such changes, many ectotherms, including most disease vectors, use behavioral thermoregulation. In addition, molecular mechanisms, such as heat-shock proteins, help other proteins keep their shape across a range of temperatures (Feder and Hofmann 1999). Furthermore, organisms might adapt to changing climates (Bradshaw and Holzapfel 2001). For instance, the mosquito *Wyeomyia smithii* uses a shortening day-length cue to enter diapause in advance of cooling weather; at higher latitudes, where temperature is cooler, the shift comes earlier (at a longer day length; Bradshaw and Holzapfel 2001). Pathogens can also locally adapt to their environment. The lineage Ia West Nile Virus strain from New York requires warmer temperatures for transmission than does the lineage II strain from South Africa (Reisen et al. 2006). So, while all species have lower and upper temperature limits, organisms often can deal with substantial variation in climate.

For cases where temperature extremes set boundaries on species distributions, global warming might alter the range (in altitude or latitude) of suitable habitat for a species. As a result, species should be closer to their physiological limits near the edges of their distribution and this is where effects of climate change should be most apparent. Global warming should initially expand the area of potential habitat for species that presently thrive in very warm places. In addition, polar and high altitude species (marmots, polar bears, penguins and their parasites) are likely to experience a net decrease in habitat suitability with global warming. However, for most species, global warming should result in a poleward shift in both the upper and lower ranges of habitat suitability. For example, while climate change may have

made Sweden more suitable for western-type tick-borne encephalitis, a parallel degradation of climatic suitability south of Sweden corresponds to a predicted Europe-wide reduction in the range of TBE (Randolph and Rogers 2000). Range limits are not the only aspect of infectious disease affected by temperature. Climate may affect the severity of disease. Most notably, climate affects the length of the transmission season for malaria. As the climate increases in temperature and humidity malaria transmission can increase from zero to epidemic, hypoendemic, mesoendemic, hyperendemic, and holoendemic (Hay et al. 2004).

Indirect effects may complicate the physiological response of a species to climate change. For instance, a pollinator may shift in distribution directly in response to climate and indirectly in response to the physiological response of flowering plants to climate (Memmott et al. 2007). Because infectious diseases, like pollinators, are parts of complex networks of species, (Lafferty et al. 2006), each with its own thermal tolerance, indirect effects of climate on disease distribution are likely. For this reason, much of the research on the effects of climate change on infectious diseases concerns the thermal tolerance of insect vectors such as mosquitoes and ticks.

#### EVIDENCE FOR EFFECTS OF CLIMATE IN INFECTIOUS DISEASES

##### *Spatial patterns*

The tendency for higher species diversity in the tropics is one of the clearest patterns in biogeography. Higher species diversity at low latitudes could result from warmer temperatures due to energy (warmth/sunlight) increasing the raw material on which speciation can act, physiological tolerances biased toward warm climates, or faster rates of speciation where high temperatures lead to shorter generation times (Currie et al. 2004). Because most host taxa decrease in diversity with latitude (MacArthur 1972), a decline in parasite diversity with latitude might occur if parasite diversity depends on host diversity (Hechinger and Lafferty 2005). An exception that proves the rule is that the diversity of helminths in marine mammals does not decline with latitude, presumably because marine mammal diversity is low in the tropics (Rohde 1982). While these patterns suggest that communities of parasites should track communities of hosts, scientists are often interested in the parasite community of a single host species, particularly humans. The diversity of infectious diseases of humans is higher in countries near the equator than in countries at higher latitude (Guernier et al. 2004). Is this a result of climate? The diversity of all disease categories increases with the maximum range of precipitation, and most disease categories increase with monthly temperature range; however, independent of latitude, there is surprisingly little effect of mean annual temperature or precipitation on the diversity of human infectious diseases (Guernier et al. 2004).

The higher diversity of important infectious diseases of humans in the tropics does not appear to be a result of higher rates of evolution in the tropics. Wolfe et al. (2007) found that infectious diseases of humans (excluding helminth parasites) were equally likely to have originated in tropical or temperate regions. The early humans that migrated out of Africa and into temperate latitudes initially left several infectious diseases behind: only one of the 10 major tropical diseases, cholera, followed into temperate latitudes. However, 11 000 years ago, several infectious diseases of newly domesticated temperate animals jumped to humans and most of these novel infectious diseases subsequently spread into the tropics (Wolfe et al. 2007).

The high diversity of infectious diseases in the tropics could result from a high diversity of vectors. For instance, mosquito diversity declines with latitude (Schafer and Lundstrom 2001) and this should affect the diversity of mosquito-transmitted diseases. Likewise, the diversity of fleas, which are vectors for bacterial diseases (e.g., plague, murine typhus), declines with altitude and latitude (Marshall 1981). Blood parasites are less prevalent in birds from the Arctic than in birds from lower latitudes (Piersma 1997), perhaps due to differences in vector diversity. The inability of human tropical diseases to spread from the tropics to temperate regions may be due to the higher fraction of tropical diseases that have a specific vector (80% tropical vs. 13% temperate) and/or a wild animal reservoir (80% tropical vs. 20% temperate; Wolfe et al. 2007). In primates, the diversity of vector-borne diseases is higher in the tropics, though this pattern does not apply to viruses or parasitic worms (Nunn et al. 2005). Thus, ecological understanding of vectors and reservoirs may be the key to predicting the effect of climate change on infectious diseases.

In parallel with broad patterns of diversity, many infectious diseases show clines in prevalence with climate. The observation that malaria is more prevalent in lowland areas (Lindsay and Martens 1998) may be the oldest observed spatial pattern in infectious diseases. For instance, in Tanzania, the annual number of mosquito bites per person drops precipitously at high elevations because the cool climate at high altitude impairs mosquito development rates (Bodker et al. 2003). In addition, cooler temperatures at high altitudes slow the development of infectious agents so that they cannot complete their life cycles. As a result, in Africa, human settlements at high altitude are relatively free of malaria (Lindsay and Martens 1998). Similarly, endemic forest birds in Hawaii are able to escape introduced avian malaria only at cool, high-altitude refuges (van Riper et al. 2003).

The present restriction of malaria to the tropics suggests a strong effect of climate on this disease. While climate does affect malaria transmission, other factors probably enforce the current distribution. Most notable is a strong increase in per-capita gross national product with latitude. This results in both greater surveillance

and increased funds for control and treatment in temperate areas. Today, malarious countries have GDPs one fifth that of non-malarious countries (Gallup and Sachs 2001), suggesting that economic forces, particularly environmental destruction, have pushed malaria out of temperate zones. Malaria is harder to control under the climatic conditions where it is holoendemic (transmitted year-round) and malaria might depress economic development in a positive feedback loop (Bruce-Chwatt and de Zulueta 1980). In other words, tropical climate might increase infectious diseases such as malaria, which then depress economic growth required for disease control (Sachs and Malaney 2002).

### Seasonality

As early as Homer's Iliad (800–900 BC), people were aware of seasonal patterns in malaria (harvest fever) that might relate to climate. Because temperature and precipitation change with the season, seasonal variability in disease transmission suggests an effect of climate on diseases. Hence, we might expect that climate change is most likely to affect diseases with seasonal patterns (Hay et al. 1998; Fig. 1). The incidence of black spot (a trematode metacercaria) in salmon is highest in the warmer days of the summer season (Cairns et al. 2005), consistent with the observation that trematodes shed more cercarial stages from snail vectors when the water is warm (Poulin 2006). Similarly, endemic cholera occurs in the season when water temperature is high (Lipp et al. 2002).

Not all seasonal patterns suggest an increase in disease with global warming. Some infectious diseases decline during warm, wet periods. For instance, meningitis peaks in the dry season (Moore 1992) and houseflies infected with the *Entomophthora muscae* fungus are more common during cool periods of the year because the fungus dies at higher temperatures (Mullens et al. 1987). A strong link between winter and flu in temperate climates has resulted in numerous hypotheses, including crowding during cold weather, physiological stress due to cold, indoor heating, and atmospheric dispersion during cold fronts (Lofgren et al. 2007). Recent experimental evidence (see *Experiments*) and outbreaks in H5N1 influenza virus in birds following temperature drops suggest a direct positive effect of cold temperature on the spread of influenza (Liu et al. 2007).

Seasonality in disease does not necessarily indicate an effect of climate on disease. For instance, seasonal variation corresponds with day length, which is important for many biological processes, but climate change will not alter day length (Fig. 1). Other patterns, such as the spring rise in egg production and transmission of trichostrongyle nematodes in domestic animals (Field et al. 1960), relate to the seasonality of host reproduction, not climate. The seasonal pattern of common human diseases (measles, pertussis, chickenpox) may occur independent of climate because the start of the school year aggregates susceptible children (Stone et al. 2007).

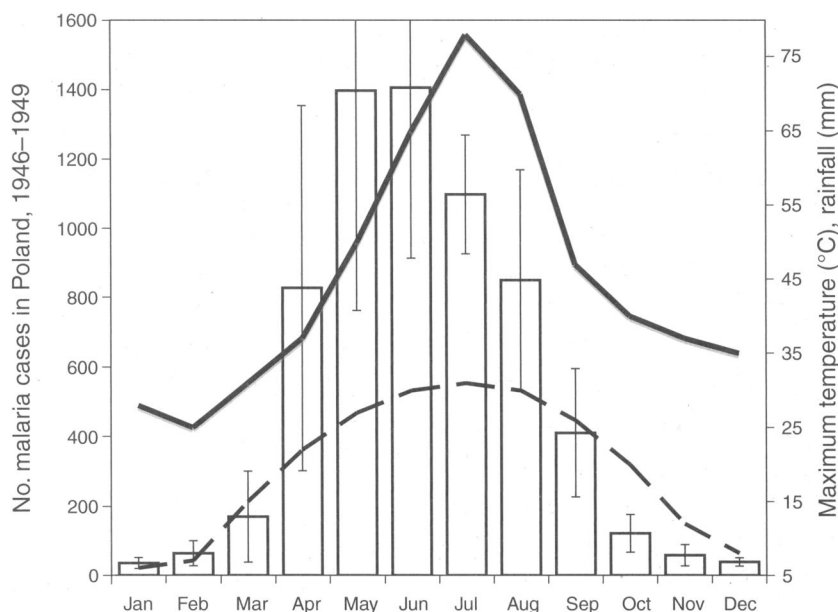


FIG. 1. Seasonality in the number of cases of malaria (bars; mean  $\pm$  SD). The histogram is superimposed on plots of seasonal variation in maximum temperature (solid line) and rainfall (dashed line). In the four years following World War II, Poland regularly suffered thousands of cases of malaria per year with a clear spring–summer peak (Reiter 2001). The log number of malaria cases is almost a perfect fit to day length ( $R^2 = 0.97$ ). Long-term (1961–1990) average measures of temperature (mean, minimum, maximum) and rainfall also increase with day length, but with a one-month time lag, so that climate lags behind malaria cases. If climate directly affected malaria transmission, one would expect human cases to lag behind the optimal temperature for transmission (because of time needed for development of the parasite in humans and mosquitoes), not the reverse.

Time lags between climate and species abundances create statistical challenges for investigating seasonal effects on infectious disease. For instance, conditions that provide good habitat for mosquito larvae do not instantly lead to infectious disease transmission because mosquito and pathogen development take time. Researchers may test a variety of lags to determine the best fit to the data. For example, Tong and Hu (2001) found the best match between climate and Ross River virus epidemics in Cairns, Australia occurred with a two-month lag for rainfall and a five-month lag for humidity. Teklehaimanot et al. (2004) explored how the fit between malaria epidemics and climate varied considerably with the lag chosen, and found that the lag with the best fit was different for different climate variables. While lag fitting may be necessary for revealing patterns, testing many lags also increases the chance of finding spurious patterns. For this reason, statistical models optimized with a variety of measures should either be corrected for multiple comparisons or, even better, be subject to independent validation (Peterson 2003) before concluding that climate affects species' distributions.

#### *Interannual variation*

Like the weather, epidemics can vary from year to year. Several authors have linked epidemics of mosquito-borne diseases to the strong interannual variation in weather associated with the Southern Oscillation, or El

Niño (Hay et al. 2000). For instance, malaria cases increase after El Niño events in Venezuela (Bouma and Dye 1997). Most interannual associations with disease relate to precipitation. The aquatic larvae of mosquitoes require aquatic habitats and several studies show a positive association between heavy rain and subsequent outbreaks of mosquito-transmitted diseases (Landesman et al. 2007). In particular, precipitation may drive much of the observed variation in malaria in Africa (Small et al. 2003). However, the effect is complex; in areas with little standing water, drought may eliminate mosquito habitat, while in areas with flowing water (which is unsuitable for mosquitoes), drought may create isolated pools suitable for breeding (Landesman et al. 2007). In the eastern United States, container-breeding mosquitoes transmit West Nile virus, and outbreaks follow the expected pattern, increasing after wet winters. However, in the western United States, wetland-breeding mosquitoes transmit West Nile virus and outbreaks follow drought years (Landesman et al. 2007). Why the opposite patterns? Mosquitoes are susceptible to a range of vertebrate and invertebrate predators found in permanent water bodies. While natural and artificial containers (important in the east) generally lack predators, wetlands (important in the west) normally contain predators. Periods of drought can eliminate predators from wetlands, resulting in safe havens for mosquitoes. For these reasons, the effect of precipitation on mosquito populations may be strongly context dependent.

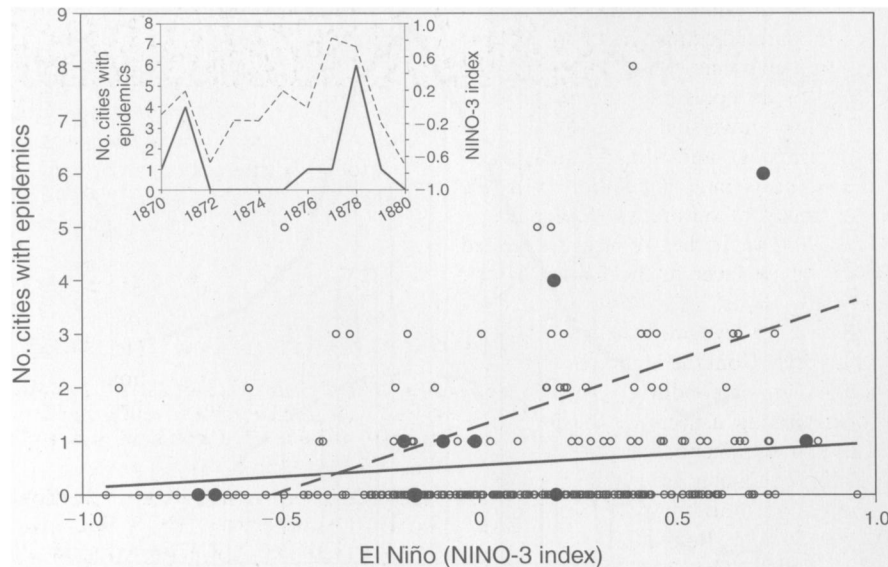


FIG. 2. Yellow fever outbreaks in the United States and El Niño. The inset shows the number of cities reporting epidemics from 1870 to 1880 (solid line) and the NINO-3 index (dashed line). In the main figure, large solid circles and the dashed regression line show the number of cities experiencing epidemics vs. the NINO-3 index from 1870 to 1880. Open circles and solid regression line show the number of cities experiencing epidemics vs. the NINO-3 index from 1688 to 1905. The NINO-3 index goes from  $-1$  to  $1$ , with positive values indicating El Niño years.

### History

Historical records of disease can provide long time series for investigating interannual associations between climate and disease. In 1878, a deadly yellow fever epidemic hit several cities in the United States after a large El Niño event. Because precipitation favors the container-breeding yellow fever vector, *Aedes aegypti*, these mosquitoes probably thrived under the unusually warm, wet El Niño conditions (Diaz and McCabe 1999). Furthermore, between 1870 and 1880, the number of cities affected by a yellow fever epidemic in a particular year increased with the global El Niño index (explaining 34% of the variation in epidemic frequency; Fig. 2 inset and large solid circles). Diaz and McCabe (1999) noted that seven of the nine major yellow fever outbreaks ( $>1000$  deaths) in the United States during the 19th century coincided with an El Niño event.

While this seems like very solid evidence for an effect of climate on yellow fever (and, by extension, an effect of climate change on the future of yellow fever), one cannot establish a statistical linkage without knowledge of the frequency of El Niño in years without epidemics. To determine the proportion of the variation in yellow fever epidemics attributable to El Niño, I analyzed data on historical yellow fever epidemics in all U.S. cities between 1668 and the last United States yellow fever epidemic in 1905 (Reiter 2001). For the strength of El Niño, I used the estimated year's ( $t$ ) and preceding year's ( $t-1$ ) cold-season NINO3 index (Mann et al. 2000). I included date as a covariate. I compared the climate in the years of Diaz and McCabe's (1999) nine deadly U.S. epidemics with non-epidemic years as controls. For the

non-epidemic controls, I considered only dates at least three years distant from a large epidemic. I ran a similar analysis for the number of cities experiencing an epidemic in a particular year, and separate analyses for epidemics in three cities: New Orleans, Philadelphia, and Charleston, South Carolina. Finally, I plotted the association between El Niño and the number of cities experiencing an epidemic from 1668 to 1905.

The analyses confirmed that the nine deadly yellow fever epidemics were more likely to follow an El Niño event ( $t-1$ ) in comparison to years not linked to an epidemic ( $\chi^2 = 4.0$ ,  $df = 1$ ,  $P = 0.047$ ), with El Niño explaining 4% of annual variation in deadly epidemics. The frequency of epidemics also increased slightly over time ( $\chi^2 = 6.1$ ,  $df = 1$ ,  $P = 0.014$ ), perhaps because of population growth. After considering the effect of El Niño on the number of cities experiencing an epidemic, a similar pattern arose, except that, in this case, it was the El Niño of the present year ( $t$ ) ( $T \text{ ratio}_{2,235} = 2.46$ ,  $P = 0.015$ ), not the prior year ( $t-1$ ), that correlated with epidemics, explaining about 2% of the variation in the frequency of deadly epidemics (Fig. 2, small open circles). Again, the frequency of epidemics increased slightly over time ( $T \text{ ratio}_{2,235} = 2.48$ ,  $P = 0.014$ ). For separate analyses of New Orleans, Philadelphia, and Charleston, there was no indication that El Niño led to epidemics. In summary, while some comparisons indicated that climate was statistically associated with historical yellow fever epidemics in the United States, El Niño did not explain a substantial proportion in the variance in epidemics.

Other factors besides El Niño likely affected yellow fever outbreaks in the United States. Susceptible hosts build up during non-epidemic years, accumulating enough susceptibles for an epidemic after three years (Hay et al. 2000). The movement of infected hosts (people or other primates) and the abundance of previously unexposed hosts in a population probably contributed to the timing of outbreaks (Reiter 2001). Furthermore, after 1905, public health measures ended the transmission of yellow fever in the United States, despite continuing El Niños, a pattern repeated in history for other diseases in developed nations. The near elimination of yellow fever from the United States under apparently favorable climatic conditions is an example of one of the most striking aspects of the long-term historical record of human infectious diseases.

Hay et al. (2000) conducted a similar historical retrospective analysis of monthly data on periodic outbreaks of dengue fever in Bangkok, Thailand and malaria in Kericho, Kenya. The data from Kenya are particularly interesting given the relative lack of control efforts in that region (permitting a clearer evaluation of the role of climate). A clear seasonal signature and a three-year periodicity emerged in both data sets, but this interannual variation in incidence among years did not correspond to changes in rainfall, temperature, or El Niño events.

Malaria in England also has an instructive history, particularly with respect to understanding the relative importance of various environmental factors on epidemiology. While malaria appears to have been common during the medieval warm period (1200) in Britain, and outbreaks may have corresponded to unusually warm years, malaria did not disappear during the little ice age beginning in the mid-1560s (Bruce-Chwatt and de Zulueta 1980). Declines in malaria deaths correspond to land-use changes more than to climate. Ironically, as malaria declined, the climate warmed and got slightly wetter. Underscoring the old saying: "malaria flees before the plough" (Najera-Morondo 1991), malaria primarily decreased from 1840 to 1910 with the increase in wetland destruction, and, to a lesser extent, with the size of the cattle population (cattle might draw mosquito bites from humans); in comparison, warm years and rainfall only marginally increased malaria (Kuhn et al. 2003).

While malaria decreased as the globe warmed in the northern hemisphere, some indications suggest malaria increased in Africa. Was this because recent climate change increased habitat suitability for malaria in Africa? A retrospective analysis on a causal link between climate change and malaria in Africa from 1911 to 1995 suggests that most areas in Africa did not change in suitability for malaria and that those areas where suitability for malaria increased (Mozambique) were offset by areas where suitability for malaria decreased (e.g., the Sahel) Small et al. (2003). Therefore, other factors besides climate change may have led to the recent increases in malaria in Africa.

### Experiments

It is possible to experimentally investigate the effects of climate variables (primarily temperature) on vital rates of some infectious diseases and their vectors. For instance, schistosomiasis is a tropical disease caused by trematode parasites. Humans become infected at water contact sites when infective cercarial stages leave the snail and penetrate the host's skin. Several authors have held infected snails at different water temperatures and counted the cercariae that emerge. Poulin (2006) conducted a meta-analysis of how trematode cercarial shedding rates changed with temperature, finding strong evidence that the production of cercariae increases dramatically with temperature. Similarly, the development rate of angiostrongyloid nematodes (lung worms) increases with warmer temperature (Lv et al. 2006). However, only if increases in development rates and productivity of parasites can outpace increases in mortality rates will warmer temperatures lead to net increases in transmission.

Experiments have indicated how temperature may determine whether a potential pathogen will or will not cause disease. Mass mortalities in Mediterranean gorgonians correspond with warmer than average temperatures and with bacterial infections (Romano et al. 2000). Experiments find that increasing the water temperature in aquaria to the level experienced by gorgonians during die offs leads to increased tissue mortality in infected and uninfected gorgonians, and that tissue damage is faster when bacteria are present, indicating that temperature both stresses gorgonians and improves conditions for pathogenic bacteria (Bally and Garrabou 2007). Such temperature-related impacts of bacterial pathogens on marine invertebrates seem to derive from a higher temperature optima for the bacteria than for the host (Harvell et al. 2002). Another example of temperature-dependent pathogenicity derives from Strongyloid nematodes, which are intestinal parasites of humans and other mammals. These worms have a plastic life cycle; larvae (found in contaminated soil) can either adopt an infectious or free-living mode of life. Laboratory experiments with *Strongyloides ratti* demonstrate that the temperature experienced by newly hatched larvae is a key determinant in this plastic life history; cool temperatures induce infectious larvae while warm temperatures induce free-living worms (Minato et al. 2008). Such a strategy seems remarkably adaptive for the parasite because higher metabolism at warmer temperatures would more rapidly use the energy reserves of an infectious larva.

Recent experimental work suggests that climate might directly affect influenza epidemics. By manipulating temperature and humidity, Lowen et al. (2007) found that cold, dry conditions favor transmission of influenza from infected to naïve guinea pigs, an effect not related to host immune response. Although the mechanisms are not yet clear, these experiments seem to

suggest that global warming could directly reduce influenza epidemics.

An advantage of experiments is that they can manipulate variables beyond normal ranges. A particularly insightful example concerns blowflies. Blowfly maggots suck blood from nestlings then detach and become subject to ambient temperatures in the nest. Dawson et al. (2005) noted that the activity and number of maggots in tree swallow nests increases linearly with ambient temperature. This positive association between temperature and blowfly abundance provides a mechanism by which climate change could reduce bird populations. However, instead of extrapolating beyond the observed natural variation in temperature, the authors conducted a notable field experiment. They placed heating pads in some Tree Swallow nest boxes. In the nests heated above the natural range of temperature variation, the blowflies did poorly, suggesting that sufficiently high increases in temperature could actually decrease parasitism, a prediction that would not have been possible without such an experiment.

Although it is not tractable to manipulate air temperature in the field across large areas, some power plants discharge thermal effluent into lakes and streams. Marcogliese (2001) reviewed studies that found thermal effluent allows fish parasites to complete their life cycles in cold months but impairs transmission during the warmest months. In addition, fish hosts may live shorter lives, decreasing the extent to which parasites may accumulate in warm sites. Sometimes, declines in host biodiversity at very warm sites lead to a reduction in parasite diversity.

The effects of warming on infectious disease will depend on the extent to which climate becomes wetter or more arid. Manipulations of precipitation are difficult, but Chase and Knight (2003) were able to investigate experimentally the effect of rainfall on mosquitoes using wetland mesocosms. The number of mosquitoes that emerged from previously dried mesocosms was 20 times higher than in consistently inundated mesocosms, which had developed a high biomass of mosquito predators. This experiment helps explain why, in the western United States, St. Louis encephalitis virus (Shaman et al. 2002) and West Nile virus (Epstein 2001b) sometimes increase after droughts.

#### EXISTING EFFECTS OF CLIMATE CHANGE

Because recent climate appears to be warmer than does past climate, we may already be experiencing changes in infectious diseases. Around 3.3% of the earth's surface changed from one climate category to another between 1951 and 2000. For the categorical shifts in climate that have occurred, the trend has been for a loss of polar and boreal climates and an increase in arid climates (Becker et al. 2006). In the Arctic, conditions may have improved for some disease vectors. For instance, lung worm of muskoxen can now develop in their intermediate host slugs in just one year, instead

of the two years historically required, suggesting that this infectious disease in the Arctic may increase in severity (Kutz et al. 2005).

We know more about shifts in the distribution of animals and plants than we do about infectious diseases. Each decade, species ranges have shifted 6 km toward the poles (and away from the equator) and 6 m in higher in altitude; the results of 41% of studies suggest that climate change has altered species distributions (62% found climate alters phenology, e.g., flowering date; Parmesan and Yohe 2003). However, a strict economic assessment (such as advocated by the Intergovernmental Panel on Climate Change) finds that climate is the primary determinant of few species ranges and that the main factor responsible for shifts in distribution is probably habitat destruction (Parmesan and Yohe 2003).

Recent increases in infectious diseases may or may not indicate an effect of climate change. Habitat alteration, invasive species, agriculture, travel and migration, drug and pesticide resistance, malnutrition, urban heat islands, population density, health service, the distribution of wealth, and education, all of which are in flux, may affect diseases. For instance, in the last three decades, as global ocean temperatures have warmed, there has been an increase in the reports of diseases for six of nine studied marine taxa; of those six taxa with increasing reports of diseases, warming was a likely factor for corals and sea turtles, while different factors, such as indirect effects of fishing, may explain the other increases (Ward and Lafferty 2004).

Increases in tick-borne encephalitis correlate significantly with increased temperature (Lindgren et al. 2000), but the correlation is weak and the increases in temperature actually followed the increases in disease, making a causal link suspect (Randolph and Rogers 2000). Furthermore, in the Baltics, a sudden jump in climate suitability for TBE in 1989 did not result in a landscape-wide increase in incidence (Sumilo et al. 2007). Statistical analyses considering a wide-range of climatic and socioeconomic data find that the best predictor of changes in TBE from 1970 to 2005 is poverty; presumably economic collapse in some areas led to a decrease in vaccinations, an increase in hosts for ticks, and an increased need for humans to forage in tick-infected areas (Sumilo et al. 2008).

Malaria in highland regions since the 1980s has been linked to global warming (Epstein et al. 1998, Epstein 2001a). Altitudinal expansion of malaria exposes populations with little resistance, leading to substantial mortality in humans (Lindsay and Martens 1998). A widely cited example is an increase in malaria in Rwanda in the warm, wet year of 1987 (Loevinsohn 1994). Analysis of a longer time series suggests that climate has warmed at four highlands sites to temperatures suitable for increased mosquito abundance (Pascual et al. 2006). This is not necessarily a distributional change; some have argued that none of the "new" reports are above the historical altitudinal limits for malaria (Reiter 2001).



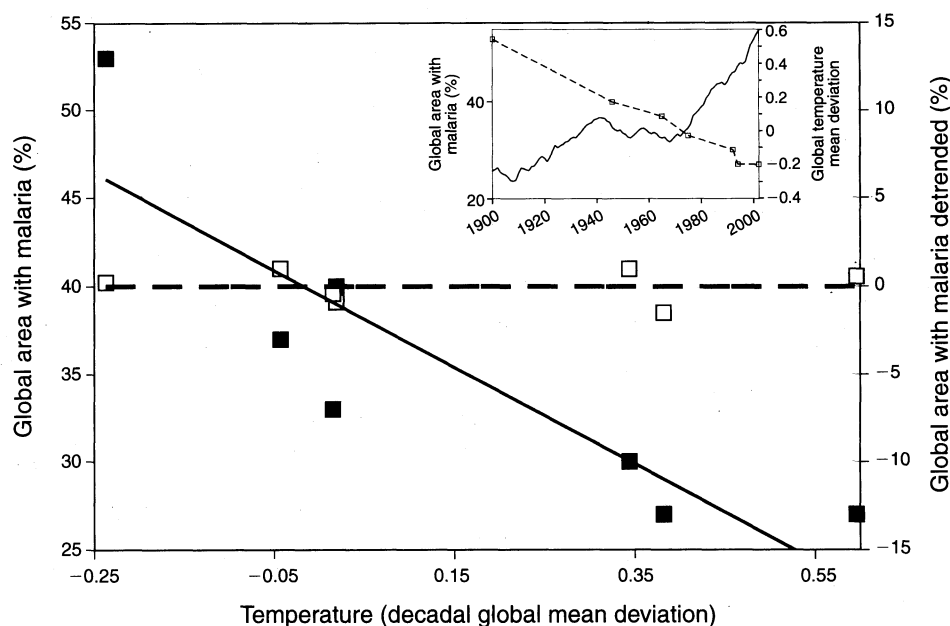


FIG. 3. A century of malaria and climate: 1900–2000. The inset shows global mean temperature (represented as a deviation, as reported from the U.S. National Climate Data Center Global Historical Climatology Network Land Surface Data) increases since 1900 while the percentage of the globe with malaria transmission decreases (data from Hay et al. [2004]). The main figure shows the data from the inset as a scatter plot (solid squares, solid line) and after detrending the decline in malaria (open squares, dashed line).

For most examples of climate-induced increases in highland malaria, logical alternative explanations exist. Control efforts, clearing for agriculture (Lindblade et al. 2000), drug resistance (Ndymugenyi and Magnussen 2004), and changes in surveillance (Reiter 2001) also correspond with the changes in malaria, making it difficult to determine the contribution of climate change. Season, epidemiology and interannual climate variation all contribute to variation in the number of malaria cases reported at highland sites, with climate explaining 12–63% of the variation in malaria, suggesting that, at some high altitude locations, recent small increases in temperature may explain some of the increase in malaria (Zhou et al. 2004).

It is easy to overlook places where infectious diseases may have declined with climate change. For instance, at the time malaria was emerging in highland regions, less attention was paid to reductions in malaria prevalence in the Sahel. Here, the brief rainy season creates a window for seasonal transmission of malaria, but an increasing frequency of drought, perhaps associated with current climate change, corresponded with a sharp reduction in malaria prevalence (Mouchet et al. 1996). Plotting published estimates of the percentage of the globe's land mass affected by malaria during the last century (Hay et al. 2004) against yearly climate records shows that as the globe warmed, malaria shrank toward the tropics (Fig. 3). This presumably occurred because warming in the last century coincided with major land-use changes, including efforts to reduce the burden of malaria in developed countries. Malaria has declined appreciably in wealthy, temperate zones and relatively

less in poor, tropical locations (Hay et al. 2004). One way to isolate the effect of climate is to detrend the data (thereby removing the temporal trend of malaria control) and look for residual associations between climate and infectious diseases (Kuhn et al. 2003). The detrended global malaria data in Fig. 3 has a slope of 0, indicating no residual effect of temperature on the historical area of the globe affected by malaria (Fig. 3).

Since the 1970s, malaria has rebounded in many areas (see Plate 1), and present increases in global warming are a possible explanation for this change (Epstein et al. 1998). However, recent events other than climate change are alternative causes. Migration and population growth can increase the potential for epidemics. Some types of economic development, particularly roads and dams, can increase habitat for mosquitoes. In other cases, economic upheavals that undermined public health systems (e.g., the 1990s post-USSR economic decline in Armenia, Azerbaijan, Tajikistan, and Turkmenistan [Sabatinelli 1998]) caused some local rebounds in malaria. Finally, the famous evolution of resistance of mosquitoes to DDT and malaria to anti-malarial drugs are potential reasons for malaria rebound (Reiter 2001).

#### FUTURE EFFECTS OF CLIMATE CHANGE

##### *Process-based models*

Process-based (also known as mechanistic or biological) models estimate how habitat suitability for a species changes with the environment. Parameterizing process-based models requires knowing relationships between climate variables and vital rates. Most process-based

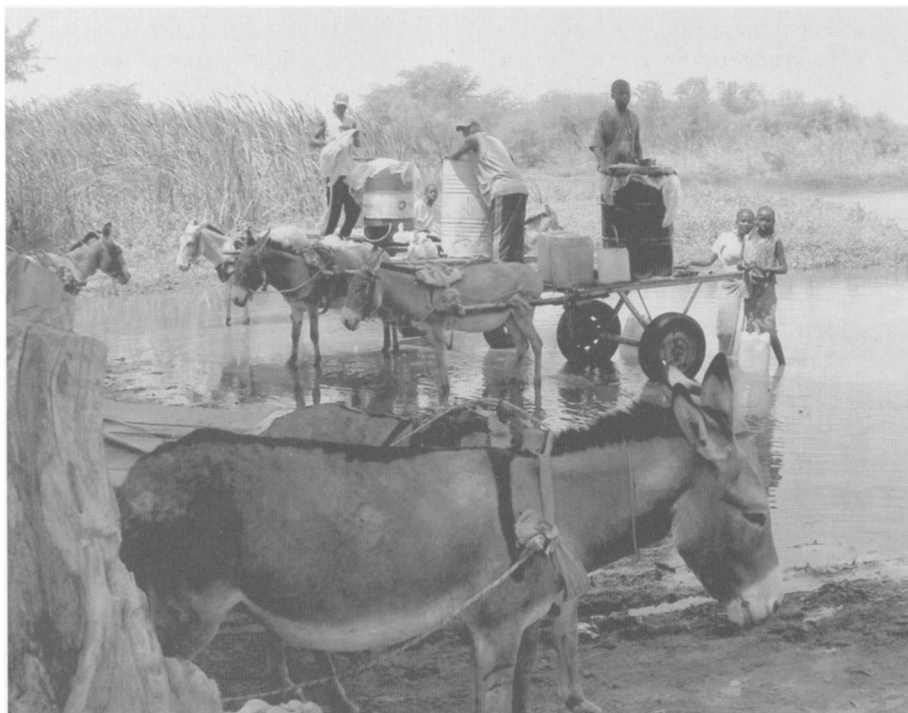


PLATE 1. Senegalese gather water and do laundry in the Senegal River at Richard Toll. This is one of the most intense transmission sites know for schistosomiasis (a blood fluke transmitted by aquatic snails). In addition, nearly everyone gets malaria during the wet season. Climate change in this region is likely to increase temperatures and reduce precipitation, impacting local agriculture, while potentially decreasing transmission of schistosomiasis and malaria. But climate is not the major issue affecting disease at Richard Toll. In 1986, damming of the Senegal River for irrigation led to spectacular increases in habitat for intermediate host snails and mosquito vectors. These changes led to an explosion of disease among an immigrant population drawn to work the new sugar cane fields. Photo credit: K. D. Lafferty.

models of infectious diseases are for vector-transmitted diseases and they consider the likelihood that the habitat will be suitable for perennial, seasonal, or epidemic transmission (Craig et al. 1999). The more sophisticated process-based models consider  $R_0$ , or the average number of infected individuals that result from the entry of a single infected host into a population of susceptible hosts (Rogers and Randolph 2006). If  $R_0$  is greater than one, the infectious disease can spread through the population. Because it is not always possible to estimate  $R_0$ , components of  $R_0$ , such as vectorial capacity (Garrett-Jones 1964), or "transmission potential," are sometimes used instead. As input, the models use mathematical relationships between climate variables (usually temperature), the vital rates of vectors (larval development rate, biting rate, adult survivorship) and, sometimes, the vital rates of pathogens (development rate; Garrett-Jones 1964).

For instance, because metabolism increases with temperature, mosquitoes must feed more to maintain positive energy balance, and increased biting rates can increase the chance of transmission of mosquito-vectored diseases. The time needed for the malaria organism to develop inside the mosquito decreases with temperature but a simultaneous increase in mosquito mortality leads to a convex-shaped association between

temperature and the proportion of infected mosquitoes that can transmit disease. If the temperature is too cold ( $<18^\circ\text{C}$ ), the parasite cannot develop, whereas if the temperature is too warm ( $>32^\circ\text{C}$ ), infected mosquitoes die before the infection is transmissible. For these reasons, the better process-based models indicate a convex relationship between climate and habitat suitability for some infectious diseases.

When parameterized with climate projections, early process-based models captured public attention by predicting a 60% increase in malaria by 2020 (Martens 1999). Comparing the ratio of transmission potential before and after climate projections resulted in maps indicating the extent to which climate change would improve conditions for malaria. These maps suggested very large increases in transmission potential in some areas (Epstein 2000). However, increases in vectorial capacity or transmission potential may not indicate actual transmission if  $R_0$  remains less than 1; in other words, an increase in suitability will not result in malaria if the new climate is still unsuitable for transmission (Rogers and Randolph 2006).

Even if process-based models could accurately define habitat suitability, they do not project actual transmission because the fundamental niche is always larger than realized niche. Barriers to dispersal and biotic interac-

tions can exclude species from parts of the fundamental niche. For instance, in Memphis, the apparent replacement of the dengue/yellow fever vector *Aedes aegypti* by the newly invasive *Aedes albopictus* suggests that competitive exclusion may have occurred (O'Meara et al. 1995). Furthermore, projected increases in malaria transmission potential in climate change scenarios might not result in epidemics if the kinds of human activities that led to the historical decline of malaria in temperate regions (wetlands destruction, vector control, chemotherapy) prevent malaria from re-emerging.

To assess the accuracy of a process-based model requires comparing predictions with actual data. For instance, before using a process-based model to project effects of climate change on dengue fever transmission, Jetten and Focks (1997) confirmed that their model corresponded with actual data from five cities. The MARA/ARMA (mapping malaria risk in Africa) process-based models of habitat suitability correspond to interpolated maps of current observations relatively well, but the correspondence breaks down at fine scales (Craig et al. 1999). Tanser et al. (2003) validated their process-based model with independent observations. Their "threshold" model of malaria transmission in Africa matched 63% of the spatial data and 90–96% of the temporal data, though this validation is controversial (Reiter et al. 2004). A goal for future maps of malaria incidence, such as the Malaria Atlas Project (Hay and Snow 2007) is to provide a means to validate process-based models to allow estimates of the uncertainty of malaria projections.

Recent process-based models predict decreases in habitat suitability offsetting increases in habitat suitability. For instance, process-based projections for malaria in India show a shift in suitability for malaria, with some higher altitude areas becoming favorable for malaria and some central areas becoming unfavorable (Bhattacharya et al. 2006). Some process-based models show little change in suitability for infectious diseases (Tanser et al. 2003, Urashima et al. 2003, Thomas et al. 2004) and several even show decreases (de Gruijl et al. 2003, Peterson 2003, Peterson and Shaw 2003).

#### Statistical models

Other attempts to predict the biological effects of climate change make use of climate mapping, or niche models. These statistical (or pattern matching) models relate field observations of a species (presence, presence-absence, or abundance) to environmental factors. This approach dates back to Johnston's (1924) correlational model of the climatic requirements of an invasive cactus in Australia. Statistical models differ from process-based models in that they do not assume known functional relationships between vital rates and environmental variables, allowing a wider range of environmental variables. The availability of remotely sensed data and spatial datasets allows complex analyses at global scales.

Statistical models estimate habitat suitability, or the fundamental niche. To approximate the fundamental niche, the statistical model often only includes positive records of disease occurrence. For instance, Peterson and Shaw (2003) modeled the current and projected distribution of leishmaniasis in Brazil, using a niche model of vectors of cutaneous leishmaniasis, three sandflies (*Lutzomyia* spp.). A genetic algorithm helped determine associations between environmental data and records of sand flies. The authors withheld half of the records for 100 validations of the projected map, choosing a model that correctly predicted all the presences in the validation set (no omission error) and minimized the prediction area (thereby minimizing commission errors under the no omission constraint). When applied to climate projections, the predicted habitat suitability of the sandflies expands to the higher southern latitudes, but retracts substantially from the lower northern latitudes, resulting in an overall reduction in the potential geographic range of each species. For malaria, apparent habitat suitability also increases at higher latitudes and contracts at lower latitudes. As a result, models estimate that by 2050, falciparum malaria will gain 23 million human hosts in previously uninfected locations, but lose 25 million human hosts in areas no longer suitable for transmission, the net result being little change in the total number of people exposed to malaria (Rogers and Randolph 2000).

Like process-based models, statistical models have weaknesses. For one, most consider simple linear relationships between climate and species distributions. As described earlier, linear projections can lead to substantial error if the actual relationship is non-linear and the projection extends beyond the range of the measured independent variable. Furthermore, using multiple independent variables with multiple possible time lags can lead to over fitting. Finally, data quality will always constrain statistical models. Although the quality of spatial climate data has improved, there is need for improved mapping of disease incidence in lesser-developed nations (Hay and Snow 2007).

Few statistical models yet include potentially important non-climate variables (limiting resources, biotic interactions, physical disturbance, dispersal barriers, human intervention) that might lead to absences of infectious diseases in areas with suitable climate (Guisan and Thuiller 2005). Statistical models that also include negative records may yield insight into the realized niche, which provides a better estimate of actual transmission. Such models could include a wide range of non-climate variables (control, predation, competition) that influence disease distributions. Future statistical models might attempt to fit observed data to the nonlinear functions known from process-based models. In addition, they could include non-climate variables, including control, but minimize over fitting through validation with independent data sets. In all cases, it is helpful when statistical models explicitly present the

unexplained variance and the errors of the estimates reported so that the confidence in projections is clear.

#### CONCLUSION

Because temperature and precipitation affect physiology, climate can affect species distributions. Climate and infectious diseases sometimes covary geographically and over time, suggesting that climate change should lead to changes in the geographic distribution of infectious diseases and their vectors. In some places, climate change will likely lead to increases in some infectious diseases. For instance, recent evidence indicates an association between thermal stress and disease in corals (Lafferty et al. 2004). Many insect vectors prefer the warm, wet conditions predicted under some climate-change scenarios. This alarms public health officials who rightly worry that climate change will broadly increase important infectious diseases such as malaria. Predictions of tropical diseases spreading into wealthy temperate nations have understandably captured the public's attention. This developing societal concern is also a challenging ecological research question.

As for most aspects of ecology, the link between climate and infectious disease is complex, requiring careful study and rigorous evaluation. There are several reasons climate change may not always lead to a net increase in the geographic distribution infectious diseases. Firstly, most species, including infectious diseases, have upper and lower limits to their temperature tolerance. This means that changes in climate should often lead to shifts, not expansions, in habitat suitability. Furthermore, while a reduction in habitat suitability should reduce a species' range, an increase in habitat suitability does not necessarily result in an increase in geographic distribution. This is because other factors besides climate, such as barriers to dispersal, competition, and predation, affect the realized niche. For infectious diseases that depend on other species for vectoring or as intermediate hosts, habitat degradation can prevent transmission even if climate is suitable. In particular, because disease control efforts have successfully reduced or eliminated the transmission of previously widespread infectious diseases from developed countries, human activities will prevent the expansion of some infectious diseases even if climate becomes more suitable. For these reasons, it seems plausible that the geographic distribution of some infectious diseases may actually experience a net decline with climate change. While this is the reverse of the conventional wisdom, it is consistent with the increasingly accepted view that climate change will reduce biodiversity. Infectious diseases, as important and sensitive components of biodiversity, may be some of the earliest casualties. This does not mean that we should welcome climate change. Reductions in disease that result from the loss of vectors and intermediate hosts will likely correspond to the loss of biodiversity in general. Furthermore, changes to climate that reduce infectious disease (e.g., drought, very

hot weather) will likely have their own set of impacts. Finally, while some areas may see reductions in infectious disease, populations in areas where infectious disease will expand have genuine cause for concern.

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