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Climate Change and Infectious Diseases: From Evidence to a Predictive Framework

Sonia Altizer,1* Richard S. Ostfeld,2 Pieter T. J. Johnson,3 Susan Kutz,4 C. Drew Harvell5

Scientists have long predicted large-scale responses of infectious diseases to climate change, giving rise to a polarizing debate, especially concerning human pathogens for which socioeconomic drivers and control measures can limit the detection of climate-mediated changes. Climate change has already increased the occurrence of diseases in some natural and agricultural systems, but in many cases, outcomes depend on the form of climate change and details of the host-pathogen system. In this review, we highlight research progress and gaps that have emerged during the past decade and develop a predictive framework that integrates knowledge from ecophysiology and community ecology with modeling approaches. Future work must continue to anticipate and monitor pathogen biodiversity and disease trends in natural ecosystems and identify opportunities to mitigate the impacts of climate-driven disease emergence.

The life cycles and transmission of many infectious agents—including those causing disease in humans, agricultural systems, and free-living animals and plants—are inextricably tied to climate (1, 2). Over the past decade, climate warming has already caused profound and often complex changes in the prevalence or severity of some infectious diseases (Fig. 1) (2–5). For human diseases, vector-control, antimicrobial treatments, and infrastructural changes can dampen or mask climate effects. Wildlife and plant diseases are generally less influenced by these control measures, making the climate signal easier to detect (4). For example, although the effects of climate warming on the dynamics of human malaria are debated, climate warming is consistently shown to increase the intensity and/or latitudinal and altitudinal range of avian malaria in wild birds (6, 7).

Predicting the consequences of climate change for infectious disease severity and distributions remains a persistent challenge surrounded by much controversy, particularly for vector-borne infections of humans [boxes S1 and S2 (8)]. Work using climate-based envelope models has predicted that modest climate-induced range expansions of human malaria in some areas will be offset by range contractions in other locations (9). An alternative approach, based on mechanistic models of physiological and demographic processes of vectors and pathogens (10), predicts large geographic range expansions of human malaria into higher latitudes (11). Both approaches have their limitations (2), and the challenge remains to accurately capture the contributions of multiple, interacting, and often nonlinear underlying responses of host, pathogen, and vector to climate. This challenge is further exacerbated by variation in the climate responses among host-pathogen systems arising from different life history characteristics and thermal niches (12).

A decade ago, Harvell et al. (1) reviewed the potential for infectious diseases to increase with climate warming. Since then, the frequency of studies examining climate-disease interactions has continued to increase (Fig. 2), producing clear evidence that changes in mean temperature or climate variability can alter disease risk. Some of the best examples of climate responses of infectious diseases to date are from ectothermic hosts and from parasites with environmental transmission stages that can persist outside the host (Fig. 1). Indeed, first principles suggest that the rates of replication, development, and transmission of these pathogens should depend more strongly on temperature relative to other host-pathogen interactions. The next challenges require integrating theoretical, observational, and experimental approaches to better predict the direction and magnitude of changes in disease risk. Identifying the contribution of other environmental variables, such as precipitation, humidity, and climate variability remains a challenge (13, 14).

Here, we review the individual, community, and landscape-level mechanisms behind climate-induced changes in infectious disease risk and illustrate how a quantitative, ecophysiological framework can predict the response of different host-pathogen relations to climate warming. We mainly focus on changes in temperature, which have been more thoroughly explored both empirically and theoretically, relative to other environmental variables. We consider impacts of climate change on human diseases and on pathogens affecting species of conservation or economic concern, including agroecosystems [box S3 (8)]. A crucial need remains for long-term ecological studies that examine the consequences of climate-disease interactions for entire communities and ecosystems, as well as for efforts that couple effective disease forecasting models with mitigation and solutions.

Ecophysiology of Host-Pathogen Interactions

More than a century of research has firmly established that temperature and other climatic variables strongly affect the physiology and demography of free-living and parasitic species [e.g., (15)], with effects on behavior, development, fecundity, and mortality (16). Because these effects can be nonlinear and sometimes conflicting, such as warmer temperatures accelerating invertebrate development but reducing life span, a central challenge has been to identify the net outcomes for fitness (1). For infectious diseases, this challenge is compounded by the interactions between at least two species—a host and a pathogen—and often vectors or intermediate hosts, which make the cumulative influence of climate on disease outcomes elusive [e.g. (17, 18)].

Immune defenses are physiological processes crucial for predicting changes in disease dynamics. Warmer temperatures can increase immune enzyme activity and bacterial resistance for insects, such as the cricket Gryllus texensis (19). Positive effects of temperature on parasite growth and replication, however, might outweigh greater immune function of the host. In gorgonian corals, for example, warmer temperatures increase cellular and humoral defenses (20), but because coral pathogens also replicate faster under these conditions, disease outbreaks have coincided with warmer sea temperatures in the Caribbean (Fig. 1) (4, 5). Warmer temperatures also can lower host immunity; for example, melanization and phagocytic cell activity in mosquitoes are depressed at higher temperatures (21). In addition, increased climate variability can interfere with host immunity, as illustrated by decreased frog resistance to the chytrid fungus Batrachochytrium dendrobatidis (Bd) in response to temperature fluctuations (14). Even though Bd grows best in culture at cooler temperatures, which suggests that warming should reduce disease, incorporating variability-induced changes in host resistance suggests a more complex relationship between climate change and Bd-induced amphibian declines (22). These issues are important for predicting the immunological efficiency of ectotherms outside of their typical climate envelope.

One promising approach for predicting how host-pathogen interactions respond to climate...
warming involves infusing epidemiological models with relations derived from the metabolic theory of ecology (MTE). This approach circumvents the need for detailed species-specific development and survival parameters by using established relations between metabolism, ambient temperature, and body size to predict responses to climate warming (23). One breakthrough study (12) used MTE coupled with traditional host-parasite transmission models to examine how changes in seasonal and annual temperature affected the basic reproduction number ($R_0$) of strongyloid nematodes with direct life cycles and transmission stages that are shed into the environment. By casting $R_0$ in terms of temperature-induced tradeoffs between parasite development and mortality, this approach facilitated both general predictions about how infection patterns change with warming and, when parameterized for Ostertagia gruehneri, a nematode of caribou and reindeer (Fig. 1), specific projections that corresponded with the observed temperature dependence of parasite stages. Moreover, this model predicted a shift from one to two peaks in nematode transmission each year under warming conditions (Fig. 3C), a result consistent with field observations (12, 24).

In some cases, ecophysiological approaches must consider multiple host species and parasite developmental stages that could show differential sensitivity to warming. Such differential responses can complicate prediction of net effects, especially for ectothermic hosts with more pronounced responses to temperature. For instance, because both infectivity of a trematode parasite (Ribeiroia ondatrae) and defenses of an amphibian host (Pseudacris regilla) increase with temperature, maximal pathology (limb malformations) (Fig. 1) occurs at intermediate temperatures (25).

Other work showed that the virulence of both a coral fungus (Aspergillus sydowi) and protozoan (Aplanochytrium sp.) increased with temperature, probably because pathogen development rate continued to increase in a temperature range where coral defenses were less potent (26). Thus, the ideal approach will be an iterative one that combines metabolic and epidemiological modeling to predict general responses and to identify knowledge gaps, followed by application of models to specific host-pathogen interactions.

Community Ecology, Biodiversity, and Climate Change

Host-pathogen interactions are embedded in diverse communities, with climate change likely leading to the loss of some host-pathogen interactions and the gain of novel species pairings. In some cases, pathogen extinction and the loss of endemic parasites could follow from climate change, potentially reducing disease or conversely releasing more pathogenic organisms from competition. In other cases, multiple pathogens can put entire host communities at risk of extinction. Although ecosystems of low biodiversity, such as occur in polar regions, can be particularly sensitive to emerging parasitic diseases (27), most knowledge of community-wide responses stems from tropical marine systems. For example, the wider Caribbean region is a “disease hot spot” characterized by the rapid, warming-induced emergence of multiple new pathogens that have caused precipitous coral declines with ecosystem-wide repercussions (28, 29). Impacts of climate-induced changes in disease can be especially large when the host is a dominant or keystone species. For example, near extinction of the once-dominant, herbivorous abalone (genus Haliotis) by warming-driven rickettsial disease caused pervasive community shifts across multiple trophic levels (5). Similarly, seagrass (Zostera marina) declines caused by infection with the protist Labyrinthula zosterae, which correlates positively with warming, have degraded nursery habitats for fish and migratory waterfowl and caused the extinction of the eelgrass limpet (30).

Microbial communities, which are often part of the extended phenotype of host defenses, are also likely to respond to climate changes. For instance, warming sea-surface temperatures in coral reefs can inhibit the growth of antibiotic-producing bacteria, sometimes causing microbial communities to shift from mutualistic to pathogenic (31). In agroecosystems, higher temperatures can suppress entomopathogenic fungi and antibiotic production by bacterial mutualists in plants (32). Warming also underlies bacterial shifts from endosymbiotic...
to lytic within host amoebas that live in human nasal passages, increasing the potential risk of respiratory disease (33). Thus, effects of warmer temperatures on the diversity and function of commensal or mutualist microbes could promote pathogen growth and pest outbreaks.

From a broader perspective, biodiversity loss is a well-established consequence of climate change (16, 34) and can have its own impact on infectious diseases. For many diseases of humans, wildlife, and plants, biodiversity loss at local or regional scales can increase rates of pathogen transmission (35–37). This pattern can result from several mechanisms, including the loss of the dilution effect (36). For example, lower parasite diversity could allow more pathogenic species to proliferate when endemic and competing parasites are lost from a system (36). Climate warming can also weaken biotic regulation of disease vectors by inhibiting their predators (38) and competitors (39). Interactions between biodiversity and infectious disease underscore the need to put climate-disease interactions into the broader context of other forms of global change, such as land-use change and habitat loss, when extending predictions from focused host-pathogen interactions to larger spatial and taxonomic scales.

**Shifts in Behavior, Movement, and Phenology of Hosts and Parasites**

Changes in climate are already affecting the phenology of interactions between plants and pollinators, predators and prey, and plants and herbivores (16). Climate-induced shifts in phenology and species movements (40) will likely affect disease dynamics. Many species are already moving toward higher elevations or latitudes (41), and an open question is whether these shifts could disrupt established interactions or bring novel groups of hosts and pathogens into contact (42). For instance, the range expansion of the Asian tiger mosquito (*Aedes albopictus*) across Europe and the Americas has created the potential for novel viral diseases such as Chikungunya to invade (10); this pathogen is already expanding in geographic range, and a recent outbreak in Europe emphasizes the need for surveillance and preparedness. Along eastern North America, warming sea temperatures and changes in host resistance facilitated a northward shift of two oyster diseases into previously unexposed populations (5).

Migratory species in particular can be sensitive to climate change (41), with the routes and timing of some species’ migrations already shifting with climate warming (16). Long-distance migrations can lower parasite transmission by allowing hosts to escape pathogens that accumulate in the environment or by strenuous journeys that dull sick animals (43). In some cases, milder winters can allow previously migratory host populations to persist year-round in temperate regions (44); this residency fosters the build-up of environmental transmission stages, and mild winters further enhance parasite over-winter survival (2). A case study of monarch butterflies (*Danaus plexippus*) and the protozoan parasite *Ophyrocystis elektroscirrha* (Fig. 1) provides support for climate-warming shifts in migration and disease. Monarchs typically leave their northern breeding grounds in early fall and fly to Mexican wintering sites. Milder winters, combined with increased planting of exotic host plants, now allow monarch populations to breed year-round in parts of the United States (45). Relative to migratory monarchs, winter-breeding monarchs suffer from higher rates of infection (43). Similarly, migration is considered an important parasite avoidance strategy for barren-ground caribou (24), but the loss of sea ice with climate warming will likely inhibit migrations and prevent them from seasonally escaping parasites (46). Thus, diminishing migration behaviors among animals that use seasonal habitats can increase the transmission of infectious diseases.

Changes in the timing of vector life stages and feeding behavior can also arise from interactions between climate and photoperiod. For several tick-borne infections (Fig. 1), pathogens are sequentially transmitted from infected vertebrate hosts to naïve larval tick vectors, and from infected nymphal ticks to naïve vertebrate hosts. Asynchrony in the seasonal activity of larval and nymphal ticks can delay transmission and select for less virulent strains of the Lyme bacterium *Borrelia burgdorferi* (47), whereas synchrony allows for more rapid transmission and the persistence of virulent strains. In the case of tick-borne encephalitis (TBE), viral transmission occurs directly between cofeeding ticks; thus, viral maintenance requires synchronous larval and nymphal feeding (48). Because synchrony of larval and nymphal ticks characterizes milder winter climates, climate change could increase tick synchrony and the transmission and virulence of several tick-borne infections.

Changes in the timing of shedding or development of environmental transmission stages could result from climate warming. Some parasites could experience earlier hatching, exposure to hosts earlier in the season, and encounters with earlier (and often more sensitive) life stages of hosts. For example, a long-term data set of lake plankton showed that warming shifted fungal prevalence patterns in diatom hosts from acute epidemics to chronic persistence, in part because of faster transmission and more widespread host population suppression under warmer temperatures (49). In contrast, Brown and Rohani (50) argued for the opposite outcome with respect to avian influenza (AI) in reservoir bird hosts. Climate-driven mismatch in the timing of bird migration and their prey resources (e.g., horseshoe crab eggs) amplified variability in epidemiological outcomes: Although mismatch increased the likelihood of AI extinction, infection prevalence and spillover potential both increased in cases where the virus persisted.

Plasticity in parasite traits could allow parasites with environmental transmission stages to
respond more rapidly to climate warming. For example, arrested development (hypobiosis) of the nematode *O. gruehneri* within its caribou host is a plastic trait more commonly expressed in areas with harsher winters as compared with milder climates (51). This arrested state prevents wasted reproductive effort for the parasites, because eggs produced in late summer in colder regions are unlikely to develop to infective-stage larvae by fall. Ultimately, plasticity in life history traits could speed parasite responses to changing environments and allow parasites to deal with climate instabilities (e.g., a series of severe winters interspersed by mild), relative to the case where selection must act on genetically variable traits (52). For example, if climate warming extends the transmission season for *O. gruehneri* on tundra, a rapid decrease in the frequency of nematode hypobiosis could shorten the life cycle and increase infection rates.

**Consequences for Conservation and Human Health**

Climate change is already contributing to species extinctions, both directly and through interactions with infectious disease (53). Roughly one-third of all coral species and the sustainability of coral reef ecosystems are threatened by human activities, including climate warming and infectious diseases (5). In contrast to tropical marine systems, the Arctic is a less diverse and minimally redundant system that is warming at least twice as fast as the global average (54) and simultaneously experiencing drastic landscape changes from an expanding human footprint. Altered transmission dynamics of parasites, poleward range expansion of hosts and parasites, and disease emergence coincident with climate warming or extremes have all been reported in the Arctic (27, 55). Together, these phenomena are altering host-parasite dynamics and causing endemic Arctic species—unable to compete or adapt rapidly enough—to decline (56). Changes in wildlife health can also compromise the livelihoods and health of indigenous people who depend on wildlife for food and cultural activities (57).

In humans, exposure to diarrheal diseases has been linked to warmer temperatures and heavy rainfall (58). Human infections of cholera, typically acquired through ingestion of contaminated water (in developing countries) or undercooked seafood (in the developed world), affect millions of people annually with a high case-fatality rate. Coastal *Vibrio* infections are associated with zooplankton blooms, warmer water, and severe storms (3). For example, in the Baltic Sea, long-term warming and temperature anomalies have been linked to increased disease from *Vibrio vulnificus*, which was first reported in 1994 along the German coast after an unusually warm summer (3). Long-term sea surface warming can increase the geographic range, concentration, and seasonal duration of *Vibrio* infections, as seen in coastal Chile, Israel, and the U.S. Pacific Northwest. Modeling approaches indicate that *Vibrio* illnesses from the Baltic region could increase nearly twofold for every 1°C increase in annual maximum water temperature (3).

Human mosquito-borne diseases, such as malaria and dengue fever, are frequently proposed...
as cases where vector and disease expansion
into the temperate zone could follow from cli-
mate warming (59). However, some researchers
have argued that ranges will shift with warming,
rather than expand, and that the best predictors
of infection risk are economic and social fac-
tors, especially poverty (17, 60). Controversy
has also arisen over which climatic variables are
most important in delimiting the distributions
of these diseases [boxes S1 and S2 (8)]. Detecting
impacts of climate change on human vector-borne
diseases remains difficult, in part, because active
mitigations, such as vector-control, antimicrobials,
and improved infrastructure can complicate de-
tection of a climate signal. Several unresolved
issues include identifying conditions under which
climate warming will cause range expansions ver-
sus contractions, understanding the impact of in-
creasing variability in precipitation, and determining
the additional economic costs associated with in-
creased disease risk caused by warming.

Ultimately, the societal implications of climate-
driven shifts in diseases of humans, crops, and
natural systems will demand solutions and mit-
igation, including early-warning programs. Re-
cently, a forecasting system linking global coupled
ocean-atmosphere climate models to malaria risk in Botswana allowed anomalously high risk to be predicted and anticipatory mitigations to be initi-
ated (61). Forecasting is well-established in crop
disease management and leads to improved timing of pesticide application and de-
ployment of planting strategies to lower disease risk [box S3 (8)]. Modeling efforts to better predict
crop loss events are also tied to improved insur-
ance returns against losses (2). Similarly, accu-
rate forecasting programs for coral bleaching have become a mainstay of marine climate resilience programs (62) and are leading to the development
of coral disease—forecasting algorithms (63). App-
propriate management actions under outbreak con-
ditions include reef closures to reduce stress and
transmission, culling of diseased parts of some
colonies, and increased surveillance (64). In the
ocean, efforts are also under way to increase the resilience of marine ecosystems to disease, including developing no-fishing zones and reducing land-based
pollution that can introduce new pathogens (5).

Outlook and Future Challenges
Climate change will continue to limit the trans-
mission of some pathogens and create opportunities
for others. To improve predictions and responses we
need to deepen our understanding of mechanistic
factors. Although the initial climatic drivers to be
expected should be temperature variables (both
mean and variability), because the data are avail-
able and we understand the mechanisms at work,
future work must concurrently explore the effects
of precipitation, relative humidity, and extreme
events. In particular, models are needed that com-
bine the principles of ecophysiology and MTE (23)
with epidemiological response variables, such as
$R_0$ or outbreak size, and that are designed to
accommodate distinct pathogen types (e.g., vector-
borne, directly transmitted, or complex life cycle)
and host types (ectotherm versus endotherm) (72).
These models should be applied, by using climate-
change projections, to evaluate how broad classes
of pathogens might respond to climate change.
Building from this foundation, the next step is to
extend such general models to specific patho-
gens, especially poverty (17, 60). Forward pro-
bands directly transmitted, or complex life cycle)
ments include identifying conditions under which
corals have multiple levels of adaptation to intense
by thermal stress that could also affect
resistance to pathogens, including symbiotic
shuffling of both algae and bacteria, and natural
selection against thermally intolerant individuals
(65). In oysters (Crassostrea virginica), warming
might have contributed to increased resistance
to the protozoan multinucleated sphere X (MSX)
disease (66), but climate variability might also
slow the evolution of oyster resistance (67). In cases
where increased rates of transmission follow from
warming, selection could favor higher pathogen
virulence, although examples are now unknown.

A persistent challenge involves the ability
to detect changes in disease risk with climate
across different systems. In the oceans, for exam-
ple, impacts of disease on sessile hosts like corals,
abalone, and oysters are readily apparent, and
for terrestrial systems, clear impacts are seen for
plant diseases and some wildlife-helminth inter-
actions. But for highly mobile species and many
human diseases, detecting signals of climate change
remains problematic. For these less tractable sys-
tems, long-term ecological studies that examine
the past distributions of pathogens, important
hosts, and severity of diseases are indispensable.
Permanent repositories of intact physical speci-
mens, as well as their DNA, can provide records
of diversity that will be critical resources as new
methodologies become available (68, 69). More-
over, new technologies can detect variability in
physiological processes and gene expression and
can improve climate projections from global
circulation models. Sophisticated experimen-
tal designs conducted under appropriate ranges
of environmental conditions and retrospective
studies to identify past climatic effects on dis-
ease (5, 70) will help advance predictive power.

An additional key challenge is predicting the
impacts of climate-disease interactions for hu-
mans and gauging how these compare with
other components of climate change, such as the
loss of arable land. By affecting food yields
and nutrition, water quality and quantity, social
disorder, population displacement, and conflict,
past climate changes have long influenced the
burden of infectious disease in many human socie-
ties (71, 72). Predicting the regions where hu-
mans and natural systems are most vulnerable
to pressures from infectious disease and how
these pressures will translate to changes in global
health and security constitute critical research pri-
orities (73). Building a mechanistic understand-
ing of climate-disease interactions will allow
public health interventions to be proactive and
will facilitate effective responses to new or ex-
panding health threats. Surveillance programs ca-
able of detecting pathogen or disease emergence
are essential and, in many instances, predicting
and detecting local-scale impacts might be more
important than predicting global-scale changes. To
this end, the value of engaging local communities
in disease surveillance is increasingly recognized,
with the goal of advancing science on climate-
disease linkages for practical solutions to pro-
tecting human and wildlife health.

References and Notes
8. Boxes S1, S2, and S3 are available as supplementary materials on Science Online.

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**Supplementary Materials**

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Materials and Methods

Supplementary Text

Fig. 51

Boxes S2 to S3

References (75–95)

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**Review: Ecological Consequences of Sea-Ice Decline**

Eric Post,* Uma S. Bhatt, Cecilia M. Bitz, Jedediah F. Brodie, Tara L. Fulton, Mark Hebblewhite, Jeffrey Kerby, Susan J. Kutz, Ian Stirling, Donald A. Walker

After a decade with nine of the lowest arctic sea-ice minima on record, including the historically low minimum in 2012, we synthesize recent developments in the study of ecological responses to sea-ice decline. Sea-ice loss emerges as an important driver of marine and terrestrial ecological dynamics, influencing productivity, species interactions, population mixing, gene flow, and pathogen and disease transmission. Major challenges in the near future include assigning clearer attribution to sea ice as a primary driver of such dynamics, especially in terrestrial systems, and addressing pressures arising from human use of arctic coastal and near-shore areas as sea ice diminishes.

As one of Earth’s major biomes, sea ice not only comprises unique ecosystems in...