

★ NEWS FEATURE

Climate change hastens disease spread across the globe

Trends in some regions are clear, but insect biology, climate quirks, and public health preparedness will determine whether outbreaks occur.

Amy McDermott, Science Writer

Late last November, a young man walked into Renee Salas' emergency room with a circular rash spreading across his leg. Salas, an attending physician at Massachusetts General Hospital in Boston, treated him for possible Lyme disease from a tick bite—a diagnosis that bloodwork later confirmed.

At the start of her career in the early 2000s, Salas would never have suspected Lyme so late in the year. Ticks used to be a summer problem. But since the 1990s, a warmer climate has shortened winters, extending Lyme's duration and expanding its reach throughout New England. Incidence of the infection has nearly

doubled. "I think about it all times of year now," Salas says. "I have to consider Lyme for every rash."

Lyme isn't the only disease whose range and seasonality is shifting, at least in part, as a result of climate change. Although the impact will likely vary based on a variety of factors, some clear trends are emerging. High latitudes and altitudes seem poised for the most dramatic spikes in disease risk. Warmer and wetter conditions in these places have started to lure ticks and mosquitoes up mountainsides and across borders into areas once too cold and dry to support them.



Field crews at the Connecticut Agricultural Experiment Station track the diversity and abundance of disease-carrying mosquitoes using traps baited with a yeast-hay infusion mixed with water. They also use traps that attract the mosquitoes using dry ice and light. Image credit: Connecticut Agricultural Experiment Station.

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Published February 9, 2022.

Some diseases are already shifting. The 2021 *Lancet* Countdown report, published in October, highlighted a 39% increase in the number of months suitable for malaria transmission in some highland areas of the world since the late 1950s (1). The area of coastline suitable for *Vibrio* bacteria, which can cause gastroenteritis, severe wound infections, and sepsis, also increased from 2011 to 2021 in several high-latitude regions according to the report, including the Baltics, the Atlantic Northeast, and the Pacific Northwest.

But while northern climes are becoming more susceptible to disease transmission, communities aren't necessarily doomed to experience bad outbreaks, says biochemist and biomedical scientist Marina Romanello, the research director of the *Lancet* report. "The risk depends on the public health measures," she says, among other factors. Public health measures can include surveillance of known diseases, as well as emergency preparedness and response plans in the event of a localized outbreak, and other measures. Even so, as environments become more and more inviting for disease transmission, "managing the risk gets more and more difficult."

Moving Up Mountains

It's no wonder that disease ranges are shifting; their geographic boundaries have always been climate-sensitive, says theoretical and computational ecologist Mercedes Pascual at the University of Chicago in Illinois. Tick vectors that spread Lyme disease and mosquito vectors that spread dengue, malaria, chikungunya, Zika, West Nile, and a host of other diseases are cold-blooded arthropods with small bodies, meaning that their internal temperatures track environmental temperatures quickly, says disease ecologist Courtney Murdock at Cornell University in Ithaca, NY. Where the vectors can go in many cases determines where the diseases can go. Many physiological traits—most importantly, how long vectors are alive, infectious, and biting—are limited or driven by temperature, as is the speed that a pathogen can develop and be transmitted from the host's gut into a person's bloodstream, Murdock says.

By the 1980s and '90s, infectious disease outbreaks had already worsened in some places. But the link to climate change wasn't conclusive. In 2014, Pascual coauthored one of the first studies to strongly suggest that warming at high altitudes in Ethiopia and Colombia had exacerbated malaria outbreaks since the 1970s (2). Historically, alpine mountain communities were too cold for the *Anopheles* mosquitoes that transmit the malaria parasite. But by the 1990s, case numbers had ballooned.

Many researchers suspected that drug resistance drove the rise in cases. But when Pascual and coauthors plotted the elevation and timing of each malaria case against yearly climate data, they found that outbreaks had marched up and down the mountains closely tracking year-to-year variations in temperature. Then, based on the tight correlation between temperature variation and outbreak size,

the researchers went on to project that Ethiopia would experience an additional 410,000 malaria infections annually per 1 degree Celsius of warming. Extrapolating from the localized 2014 findings to the entirety of Ethiopia's highlands, Pascual estimates that climate change has probably already contributed 5 to 6 million malaria cases to the country's national burden since the 1970s (3).

Around 2010 or so, medical entomologist Philip Armstrong also noticed mosquitoes on the move in New England. Rather than shifting up mountainsides, though, Armstrong saw southerly mosquito species, native to the US Mid-Atlantic, turning up in states farther north than their historical ranges. Armstrong leads the long-term mosquito monitoring program at the Connecticut Agricultural Experiment Station in New Haven, where field crews have tracked the diversity, abundance, and diseases carried by the roughly 50 mosquito species in Connecticut since 1997, beginning with 37 trapping sites statewide. The network expanded to 87 in 2001, after West Nile arrived in North America, and now totals 108.

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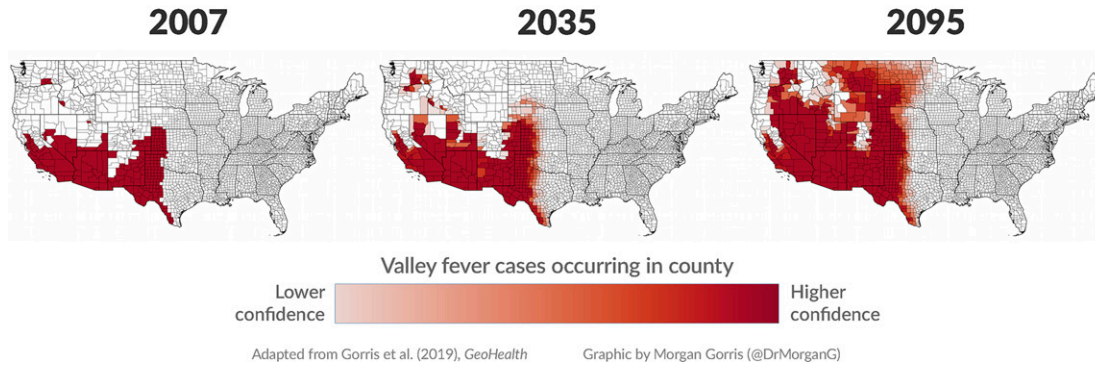
—Marina Romanello

In the evenings from June to October, the crews hang light traps in trees, baited with dry ice, which evaporates tendrils of carbon dioxide to lure female mosquitos searching for a blood meal. The next morning, researchers collect mosquitoes, identify them, and separate them into vials by species and study site. Then they grind up the insects. Liquid from the mosquito mash is injected into mammal cell lines, and if the cells begin to die after a few days then the researchers test those mosquitoes for a variety of cell-killing viruses, including the common West Nile and Eastern Equine Encephalitis (EEE), as well as Zika and others.

Since 2003, the experiment station has detected three new mosquito species in Connecticut, all of them common in more southern states, and "clearly" moving north, Armstrong says—although he notes that studies have yet to prove that the species' arrival was driven by warming. Three more Mid-Atlantic mosquito species, which were rare in New England 20 years ago, have become established and abundant, according to a 2020 report by Armstrong's group based on data from the 87 trapping sites in operation since 2001 (4). Disease-carrying species are among the new arrivals, such as the little brown *Culex erraticus*, known carrier of West Nile and EEE in other, more southeastern, states. Although *C. erraticus* hasn't yet been detected with either virus in Connecticut, "it's certainly possible that these new species may affect the transmission [of] endemic viruses," Armstrong notes, "We just haven't seen it yet."

Across the country, researchers project that the fungal disease Valley fever, primarily endemic to the

Expansion of Valley fever in the western US in response to high climate warming



Under a scenario in which the world continues high levels of CO₂ emissions, Valley fever cases will likely move out of the US Southwest and up to the Canadian border by 2095. Image credit: Morgan Gorris.

US Southwest and dry regions of Central and South America, will climb north this century. Most US cases today are concentrated in Arizona's major cities and in California's Central Valley—places with the ideal semi-arid conditions to support the *Coccidioides* fungus. Residing on and just beneath the crusty desert topsoil, the fungus can infect human lungs, causing joint pain, flu-like symptoms, and meningitis. A 2019 study used state health department data, reporting cases of the disease across the Southwest and pairing them with climate projections under two possible warming scenarios to predict where Valley fever may turn up by 2035, 2065, and 2095. That work found that as semi-arid regions shift north, so too should outbreaks (5).

Thread-like *Coccidioides* grow sporadically across the landscape. A fraction of the diameter of a human hair, field mycologists can't easily spot the fungi. So, the 2019 study relied on confirmed Valley fever case reports as a proxy. Lead author Morgan Gorris compared case numbers from health departments in California, Arizona, Nevada, New Mexico, and Utah between 2000 and 2015 with a map of climatic conditions across the Southwest. She found that counties with more than 10 Valley fever cases per 100,000 residents all had mean temperatures over 51.3 degrees Fahrenheit (10.7 Celsius) and received less than 600 millimeters of precipitation per year.

Today, counties meeting those climatic criteria are sprinkled throughout the Southwest and even up into the Central Plains of Colorado, Oklahoma, Nebraska, and Kansas—areas once thought to be too far north to be at risk for Valley fever. And the fungus may keep moving. In the same 2019 article, Gorris, a postdoctoral Earth system scientist at Los Alamos National Laboratory near Santa Fe, NM, examined moderate and severe future climate warming scenarios across the United States. She found that under the severe climate warming scenario, suitable conditions for the fungus could reach as far north as the US–Canadian border by the end of this century. It's only been a few years since Gorris' article came out, and it remains too soon to see a huge rise in cases, says climate scientist Andrew Comrie at the

University of Arizona in Tucson. He suspects that the fungus is already quietly trekking north, as desert-like conditions spread up the Mountain West. But dry expanses of Nevada, New Mexico, Utah, and Colorado are so sparsely populated that any range shift will likely go unnoticed, Comrie notes, until an outbreak hits a major city, such as Salt Lake City or Las Vegas, north of the fungus' current range.

Concerning Curves

Although many studies make projections about one or two diseases over relatively small geographic areas, one research group tried to tease apart global patterns of climate impacts on thousands of diseases (6). Jeremy Cohen, a postdoctoral wildlife ecologist at Yale University in New Haven, CT, used a database of more than 2,000 combinations of host and parasite species from more than 10,000 field surveys of wildlife disease prevalence around the world. He used statistical models to predict how a number of different factors, including short- and long-term temperatures at survey sites, as well as various host and parasite traits, could simultaneously affect the disease prevalence in wildlife.

It's well known that local weather, especially temperature, influences the prevalence of disease at a given survey site. But would, say, five degrees of warming have the same consequences for a disease in a high-latitude boreal forest as it would in a low-latitude tropical one? Or, Cohen wondered, would the regional climates of those places modulate the relationship between temperature and disease in each location? "There's been an assumption that the effects of temperature on disease are relatively consistent," he says.

Cohen's models suggest that climate can be a major factor. In cool climates, such as high latitudes and elevations, Cohen's models predict that there may be "pretty dramatic increases in disease risk under climate change." Temperate areas, on the other hand, may see only a muted increase in risk, and some tropical areas might actually see a decrease in risk. One reason: Warming in already-hot places could exceed the temperature maxima for parasites to survive and function, Cohen says (7, 8).

The risk of mosquito-borne diseases could also decline in the hottest parts of the tropics, Murdock says. Because mosquitoes are so small, their internal body temperatures track the environmental temperature quickly. And this temperature determines the rate of mosquitoes' metabolism, their cellular processes, how fast they develop, and how long they live, as well as how quickly a pathogen can replicate inside of the mosquito host, making the mosquito infectious. Every mosquito species has a thermal range in which it can survive and transmit disease.

At the cold end of this range, mosquito populations might grow too slowly or the pathogens might replicate too slowly to spread a disease. But as temperatures warm in cool regions of the world, mosquitoes could become more abundant and the pathogens they transmit may replicate faster, potentially leading to higher disease transmission, Murdock says. But if it's too hot, the mosquitoes may die before they can pass on the pathogen. In some cases, researchers expect that when cooler places warm to moderate temperatures, they'll see big mosquito-borne disease booms. Already-hot places might see a decline.

What's more, some tropical mosquitoes didn't evolve with the big seasonal temperature swings common to more temperate climes, notes Murdock. "These mosquitoes might have a lower capacity to evolve tolerance to increases in temperature or increased climate variation," she says. It's possible that some mosquitoes could change their behavior to modulate their temperature, perhaps by sheltering in favorable microclimates. But further research will have to determine how likely or feasible that may be, says Murdock.

Because roughly two thirds of human diseases come from wildlife, including the SARS-CoV-2 virus that causes COVID-19, HIV, West Nile, Lyme disease, and Ebola, it's especially important to track the factors that promote outbreaks in animals, Cohen says, to get a sense of the variety of conditions that are likely to promote wildlife disease.

Even so, existing modeling studies don't agree as to how diseases will respond to climate change. Wildlife veterinarian Lydia Franklins, a doctoral student at University College London, in the United Kingdom, coauthored a 2019 literature review that analyzed 46 modeling studies aiming to predict climate effects on mosquito-borne disease risk over various geographic and temporal scales. Just 54% of the studies predicted a positive correlation between climate change and rising incidence of disease. As a result, she says, "no consensus exists" on how climate change will impact mosquito-borne disease risk (9). Franklins suggests that future modeling should take into account mosquito biology, as well as factors including land use change, human population density, and

socioeconomic considerations such as poverty and healthcare access.

Nevertheless, some mosquito populations seem likely to shift. In the United Kingdom, where Franklins works, the *Culex* mosquitoes that carry West Nile fever could become more common in rural areas, as warmer, rainier winters riddle the countryside with flooded fields (the genus' preferred breeding grounds). The mosquitoes that carry dengue and chikungunya, *Aedes albopictus* and *Aedes aegypti*, are also likely to spread in the United Kingdom; they tend to like urban areas, often breeding in the tiny puddles that collect in old tires and plastic trash. For all three species, warming trends in London and other northern cities, and their surrounding rural areas, hold the promise of survivable winters (10).

High- and Low-Tech Solutions

Technological interventions could help mitigate spread, at least in some cases. In May of last year, Florida saw the first introductions of genetically modified *Aedes aegypti* mosquitoes in the United States, following trials in Brazil, Panama, the Cayman Islands, and Malaysia. Using a gene drive method, UK-based Oxitec is leading the release of male mosquitoes, which don't bite, that carry a gene lethal to mosquito offspring. Of course, such transgenic interventions remain controversial and their effectiveness is still a matter of debate.

The benefit of these techniques is that they can deliver control measures to mosquito breeding grounds that conventional spraying might overlook, Murdock says. But these approaches require that researchers know where the populations are and how they're connected, so that males are released in the right locations to pass the lethal gene widely enough to crash the population. Whether the technology will spread efficiently in the field also depends on the behavior of modified males. They'll need to be robust enough to compete with wild-type males to breed. "There's probably not going to be a silver bullet that cleans up all of our disease problems," she says of the gene drive technology, emphasizing the need for a combination of strategies, while adding that having "more tools in our kit for controlling mosquitoes is going to be important."

The best solution right now is likely better public health preparation. "You set up a seasonal surveillance system to detect the first case," says epidemiologist Jan Semenza, who's at the Heidelberg Institute of Global Health in Germany, and then immediately isolate and treat that patient to prevent spread. Once tick or mosquito populations are established they will be difficult to eliminate, adds Semenza. "We need sophisticated early warning systems to contain an outbreak," he says, "and prevent cross border transmission."

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