Review Article

Fossil-Fuel Pollution and Climate Change Caren G. Solomon, M.D., M.P.H., *Editor*, and Renee N. Salas, M.D., M.P.H., *Guest Editor*

Climate Change and Vectorborne Diseases

Madeleine C. Thomson, Ph.D., and Lawrence R. Stanberry, M.D., Ph.D.

HE EFFECTS OF CLIMATE CHANGE ARE WIDESPREAD AND RAPIDLY INtensifying and are largely driven by greenhouse-gas emissions from burning fossil fuels.¹ Global mean temperatures have already increased by 1.1° C since 1900 ,¹ with most of the change having occurred in the past 50 years. The extent of change is most extreme in highland and polar regions (Fig. 1), and temperatures in tropical regions are creeping closer to the thermal limits of many organisms. Given the current policies and actions, a warming of 2.5°C to 2.9°C or more by the end of this century is expected.²

Warming and other manifestations of climate change — including changes in precipitation, with increased flooding in some areas and drought in others — have important implications for vectorborne diseases through their effects on pathogens, vectors, and hosts, as well as on our ability to prevent and treat these diseases (Fig. 2). Yet attributing changes in the distribution and frequency of vectors and diseases to climate change is challenging because other factors, including land-use changes,³ the abundance of reservoir hosts,⁴ and control measures,⁵ also contribute to these changes. Furthermore, it may be difficult to distinguish between natural climate variability and human-influenced change,⁶ although scientific techniques to do so are emerging. Despite these complexities, it is clear that the components of vectorborne disease systems, including pathogens, vectors, and reservoir hosts, are highly responsive to the varied environments they inhabit and that observed changes in the rates of vectorborne diseases at given locations are often associated with concomitant changes in the local climate.

For example, warming temperatures affect the behavior, physiologic characteristics, and life history of both vectors and pathogens as well as the abundance and behavior of reservoir hosts and definitive hosts. The interactions among temperature, vector, and pathogen can change the risk of human-to-human disease spread and of spillover to humans from reservoir hosts. Thermal performance curves illustrate the ways in which temperature affects the physiological traits of pathogens, vectors, and reservoir hosts, which determine the rate of disease spread in a susceptible population. These curves are commonly used to predict the potential effects of rising temperatures resulting from climate change on vectorborne disease systems.7 Curves for individual components of a disease system must overlap in order for transmission to occur. Thermal adaptation, acclimation to a warming climate, or both can potentially shift thermal performance curves and thermal tolerance limits, with important implications for expansion of the geographic range of certain diseases. Depending on their ability to adapt, vectors may no longer carry certain pathogens or may carry new ones as climate-mediated ecosystem changes bring different pathogens, vectors, and reservoir and human hosts together.⁸

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Figure 1. Mean Surface Air Temperatures.

Shown are mean surface air temperatures from 2011 to 2021 as compared with baseline mean temperatures from 1956 to 1976. Adapted from the National Aeronautics and Space Administration Goddard Institute for Space Studies (https://data.giss.nasa.gov/gistemp/maps/index_v4.html).

CLIMATE-SENSITIVE VECTORBORNE Diseases

The Intergovernmental Panel on Climate Change reported with high confidence that the prevalence of vectorborne diseases has increased in recent decades and that the prevalences of malaria, dengue, Lyme disease, and West Nile virus infection in particular are expected to further increase during the next 80 years if measures are not taken to adapt and strengthen control strategies.1 Table 1 describes these and additional examples of vectorborne diseases that are responding to a changing climate. Additional details are provided in Figure S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org.

Malaria

Malaria, which is caused by plasmodium species and is transmitted between humans by infected female anopheles mosquitoes, is the most deadly and most studied climate-sensitive vectorborne disease. Despite control efforts, more than 600,000 deaths were attributed to malaria in 2020, predominantly among pregnant women and young children in Africa.²⁶ In many regions, malaria is a seasonal or epidemic disease that

responds to short-term changes in rainfall, humidity, and temperature. Temperature increases of 0.2°C per decade in the highlands of Colombia and Ethiopia have been associated with the spread of malaria to higher elevations in these countries.9,27 The frequency of droughts is also increasing as a result of climate change and may reduce the prevalence of malaria in certain regions. However, the broader effects of climate change on local livelihoods, food security, and migration may increase population vulnerability to the disease and undermine the effectiveness of control strategies, irrespective of the direct effects of climate change on transmission.²⁸

Dengue

In recent decades, the geographic range of dengue, the most common mosquito-borne viral disease worldwide, has expanded substantially in response to declining vector-control programs and increasing global trade and travel.²⁹ An estimated 390 million cases occur each year in more than 100 countries.³⁰ The four serotypes of dengue virus are transmitted between humans the primary reservoir host — by infected female mosquitoes, most commonly *Aedes aegypti* and *A. albopictus*. Water-storage containers, which are commonly used in regions where a piped water supply is inadequate, or rainwater-filled containers (e.g., tires, pots, and tree holes) can become mosquito breeding sites and can thus drive epidemics.31 Transovarial transmission of dengue virus (from female mosquitoes to their offspring) and the long-distance dispersal of drought-resistant aedes eggs in suitable containers facilitate efficient expansion of the virus worldwide.32 The northward expansion of *A. aegypti* and *A. albopictus* thus far is best explained by human movement patterns within regions in which the climatic conditions are suitable for geographic expansion; however, by 2030, the dominant cause of expansion of these vectors is predicted to be climate change.³³ The differential ability of *A. aegypti* and *A. albopictus* to survive normally lethal temperatures may influence their roles in future outbreaks.

Lyme Disease

Lyme disease (which is caused by the *Borrelia burgdorferi* sensu lato complex) is the most common tickborne illness worldwide, with an estimated seroprevalence of 14.5%; the reported

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The climate experienced at any location and time represents a combination of natural climate variability and, increasingly, climate change. As greenhouse gases accumulate and lead to increased global temperatures, extreme weather events are becoming more frequent, more severe, or both.

prevalence is highest in the temperate regions of Worldwide, Lyme disease involves four dominant central and western Europe and East Asia.34 tick species, although generally only one tick Without early treatment, infection can cause species is important in any given region.³⁵ Widedebilitating multisystemic chronic disease.³⁴ ranging reservoir hosts — including mammals

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1972 **n engl j med 387;21 Nejm.org November 24, 2022**

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(e.g., mice and squirrels), lizards, and birds are part of the ecologic complexities of this disease; however, humans play no role in ongoing transmission.35 The life cycle and prevalence of tick vectors, primarily *Ixodes scapularis* and *I. pacificus* ticks in North America and *I. ricinus* and *I. persulcatus* ticks in Europe, are strongly influenced by the abundance of reservoir hosts and by the ambient air temperature.36

Insurance records indicate that 470,000 cases of Lyme disease were diagnosed and treated in the United States during the period from 2010 to 2018, as compared with 329,000 cases during the period from 2005 to 2010.³⁷. Lyme disease is most common in the Northeast and rare in the Southeast; although tick vectors are found in both regions, variations in the host preferences of the ticks (e.g., lizards or mice), in the hostseeking behavior of the ticks, and in the tick density help to explain this geographic pattern.³⁶ The increases in Lyme disease cases in the Northeast are largely attributed to the recovery of white-tailed deer populations,³⁶ which are critical hosts for adult stages of the tick vector; however, increased human–tick interaction owing to the extended summer season resulting from climate change also contributes to the increases in cases. Warming temperatures have been associated with the expansion of ixodes ticks into Canada and Norway, with a corresponding increase in cases of Lyme disease.^{19,38}

West Nile Virus Infection

West Nile virus causes potentially fatal neuroinvasive disease in humans and animals worldwide.³⁹ The virus is part of a complex ecosystem that is centered around a bird–mosquito transmission cycle involving more than 300 bird species and at least 65 mosquito vectors. Mammals, including humans and horses, can be incidentally infected. Human infections are mostly asymptomatic but can cause life-threatening illness in rare cases, predominantly in older adults and in immunocompromised persons.40

West Nile virus, which was first identified in the United States (in New York City) in 1999, is the leading cause of mosquito-borne disease in the continental United States. During the period from 1999 to 2016, nearly 7 million persons were infected.41 The observed air temperature that results in a peak incidence of the virus among humans across the country was found to be 24°C, which closely matches the temperatures (which ranged from 24°C to 25°C) that were predicted by mechanistic models that were based on vector and pathogen thermal performance curves.42 Warming temperatures are expected to shift transmission of this disease northward, as is already occurring in Europe; local transmission was recently discovered in Germany after unusually warm weather.⁴⁰

Inequality and Vulnerability

Climate change exacerbates inequalities, such as those driven by systemic economic injustice.⁴³ Persons living in less developed countries bear the greatest burden of most vectorborne diseases, a circumstance that reinforces health inequities and hinders socioeconomic development. Poverty, inadequate housing, poor environmental conditions, and limited access to quality health services exacerbate the effect. Children are particularly susceptible,⁴⁴ owing in part to the effects of malnutrition⁴⁵; women and older adults are also at increased risk. Vectorborne diseases during pregnancy are associated with particularly poor health outcomes among mothers and newborns from low-income or otherwise disadvantaged groups,^{46,47} as evidenced by the devastating effects of congenital infection with Zika virus during the explosive epidemic of Zika virus infection (which was spread by aedes mosquitoes) in Brazil in 2015.48

Public Health Interventions

Investments in surveillance and control have led to improvements in the public awareness, detection, prevention, and treatment of vectorborne diseases⁴⁹ and form the basis of adaptation strategies for a changing climate (Fig. 3).¹ Specific measures to be taken vary according to disease, pathogen life cycle, and the level of risk and may include a combination of enhanced and new land-use management strategies, climate-informed early-warning systems, improved access to prevention measures (e.g., biologic mosquito control, personal protective measures, insecticides, and vaccines), and new and improved therapies⁵⁰ (Table 2). Figure S1 shows the projected benefits of adaptation strategies with respect to vectorborne disease rates. To be successful, interventions must include sustainable funding, as well

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as community and household acceptance and uptake. A 2017 survey of 1083 U.S. vector-control programs showed that 84% of the programs were rated as "needs improvement" in one or more core competencies (e.g., insecticide-resistance testing).59 The same year, the Centers for Disease Control and Prevention established five regional centers of excellence to help respond to emerging vectorborne diseases and to help create a new generation of vector experts.⁶⁰

Malaria highlights several challenges that can occur in the implementation of adaptation strategies. After two decades of concerted international and national investment and consistent declines in malaria cases and malaria-related deaths, worldwide funding has stagnated; malaria is now resurgent in several countries, owing in part to increasing drug and insecticide resistance and, to a lesser extent, to service disruptions resulting from the coronavirus disease 2019 (Covid-19) pandemic.²⁶ Innovations are needed to keep up with biologic and socioeconomic challenges and to ensure equitable access to high-quality treatment in low- and middleincome countries.

The prevention of dengue and West Nile virus infection relies mainly on community-level mosquito-control programs; the implementation of such programs varies according to several factors, including funding and management. 61 Avoidance of the vector habitat during the transmission season as a result of public communication has long been an important prevention strategy for Lyme disease.⁶² Various personal protective measures (e.g., insect repellent and protective clothing) and tick-control strategies (e.g., the culling of deer) have been proposed as approaches to reduce the risk of Lyme disease, but evidence of effectiveness is generally lacking.⁶⁰

Vaccines have been successful in the prevention of three vectorborne diseases: yellow fever, Japanese encephalitis, and tickborne encephalitis.63 Despite the fact that vaccines approved for malaria 64 and dengue 65 in the past several years have had only limited success, efforts are under way to develop new and more effective vaccines that target vectorborne diseases.⁶¹ A recent phase 2 trial showed the effectiveness of a single infusion of a monoclonal antibody against *Plasmodium falciparum* infection over a 6-month follow-up period in Mali during malaria season.⁶⁶ A formerly approved, effective vaccine for Lyme disease was withdrawn from the market,⁶⁷ but a new Lyme disease vaccine is currently being evaluated in a phase 3 trial (ClinicalTrials.gov number, NCT05477524). Similarly, a new dengue vaccine has shown promise in a phase 3 trial, and regulatory approval by European authorities is being sought (NCT02747927). According to the Intergovernmental Panel on Climate Change, successful vaccine development and uptake although made more difficult by the growing worldwide challenge of vaccine hesitancy have the potential to substantially offset the effect of climate change on vectorborne diseases.¹

Better surveillance data and climate-informed early-warning systems are needed to enhance public awareness, facilitate the targeting of resources (human and financial) for improved responses,⁵ and identify knowledge gaps and research needs. Adaptation plans must be time-sensitive and context-specific while also taking into account factors such as shifting disease patterns, extreme weather events, and current and future climate variations and trends.²⁸ This approach will require collaboration among various sectors, such as local health communities, urban planners, and climate experts.⁶⁸

IMPLICATIONS FOR CLINICAL PRACTICE

Education of health professionals is needed with respect to specific vectorborne diseases, particularly in regions in which diseases are newly emerging or anticipated to emerge. In many locations, clinicians are likely to see more cases of vectorborne diseases during longer transmission seasons, especially in regions with historically low levels of transmission. Awareness of local changes in disease rates and travel histories on the part of clinicians is important. 69 The nonspecific clinical manifestations of many vectorborne diseases often make diagnosis difficult.⁷⁰ Strategies for the prevention and treatment of vectorborne diseases are reviewed in Table 2. To help address the additional burden of health care delivery created by a changing climate, health professionals can advocate for more climate-resilient health systems⁷¹ and for programs that focus on the current worldwide shortages of health professionals, including infectious-disease experts.

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The panel on the left shows key community-based strategies for responding to the threat of vectorborne diseases. These include public policies that regulate land use and home construction, both of which can affect vector breeding sites and reduce the risk of indoor mosquito bites; surveillance for vector abundance and the incidence and prevalence of disease; and syndromic surveillance. Surveillance may be enhanced through multisectoral collaborations (e.g., meteorologic services that might predict conditions that are suitable for enhanced mosquito survival and parasite development). If early-warning systems can be developed, they could be used to enhance vector and disease surveillance in targeted areas. Then, if a surveillance threshold is exceeded, certain measures could be taken or reinforced (e.g., initiation of public-awareness campaigns that educate and provide guidance). The panel on the right shows the strategies that individual persons and households can use to prevent or respond to a vectorborne disease. For adaptation measures to be successful, community and household acceptance and uptake are needed.

MITIGATION OF CLIMATE CHANGE

Reducing the risks of vectorborne diseases and other health consequences of climate change requires not only adaptation but also a rapid and equitable transition away from fossil fuels. The signing of the Inflation Reduction Act of 2022 represents a necessary (although insufficient) move toward decarbonizing the U.S. economy in line with the goals set under the Paris Agreement in 2015. The health care sector, which contributes an estimated 4.9% of the total car-

process.72 As trusted voices,73 health professionals can weigh in regarding the importance and urgency of mitigation.⁷⁴

Conclusions

bon footprint worldwide, must be part of the are expected to continue as the climate continues Climate change has substantial effects on pathogens, vectors, and reservoir hosts, with implications for the health sector worldwide. Many vectors are already expanding their latitude and altitude ranges, and the length of season during which they are active is increasing; these trends

n engl j med 387;21 nejm.org November 24, 2022 1975

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* The development and implementation of adaptation measures are associated with considerable challenges, including the need to ensure adequate funding for research and development and for the establishment and sustaining of programs and to ensure equitable access to adaptation measures.

† Insecticides such as dichlorodiphenyltrichloroethane (DDT) have historically been the cornerstone of vector-control programs but have become less effective and have unacceptable environmental and toxicologic effects.

to warm. Changes at the local level will be context- and disease-specific. Clinicians should be alert to changes in risk for the population they serve. To protect health and equity in a warmer world, investments are needed in vector control with respect to tailoring measures to rapidly the full text of this article at NEJM.org. emerging situations and in new forms of technology and approaches, including vaccines. Unfortunately, adaptation strategies will not be viable

as a long-term solution without the implementation of sufficient, urgent mitigation efforts to maintain global temperatures below critical thresholds.¹

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