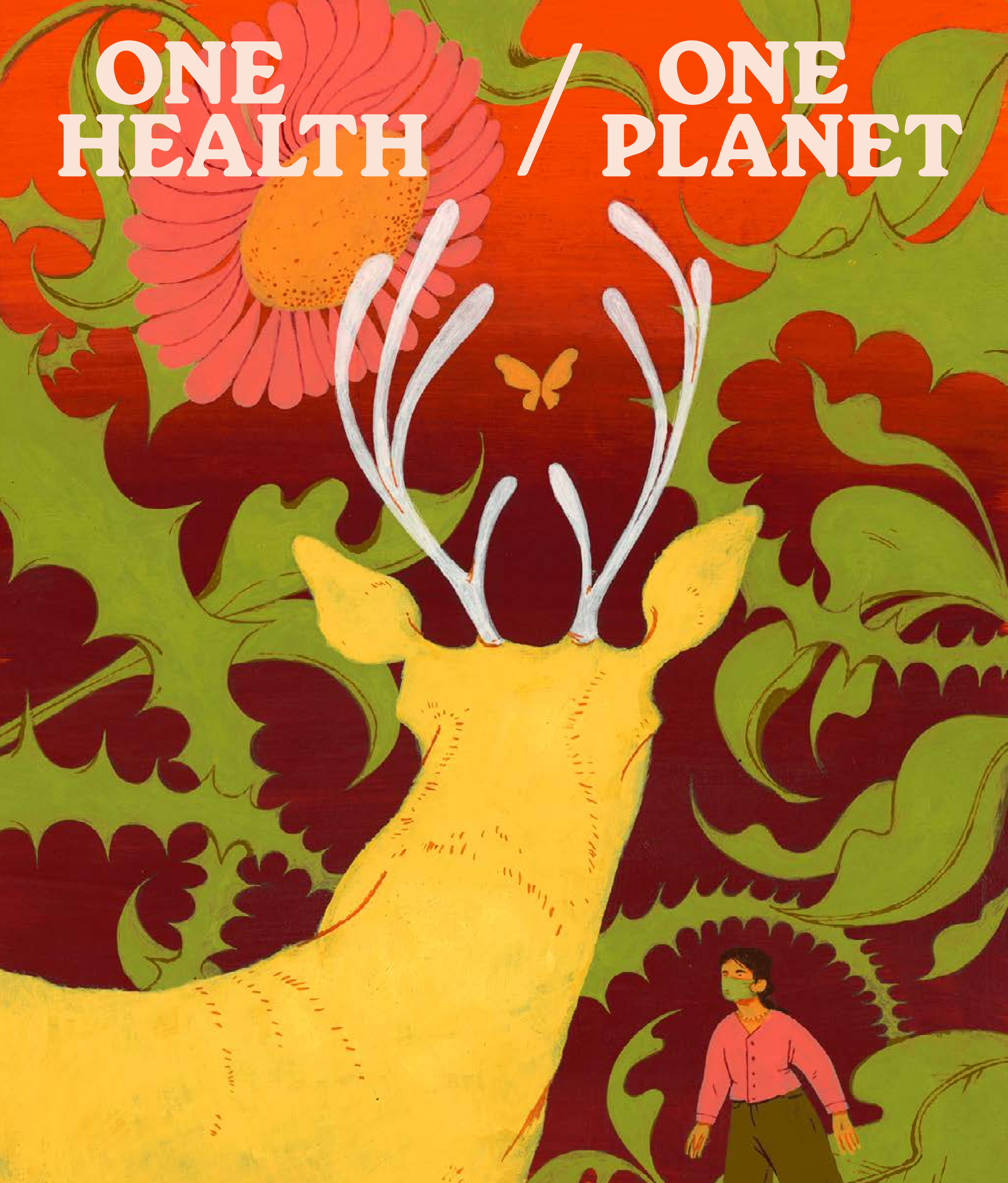
ONE HEALTH / ONE PLANET



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SCIENCE PHILANTHROPY ALLIANCE

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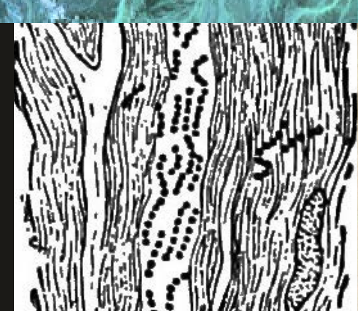
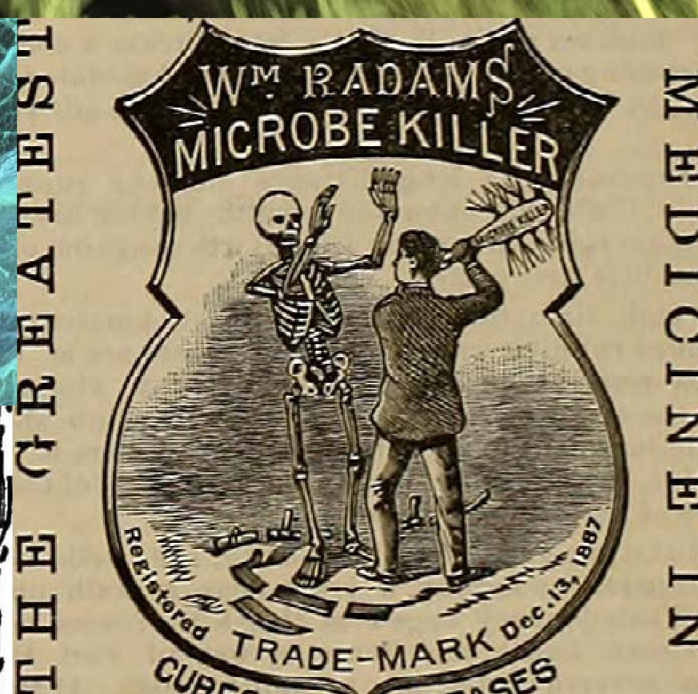
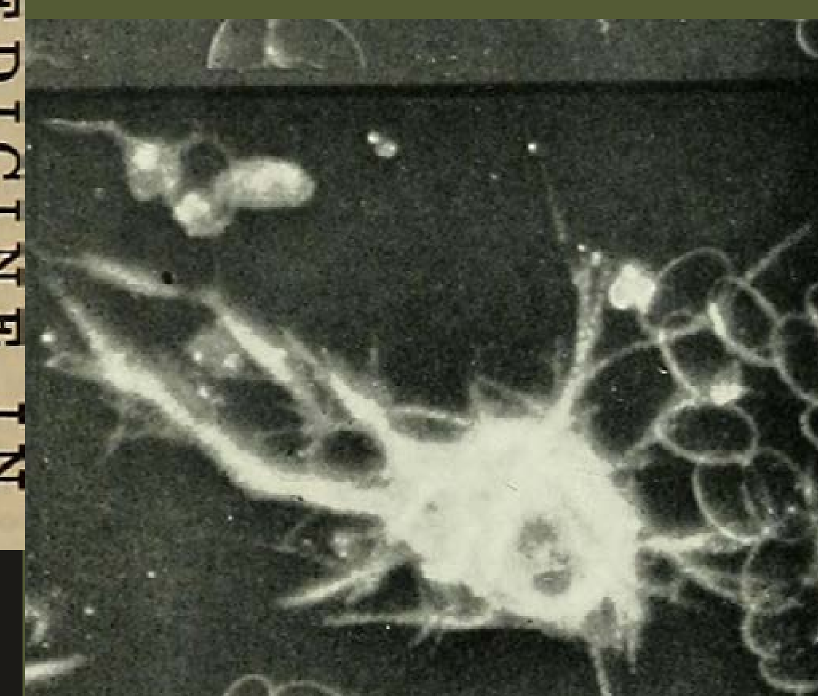
EXPLORING THE INTERSECTION OF CLIMATE CHANGE + AND INFECTIOUS DISEASE

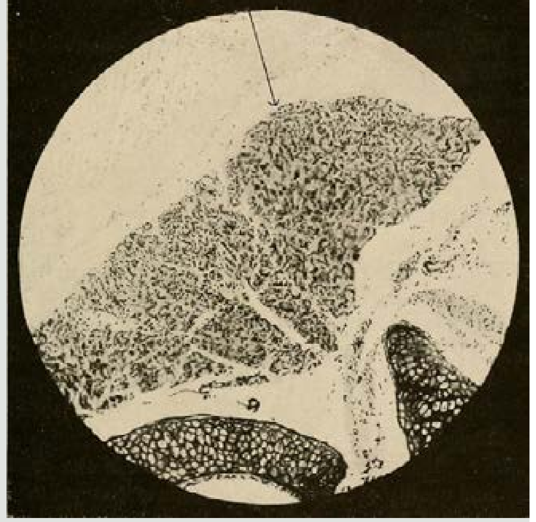






About the Science Philanthropy Alliance

The Science Philanthropy Alliance works to advance scientific discovery through visionary philanthropy. Drawing on its distinguished external science advisors, skilled team of philanthropic advisers, and a membership base of leading science funders, the Alliance provides advising services and learning opportunities to help philanthropists expand the world's knowledge and lay the scientific groundwork for lifesaving, economy-changing breakthroughs.



Introduction

In recent years, headlines about extreme weather events and the COVID-19 pandemic have put climate change and infectious diseases at the forefront of the public discourse. That's equally true within the philanthropic community. Members of the Science Philanthropy Alliance, which include many of the world's most prominent science funders, are grappling with where and how their resources and unique position within the research enterprise can have the greatest impact on these dual threats. Through conversations with our members, two important points emerged that sparked the genesis of this special edition of Leaps.org in collaboration with the Aspen Institute and GOOD Worldwide.

The first is that these seemingly disparate issues of climate change and infectious disease are, in fact, interwoven across the fabric of nature. This stands out perhaps most notably in the growing risk of disease spillover from animals to humans as climate and habitat changes drive them together. As highlighted throughout this edition, though, the connections run much deeper and the complex systems at play have little regard for the traditional siloes of academia. Although far from a novel concept–especially for many Indigenous communities–there's growing recognition that a holistic, interdisciplinary lens is crucial to advancing how we understand, interact with, and respond to our changing planet. The "one health" framework described in this edition takes this into account but is by no means the only approach.

Second, important gaps remain in our fundamental understanding of climate change, infectious disease, and the interplay between the two. It's this often-overlooked basic research that builds the bedrock of knowledge upon which breakthroughs are made. As you'll read in these digital pages, though, the relationship between basic research, applied research, and technological breakthroughs isn't a linear one. Rather, as Simons Foundation President David Spergel has said, it's a "complex dance" with each fueling the other along the way. This means that pressing basic research questions carry with them the potential to catalyze science, often in unexpected ways.

Thankfully, although small in comparison to government funding for science, philanthropic funding is uniquely positioned to address both points–breaking down silos and filling high-leverage gaps in research. It's our hope that this edition of Leaps.org will prompt important conversations on the topic and encourage more philanthropists to lend their support to the inspiring researchers expanding our knowledge at the intersection of climate change and infectious disease.

France A. Córdova, Ph.D.
President, Science Philanthropy Alliance

Editors
Matt Fuchs
Jylana L. Sheats
Lina Zeldovich
Aaron F. Mertz

Art Direction & Design
Tatiana Cárdenas-Mejía

Design Support
Lysistrata Karch-Coar
Cristina Mejia

Concept Strategy
Sue Merrilees
Jason Maier
Diane Matar
Daren Ginete
Andrew Golnar

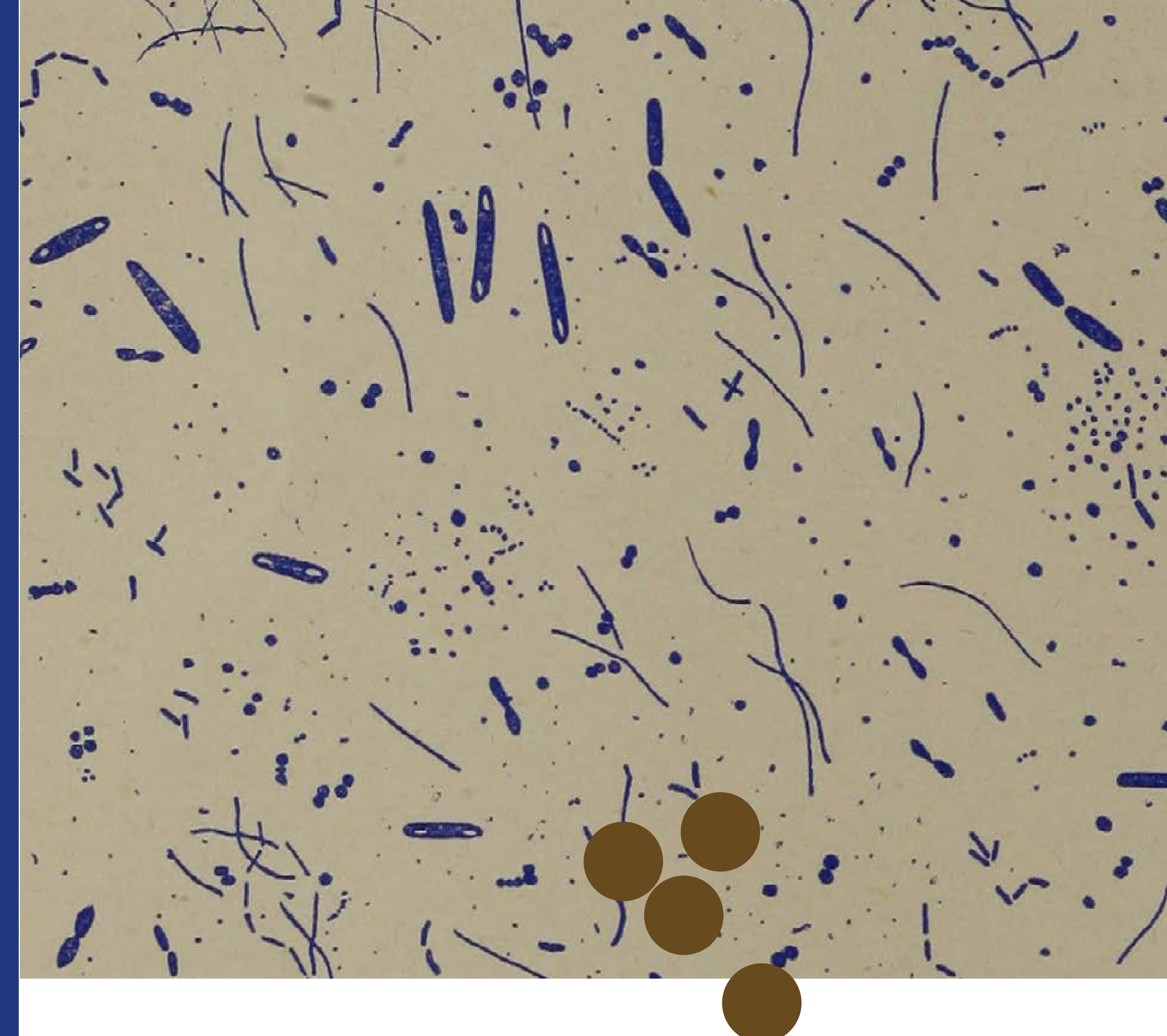
Front & Back Covers
Illustration by
Celia Jacobs

Fonts
VC Henrietta
Simplon BP Mono
Domine
DM Sans

Writers
Temma Ehrenfeld
Susan Kreimer
Stav Dimotoupolos
Matt Fuchs
Linda Marsa
Lina Zeldovich
Kristina Campbell
Eve Glicksman
David Levine
David Cox

Illustrators
Juli Tudisco
Lisa Larson Walker
Gabrielle Delabarre

Contact
aaron.mertz@aspeninstitute.org
matt.fuchs@leaps.org



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Dismantling the silos

By Jylana L. Sheats, Ph.D. and Aaron F. Mertz, Ph.D.

Whether called a concept, methodology, strategy, approach or framework, "One Health" recognizes the interconnectedness between humans, animals and the environment. In an increasingly globalized world, "One Health" activities can prevent zoonotic disease outbreaks where diseases are transmitted from animals to humans (e.g., West Nile virus, avian influenza, SARS), ensure food safety and security, improve human health (such as reducing antibiotic-resistant infections) and protect global health security, according to the Centers for Disease Control and Prevention (CDC). Yet, public health activities are not the only forces that shape outcomes. Culture and geographies have direct and indirect impacts on how health, illness and disease are conceptualized—and diagnosed, treated or cured–as well as influencing who is responsible for said treatments or cures (e.g., medical doctor, shaman, curandero). The nature in which humans, animals and the environment are interconnected differs depending on context. For example, a paper by Cunningham and colleagues notes that "animals and people are not seen as separate in many cultural contexts, but integrated as part of interconnected social–natural worlds." These beliefs are central to Indigenous communities, which have a deeply significant spiritual, physical and social relationship with land, water and other elements of nature. A brief from the United Nations states that land is a "core part of their identity and spirituality and to be deeply rooted in their culture and history."

In the introduction of a special issue of the *Philosophical Transactions of the Royal Society* journal, the authors argue for understanding place, culture, context and nuances of how "dis-ease" is conceptualized. To do so requires not only collaborative, interdisciplinary understanding of disease, people and their behaviors to optimize and advance interventions, but also participatory methods that value diverse perspectives and seek out local knowledge and histories. A key element of community engagement and participatory methods is understanding that community members are experts of their own lived experiences.

> **"We should dismantle the silos in which we focus much of our attention, education and research."**

Across the topics discussed in this *One Health/One Planet* magazine, thoughtful experts propose a number of fruitful areas of research, with some recommendations for who should be the members of inter- and trans-disciplinary teams that lead progress in these areas. A major consideration should be to whom, by whom and how that research should be disseminated. Diversity within the context of perspectives and who is conducting research activities—as well as multi-level and -sectoral collaborations, communication and coordination—should be paramount. In a recent *Lancet* article, the authors affirm that we should dismantle the silos in which we focus much of our attention, education and research. By valuing the contributions of myriad fields that explain the interconnectedness of relationships among humans, animals and the environment, we will further our understanding of current and new strategies toward improving human health—and facilitate and inform new research and funding priorities.

Editor's note:

In the spirit of rising to difficult challenges and erasing pointless divisions, we present *One Health/One Planet*, a single-issue magazine that explores how climate change and other environmental shifts are increasing vulnerabilities to infectious diseases by land and by sea. The magazine probes how scientists are making progress with leaders in other fields toward solutions that embrace diverse perspectives and the interconnectedness of all lifeforms and our precious blue dot.

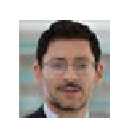
This special issue is a collaboration among the science outlet *Leaps.org*, the impact and engagement company GOOD, the Aspen Institute Science & Society Program and the Science Philanthropy Alliance.

The articles explore potential breakthroughs that are taking single-aim at the overlapping dilemmas of a warming planet and more frequent global pandemics. These predicaments, while certainly not new, have begun to seem more tangible and ominous in the midst of COVID-19, a tragedy that could very well repeat itself on an even more disastrous scale as deforestation and changing temperatures force new interactions among species, increasing the risk of disease transmission—including viral jumps to humans. Recognizing this reality, some scientists are making unprecedented advances in use-inspired research and technological development for a safer, healthier, more sustainable future that contemplates every planetary organism and ecosystem as essential parts that sum to a greater whole.

Going forward, we must do more to support scientific efforts that address at least ten complex and interrelated areas, around which this magazine issue is organized: PARTNERSHIPS, NEW FRAMEWORKS, MICROBES, SPILLOVERS, ANIMAL & PLANT HEALTH, HUMAN HEALTH, INSECTS, SURVEILLANCE, CHANGING HABITATS and MODELING.

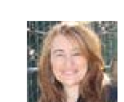
When historians of the 22nd century judge how we protected our own health, the health of our planetary cohabitants and the planet itself, the criteria will take account of, but extend far beyond the work and achievements of modern science. Their benchmarks will include how we met the need to engage diverse audiences—such as our farmers, historically underrepresented and underserved communities, conservationists, frontline medical workers, artists, politicians and communicators. We need their contributions in order to pursue the questions that are the most relevant, incisive and holistic. Only then can we be sure that we are allocating scarce resources toward the best possible answers. Nothing less will work against such steep challenges. Only with the broadest, most collaborative and transdisciplinary engagement can we truly hope to embrace the *One Health/One Planet* paradigm needed for *our* future salvation and prosperity.

Sincerely,


Matt Fuchs, J.D.
Editor-in-Chief, *Leaps.org*
Science Editor, GOOD and Upworthy


Jylana L. Sheats, Ph.D.
Civic Science Fellow
Science & Society Program, Aspen Institute


Aaron F. Mertz, Ph.D.
Director
Science & Society Program, Aspen Institute


Lina Zeldovich, M.S.
Contributing Deputy Editor, *Leaps.org*

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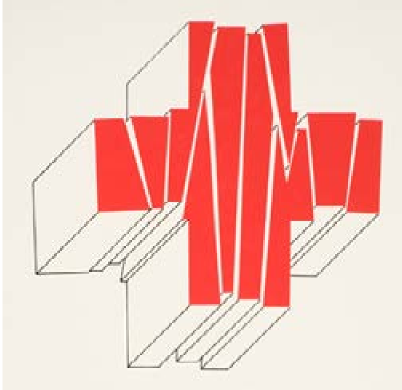


1. Partnerships in One Health/One Planet:

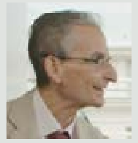
A Conversation between Rajiv J. Shah and Louis J. Muglia

Louis J. Muglia, the President and CEO of the Burroughs Wellcome Fund, sat down with Rajiv J. Shah, the President of The Rockefeller Foundation, to discuss the future of research on health and the environment, among other issues, at a members' meeting of the Science Philanthropy Alliance in May 2022.

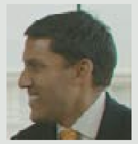
This conversation was lightly edited by Leaps.org for style and format.

Louis Muglia: Good evening. Given your experience at the Gates Foundation, government administration and the philanthropy sector, what lessons have you learned about data use and interpretation?

Rajiv Shah: Thank you. It's great to be with you. I've had a chance, as you have, to work on so many different issues that affect the lives of people who are vulnerable at home and around the world. And too often, when people try to do good, they assume that this good intention is sufficient proof that you're in fact making a difference. I've learned over time that you actually need to measure results, track data and study where you can have the greatest impact to use your resources to create the kind of massive changes that help lift up the most people.



LM: We could argue that's more important than ever with the issues that we're facing as a community and as a global community. How do you think about investing in shorter term interventions that are "boots ready," ready to implement, versus strategies with longer timelines, like developing new energy systems that require discovery science? There's a balance between those things, and I'm wondering how you process that.



RS: There's an absolute balance between what can we do right now to lift people, and what can we do if we invest in new scientific frontiers with even more potential over the long run. Every day we all struggle with how to get that balance right. If you just take the health space, for example, the Foundation for more than 100 years has invested both in tools and technologies—from inventing the yellow fever vaccine, to more recently, the development of other types of health technologies and digital tracking tools to help deliver vaccines and other commodities to people where they're most needed.

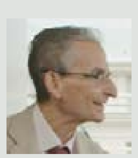
But we also have tried to invest in and create institutions that serve people now. We saw that during the pandemic here in the United States. We worked with states and local governments and built networks to make testing much more prevalent in America. It was unbelievable that early in the pandemic, you couldn't appropriately get a free test in the U.S., and then we wondered why we had an out-of-control pandemic. To solve that problem, yes, we needed to invest in some technology. We needed to work with companies to make sure they were going to manufacture antigen tests at scale, for example. But we also had to work on the ground in Navajo Nation in Los Angeles, New Orleans, Detroit, Washington, DC, and New York City, in order to really be connected to the communities we want to serve.

So, for our institution, we try to get that balance right of investing in future frontiers but also recognizing that we need to listen and learn from the needs of those we hope to serve right now.

"I believe that anyone, no matter the size of their resource base, is an important potential partner."

– RAJIV SHAH,

THE PRESIDENT OF THE ROCKEFELLER FOUNDATION



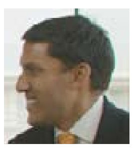
LM: One of the areas that I've been particularly impressed with The Rockefeller Foundation is the water surveillance initiative. It's a wonderful example of using new science to strategize ways to identify and intervene in problems. I wonder if you could talk a little bit about that.

RS: I have a history here. I was at USAID when Ebola hit in West Africa and had responsibility for managing the response there. What I saw was, if you don't have real-time data around cases--who's positive in which districts of a country--no matter how many resources you throw at a problem, you're not going to solve it. You need that real-time, accurate, geospatial data, and then you need to act.

In our international public health architecture, and even our domestic one, data doesn't get liberated very easily. When COVID hit in this country, we said, look, if we're ever going to avoid a future pandemic, we have to build a data architecture for the planet that allows positive cases anywhere to be visible. We've launched a Pandemic Prevention Institute to do just that. We recruited Dr. Rick Bright to lead it. We have an outstanding team of data scientists working day and night to put it together. It collects data from two basic platforms. One is, of course, clinical data from labs in the U.S. and around the world. That's how we knew that genome sequence for Omicron out of the Centre for Epidemic Response and Innovation (CERI) at Stellenbosch University so quickly. We provided them with support alongside Wellcome. In fact, we saw that they shared that information three to four weeks before official agencies shared their information.

But we're also building a wastewater surveillance system so that we can use new environmental signals to identify where outbreaks are likely to occur in the near future and act ahead of time. In addition to that, we're exploring looking at data mining across social media data search terms, to identify platforms that allow data science and AI to help predict where pandemics are likely to emerge. If we can start to visualize the 200-plus epidemics that hit every year, the goal is to make sure they don't become pandemics by getting ahead of them quickly.

LM: The example of the water surveillance project requires genomic scientists, epidemiologists, environmental ecologists—people who often don't talk to each other in the same place at the same time. How did you bring all these folks together?



RS: Consistently across the partners in the Science Philanthropy Alliance, we have philanthropy platforms to bring people together. Folks trust The Rockefeller Foundation because we've worked on behalf of humanity and its health for 110 years almost. People trust institutions that represent scientists because they understanding that the goal is to bring people together, share data, solve problems.

We've been able to leverage that trust and access data. We make grants to partners all around the world. Grant making, of course, is what we all do together. And it gives frontline institutions, whether they're university labs or platforms for wastewater or water surveillance, within departments of public health all around the world, the resources to build data collection platforms. We're creating a data architecture that allows them to share that data in real-time so that it can be searched, visualized and acted upon.

It's not such a big breakthrough concept, right? We do that for real estate in America, through Zillow. Why can't we do this for pandemic data?

LM: Problems like the pandemic and climate change have often disproportionately affected the most marginalized populations. How has Rockefeller prioritized diversity, equity, and inclusion in its grant making and its general targets?

RS: First, we try to focus on diversity, equity and inclusion in our grant making, our hiring, and who we choose to partner with. We do that in the U.S. where the DEI construct has a very specific and important interpretation. And we try to do that globally, so that we're not giving all our resources, for example, to U.S. or European institutions to work in Africa or Asia. We're finding local institutions and nurturing them. That's critically important.

A second answer is a bit of my perspective on where we are right now, especially on the global front in terms of equity. The truth is the pandemic uncovered and exacerbated deep inequities in our global economy. The people who live in the lowest income countries, and the people who had the least access to health and education, energy and livelihoods were also the people most severely affected in many ways. It was the health consequences of COVID but also the fact that rich countries were able to put more than 20% of their GDP into efforts to stimulate their economies and [provide] a protective floor for the vulnerable. Whereas developing countries could only do 3%.

And right now, because of the war with Ukraine and Russia, we're facing a food and hunger crisis that's only going to get worse because those countries were

"The intersection of climate change and health will only get more intense and consequential for the most vulnerable people on the planet."

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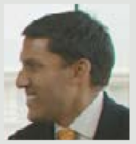
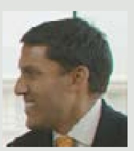
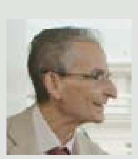


RS: both the breadbasket for many parts of the world for certain commodities and the world's primary source of ammonia for fertilizer. I'm very concerned that for the first time in the post World War II era, developing nations, which have traditionally grown a little bit faster in order to catch up, are actually going to be mired in long-term debt, with fuel and food crises. We all have to redouble our efforts to focus on those most vulnerable, globally, due to a conflict they had nothing to do.

LM: For organizations like Burroughs Wellcome Fund with a much smaller asset portfolio, how do we think about partnering with The Rockefeller Foundation in a way that is complementary, that we might think of as being catalytic.



RS: I believe that anyone, no matter the size of their resource base, is an important potential partner. A foundation, individual, university team, or corporate leadership group can craft a set of ideas that help solve a problem that others get behind. You do great work at the intersection of health and environmental futures. Really understanding that and bringing people to that mission is a tremendous role you can play, and we are eager to participate and follow. We did some work in planetary health and, as our world gets smaller, as we saw with COVID, we'll see with other crises. The intersection of climate change and health will only get more intense and consequential for the most vulnerable people on the planet.



LM: I've enjoyed the conversation, Raj. It’s been very inspirational for me. We will all look forward to seeing great things that the Rockefeller Foundation supports and that we can potentially partner around. Do you have any comments in closing?

RS: Let me thank you. I'm so excited to be part of the Science Philanthropy Alliance. And I think if you look across history, there's perhaps no other time when the creation of new knowledge and technology, [while] making sure it's equitably distributed, has been more consequential for human health. We see this with COVID and with food security where 810 million people will go to bed hungry tonight, and that number is going up. Where we're facing the existential threat of climate change, and 97 percent of all renewable energy infrastructure built last year is in rich countries, not developing ones. This Alliance is very special in bringing both the ethic of serving everyone and the faith in what science and innovation can do to tackle our biggest problems. I hope the whole community moves forward boldly. And I thank you for your time.

2. Frameworks & Approaches:

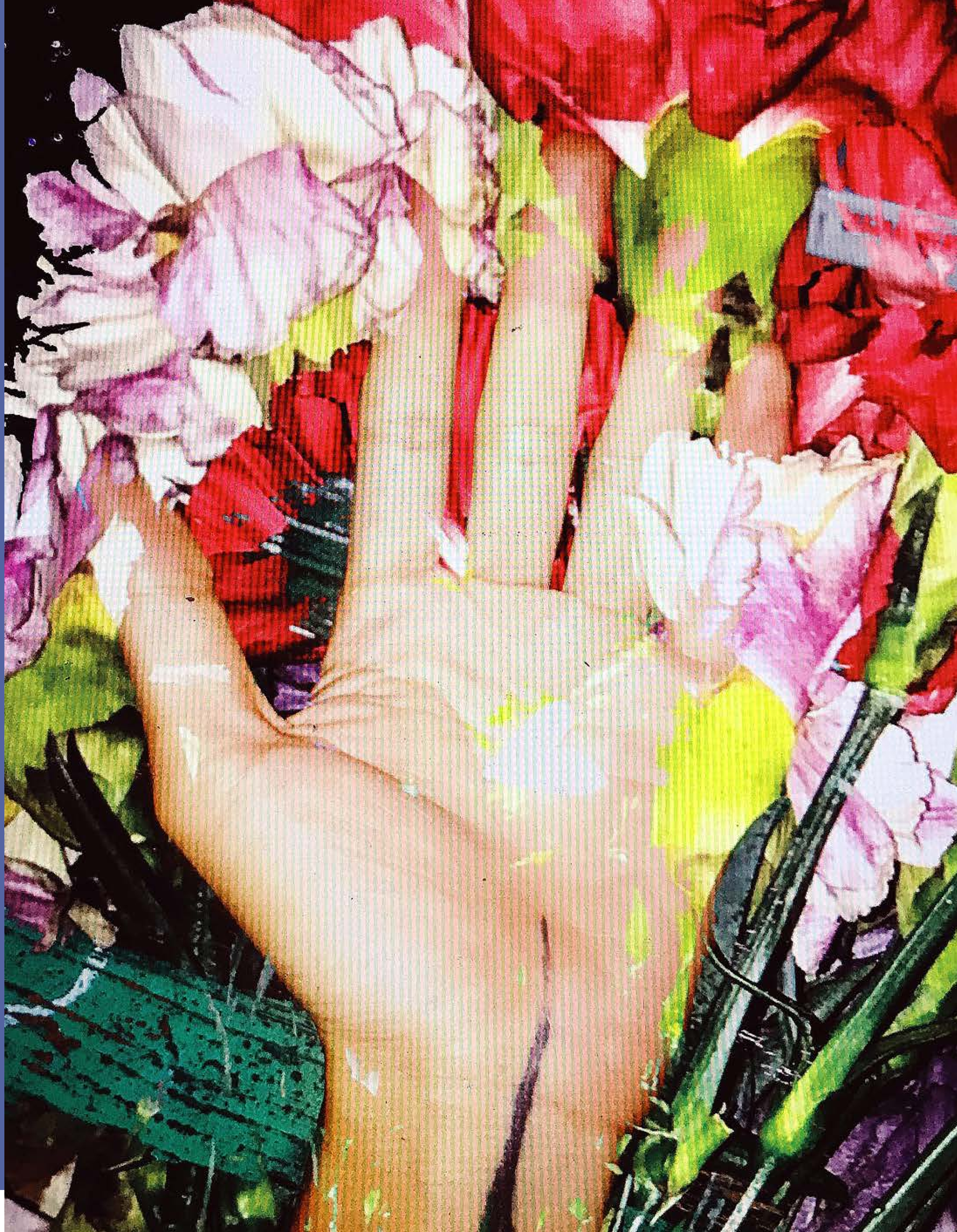
A Complex Problem Calls for New Strategies Plus the Wisdom of Our Ancestors

Credit:
Lisa Larson Walker
and Faisal Amir

By 1951, malaria was considered an eliminated disease in countries like the U.S. Over the past few decades, though, malaria cases in the U.S. have been steadily on the rise. In 2016 alone, a total of 2078 cases were reported, the highest number since 1972, which led experts to sound the alarm about potential future outbreaks.

By Stav Dimitropoulos

A major culprit in malaria's transmission is the environment. An increase in temperature, rainfall and humidity may cause malaria-carrying mosquitoes to



thrive at higher altitudes, facilitating transmission in places where the disease was previously rare. And it's not only malaria: Lyme, West Nile virus, yellow fever, and diseases transmitted by mosquito and tick bites, contact with animals, fungi, and water, are spreading fast. There is a complicated interplay between humans, animals, parasites, the habitat, society, and climate change that facilitates infectious diseases in their quest to expand their enormous reservoir of pathogens into new geographic terrains.

That complexity is why interdisciplinary approaches are eliciting trust among scientists and the community alike. An example is One Health, a concept that originated in 2004 to recognize linkages in animal and human health, but has expanded since then to embrace environmental health. Some scientists say, however, that new frameworks can help to integrate long overlooked perspectives.

One Health and other major frameworks

When the people, animals, and environment come together they make up the One Health Triad. It is a collaborative, multisectoral, and transdisciplinary approach that works at the local, national, and global level concurrently, but without losing its singlehanded focus: to achieve optimal health. So, if climate change threatens sustainability, it also threatens One Health – the one health of the environment, animals, and humans.

"Often, when we're looking at infectious disease prevention and control, it's from a very narrow focus. What One Health does is provide a framework for looking at things from a systems perspective," sometimes factoring in very indirect and subtle causes, says Lina Moses, an epidemiologist and disease ecologist at Tulane University School of Public Health and Tropical Medicine. Moses believes One Health is the most appropriate path to tackling the combined threat of climate change and infectious diseases.

It is only through interdisciplinary frameworks like One Health that climate modelers can meet up with health scientists, agrees Cecilia Sorensen, an emergency medicine physician-investigator and director of the Global Consortium on Climate and Health Education at Columbia University. "Climate modelers can tell us - with different levels of certainty or probability - what future climates could look like, but if we don't translate that into the level of granularity that we need in terms of what specific regions are going to look like, then we cannot know what to do in terms of public health preparedness," Sorensen says. Health experts, climate modelers and environmental experts need to talk to each other; only then will they translate climate models to health outcomes. They need funding to support such collaboration, Sorensen explains.

But this is only the start of what she describes as a chain reaction. "How will health and environmental agencies use that information to direct their policy?" asks Sorensen. Columbia's Global Consortium has developed its own framework, Core Competencies, to unite issues of the climate with the health sector. It's intended to guide health professionals in developing certain skills and abilities related to how health and climate interact.

EcoHealth is another major framework that examines the complex relationships between humans, animals, and the environment, and how these relationships affect the health of all three. Similarly, the Planetary Health framework seeks to understand the interrelations between human-caused disruptions of Earth's natural systems, while placing greater emphasis on human health compared to EcoHealth, although that may be changing.

Frameworks that bring multidisciplinary science to the people

In the last 20 years, transcending the boundaries of science or achieving transdisciplinarity has emerged as a new principle of scientific inquiry. Based on the mental models approach, for instance, which says that people are restricted by their mental models when interpreting new information, natural scientists from Hamerschlag University and psychologists and behavioral scientists from the University of Leeds have been working together for 15 years to develop materials that will sensitize people to the severity of climate change and inform them about mitigation methods.

Another way to reach the public is through science shops, typically housed within the facilities of a university department or an NGO. In these "shops," scientists carry out research in a wide range of disciplines on behalf of citizens and local civil society. "The shared physical space not only between scientists but between scientists and the public is very important," says Moses. "Communities help to ground scientists in what's real, what's relevant, and what's important." In fact, it's the community that defines the goals. "Success for a scientist would be the development of a new drug therapy, and the approval of that," Moses says. "But communities won't consider that successful until they start to see actual improvement in their lives, on the ground."

Single-bullet, high-tech solutions are not a magic sauce. Once you roll out a climate change solution in the real world, where you're dealing with human behaviors, economics, politics and social issues, it doesn't take long before you see the interactions with infectious disease and other frameworks, and vice-versa, suggests Moses. "And this becomes particularly challenging in historically marginalized communities." In fact, these communities sometimes harbor the best answers for streamlining these frameworks.

Time is intergenerational—a perspective rooted in cyclicality, through which the Potawatomi walk through life "together" with relatives that both passed and have yet to be born.

Looking to Indigenous perspectives – and preserving them

The pandemic found Sorensen, the physician-investigator at Columbia University, working on the Navajo reservation in the Southwest. The Navajo Nation is a Native American territory covering about 27,000 square miles, the largest land area retained by a Native American tribe in the country. By April 2021, 88 percent of the Navajo Nation's eligible population had received at least one dose of the COVID-19 vaccine, and 38 percent had been fully vaccinated – significantly more than the broader U.S. population.

"They did that because they wanted to protect their elders, so they were able to create a cultural response to COVID-19 and to mobilize as a singular identity against it," says Sorensen. Families isolated their elders with a single caregiver and restricted contact with others to protect them. "Family members would bring food and supplies to the elder's house, leave them on the front step, and wave from the window," remembers Sorensen. A strategic vaccination campaign supported these efforts, ultimately leading to a low mortality rate among the elderly. This level of engagement is an example of how Indigenous cultures have such a deep knowledge of themselves, says Sorensen.

In stark contrast to the Western, fragmented, and hierarchical relations among humans and the rest - animals and the environment – many Indigenous Peoples view humans, animals, the environment and time itself as oneness. Time is nonlinear in the Indigenous cosmotheory. The Māori, the indigenous Polynesian people of mainland New Zealand, for instance, cannot conceive the past, present and future as distinct entities, "for the past is constitutive of the present and, as such, is inherently reconstituted within the future," as outlined in a *Policy Futures in Education* paper.

In the Anishinaabemowin language of the Potawatomi, a Native American tribe of the western Great Lakes region, upper Mississippi River and Great Plains, the expression aanikoobijigan means ancestor and descendant at the same time. Time is intergenerational—a perspective rooted in cyclicality, through which the Potawatomi walk through life "together" with relatives that both passed and have yet to be born. It's a perspective that, if embraced by scientists and our frameworks, could portend greater protection for the planet for its future inhabitants.

There are around 476 million Indigenous Peoples worldwide, making up just 6 percent of the global population, but they nurture 80 percent of the world's cultural and biological diversity, occupying 20 percent of the world's land surface. "Imagine what would happen if we could get more lands in the hands of Indigenous Peoples?" asks Nicole Redvers, a naturopathic physician at the University of North Dakota, who is a member of the Deninu Kųę́ First Nation, an Indigenous First Nations band government in Canada's Northwest Territories. She is confident that Indigenous Peoples would take better care of the land if they were placed in positions of power, resulting in positive downstream effects for how the rest of society confronts infectious diseases, since protecting biodiversity decreases the risk of infectious disease.

Redvers is skeptical that One Health can really produce the diversity of perspectives it promises, though. "They say they have diverse voices, but if you actually look at the evidence in the published literature, there is no sense of incorporation of diverse epistemologies," she says. "There is currently very little under the published One Health banner with things like traditional Indigenous knowledges, for example, or being inclusive of other systems, economic, social determinants, equity and more. In addition, the field has been very much dominated with epidemiological evidence, without too much furrow into other types of spaces."

Redvers believes the Planetary Health framework has more potential, particularly because it has a better record of including diverse voices thus far. "Planetary Health was also arguably very human-centric in the beginning," Redvers says, while adding that the Planetary Health Alliance consortium recently expanded its definition to be more inclusive, beyond humans and animals, to political systems, business systems, and ecosystems – and beyond climate change to pollution and biodiversity loss, because they're all multi-connected.

In a paper in *The Lancet* in February 2022, Redvers and other authors invited a group of Indigenous scholars, practitioners, land and water defenders, respected Elders, and knowledge-holders from multiple continents to join a consensus process for defining

"There is currently very little under the published One Health banner with things like traditional Indigenous knowledges, or being inclusive of other systems, economic, social determinants, equity and more. In addition, the field has been very much dominated with epidemiological evidence, without too much furrow into other types of spaces."

– **NICOLE REDVERS**, NATUROPATHIC PHYSICIAN AT THE UNIVERSITY OF NORTH DAKOTA

the determinants of Planetary Health from an Indigenous perspective. Three overarching themes were identified: Mother Earth Level, Interconnecting Level and Indigenous People's Level. They identified ten additional individual determinants of health across the planet, such as legal designations for ancestral personhood, respect of the feminine, the modern scientific paradigm, governance, law, and Indigenous land tenure rights.

While international scholarship is increasingly looking at Indigenous People's intergenerational wisdom in its breathless fight against climate change, there is one word that ricochets across the various reports: "Knowledge, knowledge, knowledge," protests Redvers. "I often remind people that Traditional Knowledge doesn't come without the people and the people don't come without their lands, however. The biggest step that Western allies and others can take in the fight against climate change and infectious diseases is to ensure Indigenous lands are protected." These lands are integral to the worldviews that, if we embrace them, have potential to integrate our modern scientific stovepipes.

Yet, multilateral corporations, political enterprises, even conservation efforts, says Redvers, are continually moving Indigenous Peoples off their lands, which removes them from their much-cherished Traditional Knowledge. "To kill the Indian, and save the child," the program sought to assimilate Native Americans into the white educational system, led not only to inhumane and genocidal practices; it also became very dangerous for the planet, says Redvers.

Can Western scientists and Indigenous Peoples sit at the same table today? Yes, probably, but they may need to engage in some mental gymnastics beforehand. "Most contact between Indigenous communities and Western science has taken place on an exploitative and extractive basis," says Sorensen. Fostering trust and rebuilding these relationships is challenging. "The process requires Western scientists to give up a lot of power they've been taught to have, which is scary," says Moses.

Rewarding this shift may help; funding scientific projects favoring new evaluation processes for scholars, not just the type and amount of publications they generate, might be good leverage points, says Moses. Whatever path we choose, we need to adopt a new narrative, says Redvers. "But if you really think about it, it's an old narrative."

STAV DIMITROPOULOS has written for the BBC, Popular Mechanics, National Geographic, Nature, Scientific American, Fortune, Neo.Life, and more.

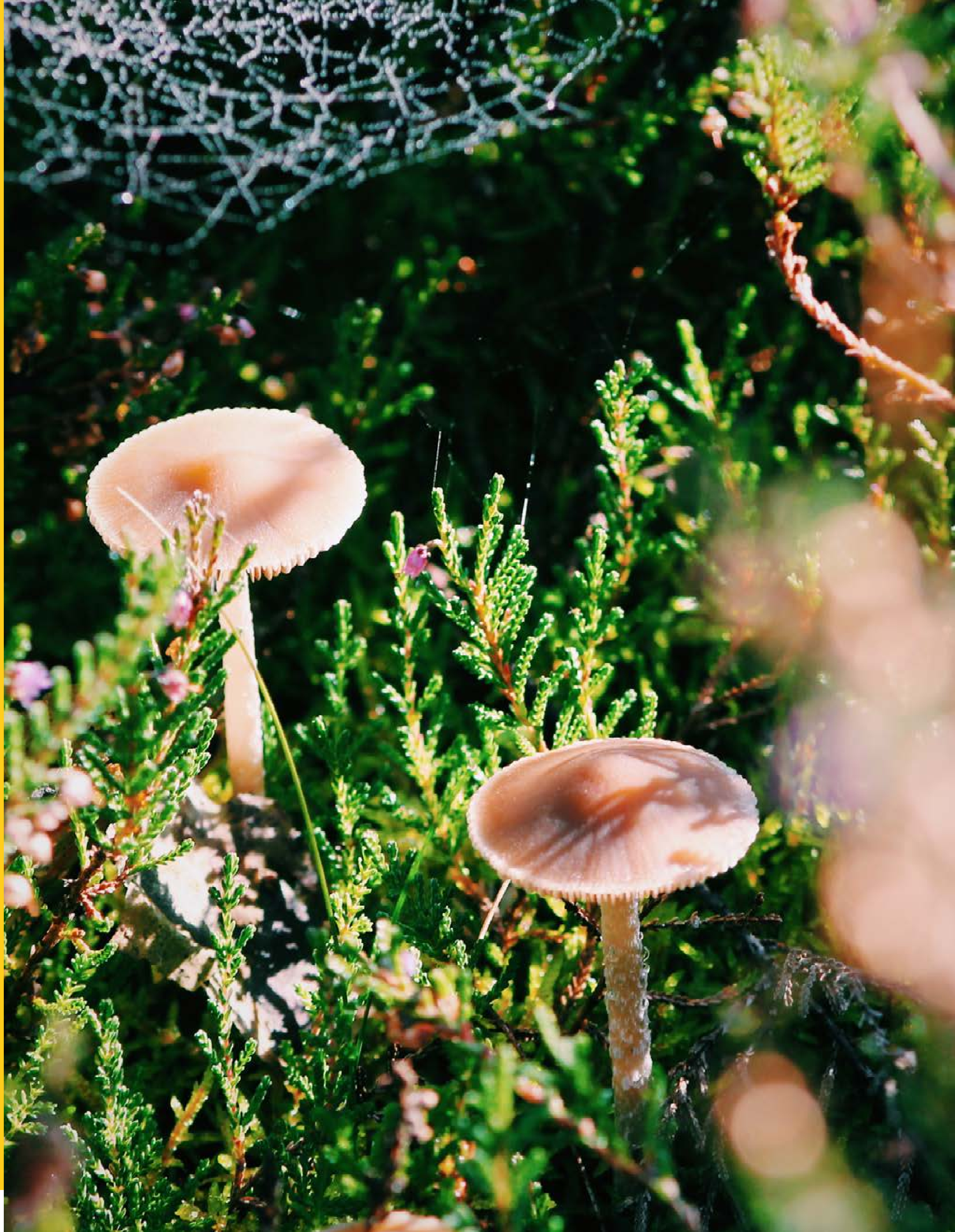
3. Microbes:

With Infections, We've Been Playing 'Pin the Blame on the Microbe.' Is It Time to Change the Game?

Credit: Erik Jan Leusink

If a doctor from the early 1900s could visit a hospital today and look at patients' lab work, some of the most common microorganisms that cause disease would be grimly familiar: *Salmonella* and pneumonia-causing *Streptococcus*. But some of the other pathogens would be surprising: for example, infections and deaths caused by the fungal species *Candida albicans* or *Cryptococcus neoformans* would certainly raise eyebrows. In fact, prevalent fungal

By Kristina Campbell

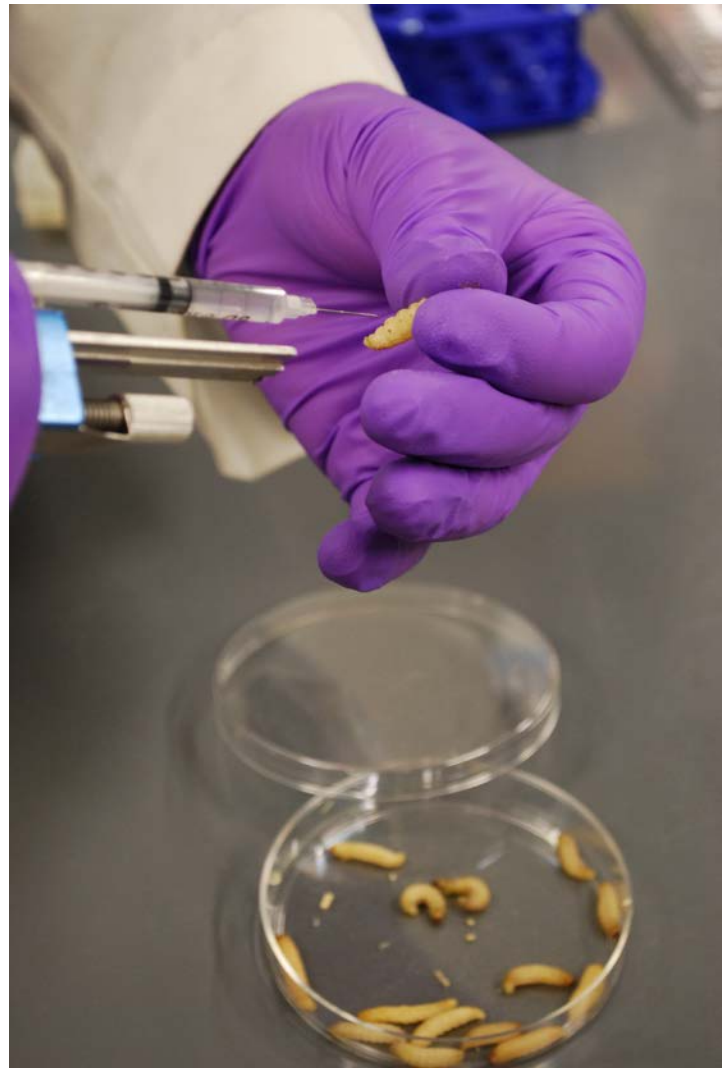


disease would be a whole new phenomenon. How did the fungi become a bigger risk to human health over time?

In the 19th and early 20th centuries, German microbiologist Robert Koch established a set of rules known as Koch's postulates that allowed scientists to determine whether a disease was caused by a particular microorganism. It seemed to allow for easy classification: either a microbe was a pathogen, or it was not. In this way, Koch advanced the germ theory of disease, essentially formalizing the rules of the game 'pin the blame on the microbe' and inviting every microbiologist in the world to play along.

Many benefits came from this approach: by focusing on microbial bad actors, Koch's postulates led to immense progress in understanding and controlling infectious diseases such as cholera and tuberculosis over the following two centuries. Yet the germ theory framework, which persists to this day, falls short when it comes to understanding changes that occur in the ability of microorganisms to cause disease.

The planet, and all creatures dwelling on it, are covered in microorganisms—an estimated one trillion different species. Although just a tiny minority of these microbes cause disease in humans, climate change means we can count on a growing number of them becoming problematic for our health. Understanding these infections through the limited lens of germ theory is no longer adequate, so scientists are working on new frameworks and research areas that focus on the relationships microbes have—with other microbes as part of complex ecosystems, and with other ecosystems—that lead to health or disease outcomes.



ABOVE: Daniel Smith injecting *Galleria mellonella*. Credit: Quigly Dragotakes

It is only by focusing on these relationships—and where they go wrong—that scientists will succeed in supporting human health through a changing climate.

Caution: more infectious disease ahead

Global reports, including those of the Intergovernmental Panel on Climate Change, have documented an increased risk of infectious disease as the climate warms. Transmission of dengue fever and tick-borne diseases, for example, as well as diarrheal disease, are increasing in many areas of the world. In addition, the latest models predict a heightened threat from novel pathogens, as many species of wildlife expand their range and interact with unfamiliar species, providing opportunities for viruses to mutate and spill over to human populations.

With climate-driven changes in infectious disease, scientists are faced with more difficulty fitting various microorganisms into the discrete categories of pathogenic and non-pathogenic. Some microbes, in trying to survive in a changing climate, gain a new ability to cause disease in a particular host. Arturo Casadevall, a microbiologist and immunologist at Johns Hopkins Bloomberg School of Public Health, has published a paper on the emergence of fungal diseases in humans and other mammals, hypothesizing that not only does climate change bring mammals into contact with fungi they never would have encountered, but it also provides impetus for the fungi themselves to become more tolerant to higher temperatures, allowing them to survive at human body temperature and cause infection. "The world's getting warmer," says Casadevall. "The microbes are adapting. That's a prescription for trouble ahead."

All of this means we may be headed toward an era dominated by infectious diseases and future pandemics—in the words of science writer Ed Yong, a

Pandemicene. A key task for scientists, then, is to stay on top of the shifting contributions of specific microorganisms to infectious diseases, so surveillance and control strategies can be deployed in a timely manner.

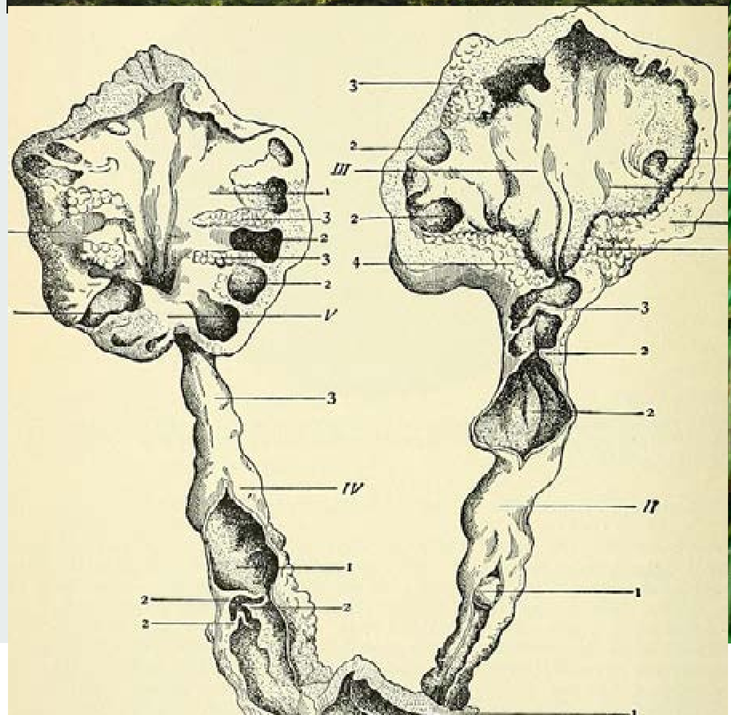
From pathogen to pathogenic potential

In the microbiology textbooks, 'pathogen' is a label for a microbe that causes disease using a number of genetically-encoded strategies called 'virulence factors.' But Casadevall says this classic definition fails to clearly convey that disease is a shared responsibility between the pathogen and the host that harbors it. He says, "No microbe can be a pathogen without a susceptible host. Trying to define a pathogen based on microbial characteristics is doomed to fail."

Casadevall advanced the idea of pathogenic potential in a 2017 paper, attempting to capture the likelihood that a microbe will cause disease in a particular host. The pathogenic potential equation takes into account the dose of the microorganism that's required to cause disease in the host, since this quantity of 'inoculum' matters as much as, or more than, the presence of virulence factors. "For organisms that are non-pathogenic," says Casadevall, "if you increase the inoculum you can still kill the host."

Recently, Casadevall's postdoctoral fellow, Daniel Smith, provided a proof-of-concept by testing the pathogenic potential of various fungi and bacteria in moths. He confirmed that certain species and amounts of the microorganisms led to sometimes-unpredictable host symptoms. In one case, to his surprise, higher initial doses of a fungus ended up reducing its pathogenic potential in the moths.

Smith also took inspiration from a recently published study to calculate the pathogenic potential of the infamous pandemic virus, SARS-CoV-2, which causes COVID-19 in humans. He confirmed quantitatively that its pathogenic potential was high, since the virus was shown to cause symptoms in 89 percent of participants who were inoculated with just 10 virions (or viral particles). The formula captures the nuances of the virus's ability to cause disease, since SARS-CoV-2 was not strictly a pathogen for the 11 percent of people who experienced no symptoms.



A human walking in a forest can be seen as a set of nested ecolo-systems: microbiomes inside the body and on the skin, moving through a forest ecosystem, which is in a biosphere, in the overall planetary ecosystem.

ABOVE:
Daniel Smith holding a plate of *Cryptococcus neoformans*.
Credit: Quigly Dragotakes

Margaret McFall-Ngai, an animal biologist and biochemist based at Carnegie Institution for Science, agrees the give-and-take of microbe-host relationships are key to understanding the true causes of disease. Having shown in her own work that a host can interpret bacterial signals in different ways, she says, "A given microbe may be a pathogen in one circumstance and a mutualist in another. Pathogenesis is context-dependent and depends on the outcome."

A microbiome movement

The idea that pathogenicity depends on a two-way 'conversation' between a host and a microbe aligns with a broader movement in microbiology that puts the spotlight on the relationships of microbes with other biological entities. Scientists in the field are increasingly drawn to studying microbiomes, which are mixed microbial communities occupying specific habitats. Studies on microbiomes have increased exponentially over the past two decades as improvements in next-generation gene sequencing technologies have allowed scientists to take 'snapshots' of an entire microbial community at any point in time.

"Microbiome science is a relationship science," says Nicole Redvers, an Indigenous health researcher from the University of North Dakota School of Medicine & Health Sciences. "It's all of the organisms that we host, in relationship, as a part of our living and being." Redvers says Indigenous worldviews have long held the natural world as interconnected and dependent, with humans as only one part of it. For some people, the microbiome may be an entrée to this powerful idea. She says, "We've forgotten that we have ecosystems inside of us that are microbial. Thinking through that relationally helps people understand the connections to the broader environment of microbes that we swim in every day."

This means a human walking in a forest can thus be seen as a set of nested ecosystems: microbiomes inside the body and on the skin, moving through a forest ecosystem, which is in a biosphere, in the overall planetary ecosystem. Acknowledging these connections means no microorganism—not even one that causes disease—can possibly act alone. Rather, microorganisms operate according to the constraints and opportunities offered by fellow microbes, which in turn are influenced by successively larger ecosystems. A disturbed environmental ecosystem (triggered, say, by climate change) could conceivably alter normal microbial exposures for humans, who could experience disturbed gut microbial ecosystems that make them less resilient to infections. An ecosystem-focused perspective makes it easier to see how a pathogen's ability to cause disease could depend, in part, on the microbiome it encounters in a host. Scientists have demonstrated this with *Clostridioides difficile* diarrhea, which is an increasing problem in hospitals globally. *C. difficile* bacteria often exist peacefully in a healthy digestive tract, but when the gut microbiome is disturbed by antibiotics, the bacteria take the opportunity to expand and cause serious illness in the human host.

Resilience through relationships

The good news is that seeing disease-causing microbes in the context of microbiomes and larger ecosystems could help humans become more resilient to infections while the climate changes.

When it comes to developing strategies for disease control, a 2019 consensus statement on microorganisms and climate change, as well as a more recent climate change report from the American Society for Microbiology, both highlighted the need to understand more about microbial community ecology. Rick Cavicchioli, an environmental microbiologist at University of New South Wales in Australia and first author of the consensus statement, says, "A very important aspect of the microbiology is to ask, if I push here and I perturb the ecosystem like this, what's going to be the flow-on effect?” By acquiring more basic knowledge of microbial ecosystems, and using observations from natural environments, scientists can determine the positive or negative effects of perturbations on a specific host all the way up to large, complex ecosystems.

To take one example relevant to humans, microbiome scientists are experimenting with diet-driven shifts of the gut microbiome that increase or decrease the host’s resistance to disease-causing microbes. Dietary fibers encourage the growth of diverse microbes in the colon, successfully shifting the ecosystem and reducing the ability of disease-causing microbes such as *C. difficile* to take up residence. Casadevall sees a future where scientists input scientific knowledge about each microbe and host to yield probabilities for how novel microorganisms might cause disease—akin to a weather forecast. Smith adds that studying how fungi in the environment adapt to climate-induced temperature changes will also be important, to get a heads-up on how they may increase their pathogenic potential for human hosts. Various mammals and individual people, too, can be studied to determine whether they are becoming more hospitable to fungi, perhaps through changes in their microbiomes.

Doubling down on this science could help us address the threat of disease-causing microorganisms across the globe in an era of climate change. But above all, it’s a change in perspective from ‘pathogen’ to ‘microbial relationships’ that will open our eyes to solutions that leverage the entire biological context—ecosystems within ecosystems—for increasing human resilience to infectious disease.

KRISTINA CAMPBELL covers microbiome science and biotechnology for media throughout Europe and North America.

She is co-author of *Gut Microbiota: Interactive Effects on Nutrition and Health*, published by Elsevier, with a second edition forthcoming.

Kristina currently lives in Victoria, Canada.

“No microbe can be a pathogen without a susceptive host. Trying to define a pathogen based on microbial characteristics is doomed to fail.”

– **ARTURO CASADEVALL**, MICROBIOLOGIST AND IMMUNOLOGIST AT JOHNS HOPKINS

4. Spillover:

Climate Change and the New Pandemic Age

When West Nile virus arrived in New York in the summer of 1999, most likely hiding in a mosquito stowaway on a plane landing at JFK or in the bloodstream of someone already infected, the scorching temperatures helped the deadly pathogen gain a foothold in North America. That summer had been unusually hot and dry in New York—the hottest July on record at that time—and by mid-August, there were 10 days over 100 degrees, followed by heavy rains, and flooding. These weather conditions created the perfect incubator for the populations of *Culex pipiens*, the common house mosquito that transmits West Nile, to explode.

Credit: Pete Hudson

By Linda Marsa

Reports started appearing in the press that there was some kind of bird plague spreading through northern Queens, not far from the airport, and that local sanitation workers and highway cleaning crews

were finding hundreds of dead robins and crows on sidewalks, in parks and city streets. By Labor Day, whatever killed the crows was infecting humans, too: a family physician at Flushing Hospital Medical Center, in Queens, had a cluster of five elderly patients in the intensive care unit who were deathly ill from a mysterious neurological disease that was causing encephalitis. They seemed confused, complained of headaches and severe gastrointestinal pain, and experienced muscle weakness and fevers as high as 103 degrees.

Routine diagnostic tests hadn't been able to identify the culprit because West Nile virus had never been seen before in the Western Hemisphere. But we now know that bird species, depending on the local ecology, can be the primary hosts of this deadly pathogen, which is transmitted when a mosquito bites an infected bird and then delivers its lethal payload to humans.

First identified in the West Nile district of Uganda in 1937, the virus is fairly common in Africa, West Asia and the Middle East. But climate driven changes in the ecosystems of disease vectors, like mosquitoes—which can now survive in newly temperate regions—along with large increases over recent decades in international travel on a hotter, wetter planet, have created the perfect conditions for greater transmission of these deadly microscopic invaders from remote rural areas to industrialized nations. When another hot, dry summer hit in 2002, West Nile tore through the U.S. and into Canada. West Nile is now entrenched in the continental U.S., with every state reporting infections.

ABOVE: Devin Jones, PhD. student and member of Raina Plowright's research team, in Australia untangles a black flying fox from a net so that the animal can be anesthetized, after which the researchers collect samples and then release it. Credit: Manuel Ruiz Aravena.

SPILL*BACK*

Spill**over** occurs when disease-causing microbes travel from one species into another, but spill**back** can be equally dangerous. Also known as reverse zoonosis, spillback happens when people spread an agent of disease back to animals. Once these microorganisms have been passed to animals, they can spark pandemics among wildlife, cross over to multiple species and harm entire ecosystems. They can also mutate in the bodies of animals, evolving into strains that can then re-infect humans with greater wrath, becoming much deadlier than their predecessors. Notable examples of spillback include Ebola, tuberculosis and yellow fever.

Throughout history, we've had what are called spillover epidemics of zoonotic diseases, when deadly viruses or bacteria leap from their traditional hosts in animals to humans. Records of plagues date back more than two millennia, ravaging ancient civilizations like Egypt, Greece, India and China. More than 60 percent of the most lethal pathogens have originated in animals, including smallpox, cholera, influenza. The biggest killer of them all, the bubonic plague, carried by rats infected with the bacteria Yersinia pestis, swept through Europe in the mid-14th century, killing 34 to 50 million people—up to half the population.

But the pace of spillover is accelerating, according to recent studies, and we're seeing the emergence of new diseases for which we have no natural immunity. The list of potential miscreants includes West Nile, Zika, Ebola, HIV, Marburg virus, SARS and, of course, COVID-19, which most likely originated somewhere in southern China, Laos or Vietnam, before it made itself at home in horseshoe bats. No one really knows precisely how the SARS-CoV2, the virus that causes COVID-19, first made the jump from its animal host to humans but it infected enough people in Wuhan, China for the world to finally notice.

Several factors are ushering in what experts are calling a new pandemic era. Soaring temperatures create more hospitable conditions for the incubation and spread of infectious pathogens and expand the range of vectors that carry diseases. Intensive agriculture, global urbanization and a dramatically changing climate are pushing wildlife out of their natural habitats, causing more interaction between animals and humans in increasingly dense cities.

We saw this play out in 1998, when the Nipah virus, which is fatal in 40 percent of cases, spread through Malaysia. It took years for researchers to piece together the chain of events that led to this spillover event: flying foxes, a type of bat, were the culprits. As their habitat was destroyed by climate change and urbanization, the bats lost their traditional food sources. The stress and hunger weakened their immune systems, increasing their viral load and prompting a lot of virus to spill out in their saliva urine. The starving animals were forced to migrate closer to urban areas in search of food.

When animals are driven out of their natural environments, they're often in poorer health because of the stress. "If they're sicker, they shed more virus," says Colin Parrish, a virologist at Cornell University, "so there's more opportunity for things to be shared in different species."

"Climate change is a huge trigger," says Raina Plowright, a disease ecologist who also works at Cornell. "And we're going to see more of this."

Mammals and birds alone harbor about 1.7 million viruses, and that number doesn't include other pathogens, like fungi and bacteria, that can also make us very sick. But few of them pose a serious threat. Scientists are now trying to decipher which traits explain why some viruses make the hop into humans, and others do not. In most instances of human spillover, the infections are a dead end and don't spread beyond that initial individual.

For a new virus to trigger an outbreak, it has to surmount numerous obstacles, and a whole array of factors need to align. The chain of transmission ranges from simple geography—the viruses must be in close proximity to humans and shed at a specific time—to whether they are biologically compatible. In other words, can they actually establish an infection in the new host, namely us? The SARS-CoV-2 virus, for instance, was especially adept at this, and its surface is studded with molecular hook proteins that enable it to latch on to human cells. What's more, SARS-CoV-2 is an RNA virus, a class of viruses that are notorious shape shifters and constantly mutate, which in turn creates more variants and more possibilities of infection.

The crucial step is what happens after a pathogen infects its initial spillover host. If it can be transmitted from there, and cause an outbreak in a new host population, then it is on the pathway to becoming an epidemic. But it's difficult to predict which pathogen can circumvent all these hurdles. "When you have 20,000 potential hosts, probably a million viruses and 50 different environments, can we predict what it is going to do next?" observes Parrish. "How is it going to interact with the new host? Will it be able to establish infections? Will it be able to replicate and spread?

We have a problem we should be approaching in a holistic way."

Plowright is one of the principal investigators on a global research team, which includes a network of scientists from universities and labs in North America, Europe and Australia, that is trying to decipher the mechanisms that prompt viruses that originate in bats to infect humans. Understanding what makes bats excrete the deadly pathogens could shed light on ways to prevent spillover.

In the initial research phase, scientists such as Plowright collected samples from bats in Asia, Africa and Australia (there are more than 1,400 bat species in the world). Bats normally shed viruses through urine or droppings, which can sicken humans who come in contact with these droppings more often due to loss of habitat from climate change or urbanization.

"We're testing hundreds of animals—taking blood and urine samples, putting on GPS tags to see where they move," says Plowright. "We're looking for patterns, such as changes in temperature, rainfall or the availability of food, that may drive the excretion of viruses. And there is definitely a climate signal, with

ABOVE: Bats fly near their roosting places at dawn, when they return from foraging during the night. Credit: Tamika Lunn.

"When you have 20,000 potential hosts, probably a million viruses and 50 different environments, can we predict what it is going to do next?"

– **COLIN PARRISH**, VIROLOGIST AT CORNELL UNIVERSITY

an interaction between extreme climate events and the loss of crucial habitats."

In fact, changing weather patterns amplify and accelerate these opportunities for human populations to mingle with entirely new pathogens and resulting spillovers. Recent research indicates that climate change may make these uncute-meets happen much more frequently as the temperature rises, forcing animals to migrate to more hospitable environments, according to a disturbing April 2022 study in nature. In a massive computer simulation, two Georgetown University researchers built a model of potential spillovers that mapped out how more than 3,100 mammal species would change their ranges as the world heats up.

What they found was in the next several decades, we'll see at least 300,000 first encounters between species that don't normally interact. This could open up entirely new pathways for viruses to infect new hosts, and result in about 15,000 spillovers when these pathogens enter humans.

These new connections happen as animals lose their natural habitats, an unfortunate byproduct of the explosive growth of cities and more frequent and intense weather events as the world heats up. Floods, fires, hurricanes and drought destroy land and trigger the migration of millions of displaced populations to new regions.

"The one unifying feature in emerging infectious diseases is that they're all, in one way or another, associated with habitat loss," says Sarah Zohdy, a disease ecologist in the School of Forestry and Wildlife Sciences and College of Veterinary Medicine at Auburn University. "When you chop up the rain forest into different, isolated fragments, you create mini-islands of ecosystems, and the ecology changes because of that. And each fragment produces a different viral strain so you have ten times the number of variants and more potential variants that can spill out into human communities."

The spread of Lyme disease across the U.S. is a case study in how this happens, according to Zohdy. First identified in Connecticut in the mid-1970s, the tick-borne disease emerged in an area where the forests had been cut up for subdivisions, creating what scientists call fragmented landscapes. Normally, these forests were teeming with wildlife—rodents, possums, foxes and owls. "But these fragmented forests were so

LEFT: Raina Plowright, a disease ecologist at Cornell University, is testing hundreds of animals—taking blood and urine samples, and putting on GPS tags to see where they move. Credit: Kelly Gorham.

> **“The one unifying feature in emerging infectious diseases is that they’re all, in one way or another, associated with habitat loss.”**
>
> – **SARAH ZOHDY**, DISEASE ECOLOGIST AT AUBURN UNIVERSITY

small, the only animals that could survive were white-footed mice—they’re like petri dishes for white-footed mice, which are the main hosts of the bacteria that causes Lyme,” says Zohdy.

Young ticks feed on the infected mice, pick up Lyme and then spread it to humans they come in contact with. “When a habitat is more diverse, you get less chance of spillover because of the dilution effect: having more species dilutes that opportunity for Lyme to escape into the human populations,” says Plowright, the disease ecologist at disease ecologist at Cornell. “But we’ve found with fragmented habitats, when the natural predators die off, at the perimeter, you have much more interface between animals and people and you get the most spillover.”

Lyme disease is now the number one vector-borne disease in the U.S.. It’s incidence has doubled since 1991 and now affects nearly 300,000 annually. The hardy blacklegged ticks that spread the Lyme-causing bacteria, called Borrelia burgdorferi, thrive in heat, and have already taken up residence along the Canadian border thanks to rising temperatures. To prevent more zoonotic epidemics like this, Plowright and her colleagues are calling for the establishment of policy directives that manage, regulate and protect forests and wilderness areas in order to interrupt what Plowright calls “the full zoonotic pathogens’ cascade of ‘infect-shed-spill-spread’ that happens after habitat loss. Restoring habitats is a clear way to stop spillover.” To better predict who and where the bad actors are, scientists are devising surveillance systems for global hot spots where pathogens are most likely to make the jump from animals to humans. Computer modeling tools are critical as well. Jonna Mazet, an epidemiologist and disease ecologist at the UC Davis School of Veterinary Medicine, and her colleagues, devised an interactive web tool, SpillOver, a risk assessment model to evaluate the zoonotic spillover and spread potential of new viruses found in wildlife. Using data from testing more than half a million samples from nearly 75,000 animals, they identified 31 factors that pertain to animal viruses (how they are transmitted), to their hosts, and to the environment (human population density, frequency of interaction with hosts, urbanization and deforestation).

They ranked the spillover potential of 887 wildlife viruses. Not surprisingly, SARS-CoV-2 ranked in the top twelve, although several newly detected wildlife viruses ranked higher. The hope is that the resulting watchlist of potential troublemakers can serve as an early warning for public health ministries to contain these emerging diseases. “Even though the COVID pandemic was incredibly devastating, it could have been so much worse if the virus was more deadly,” says Mazet. “I am worried because it’s human nature to go back to business as usual. If that happens, we’ll be sitting ducks for the next one. But if people are more proactive, we’ll be in much better shape.”

LINDA MARSA is an award-winning Los Angeles science journalist and author of *Fevered: Why a Hotter Planet Will Harm Our Health*. She is currently working on a book for Random House on the history of public health.

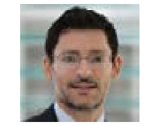
5. An Exclusive Interview with Raina Plowright, Disease Ecologist at Cornell:

What's Better than a Swift Response to Pandemics? Preventing Them in the First Place

By Matt Fuchs

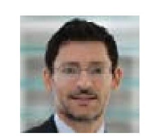
Leaps.org had a chance to speak with Raina Plowright, a Cornell Atkinson Scholar and Professor in the Department of Public and Ecosystem Health at the College of Veterinary Medicine. Plowright researches pandemic prevention through a holistic approach that focuses on how pathogens, or disease-causing microbes, get transmitted between species, a process known as spillover, and the connections between land-use change and spillovers, among other areas. She is a fellow of the American Association for the Advancement of Sciences. Read her full bio here.

This conversation was lightly edited by *Leaps.org* for style and format.



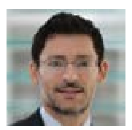
Matt Fuchs: You made wonderful contributions to this special magazine issue in Linda Marsa's article on spillover. You're a very accomplished disease ecologist. How did you develop such a passion for this field?

Raina Plowright: I was very fortunate to train as a veterinarian and start working in practice when I was relatively young. That gave me many opportunities to explore other career avenues. I always wanted to do research and something related to conservation, but I wasn't sure about the pathway. I went to U.C. Davis to do a PhD in epidemiology. While I was there, I thought that given I was interested in wildlife, I should take some courses in ecology. I just couldn't believe this whole field existed and I didn't know about it. I found my passion and how my mind works. As a veterinarian, as a medical professional, I was trained to think in a very logical progression of steps. That is a very useful style of thinking, but it's so different from ecology, where you have every piece of complexity thrown at you. You're trying to figure out how all of these processes, from molecular scales within the cell all the way to the global climate, interact at the scale of landscapes to create patterns and processes. And everything's changing in space and time. It's really exciting. I became a disease ecologist when I learned that pathogens like viruses are an important part of that complexity.



MF: I've heard you talk about your "long road to bats." They're fascinating animals. They show remarkable immunity to the negative effects of the viruses that they harbor, such as inflammation. Is that what makes them perfect hosts for diseases? Do they have special powers?

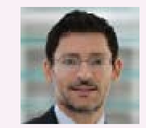
RP: They really do. They are such unusual creatures. Whereas birds have hollow bones, bats are mammals without that same light structure. It takes quite a lot of effort to get themselves up in the air and then sustain flight. They have to have extremely high metabolic rates, like 16-fold their resting metabolic rate. And even more interesting is they must sustain that metabolic rate for long periods of time. Some bats can fly for hundreds of miles during a migration. It's not really understood why, but it comes back to this potential DNA repair mechanism to withstand the effects of oxidative stress. Their bodies should be under this oxidative stress with free radicals interfering with cell processes. They have these mechanisms to withstand that. It could tie in with their ability to host infectious diseases without getting sick.



MF: What's the latest understanding of what makes bats excrete deadly pathogens? And how could that knowledge help with preventing spillovers?

RP: There's a lot that we need to learn. It's a really important area. There's this whole suite of processes that lead to the pathogen leaving the bat and entering the human population. Firstly, these bats have to be infected, and they have to be shedding virus at levels that are large enough to produce a dose that can infect another species. Often we see that happening when they are stressed. For example, with our field studies, we go back to the same populations again and again. We take samples and look for virus. We then calculate how much virus there is at every point in time and space, and we often have real difficulty finding these viruses. They're often not there at all or they're at very low levels. And then all of a sudden, we'll go back to the field site and we'll see a lot of virus.

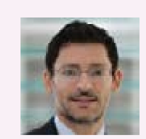
Those periods coincide with when the animals are stressed. For example, they don't have enough food to eat. It could be from loss of habitat that provides the food, or extreme climatic events that change food availability, or a whole suite of different reasons. So there has to be this excretion of virus but then there has to also be a contact with another species. We think the coronaviruses are probably entering the human population through an intermediate host.



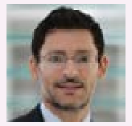
MF: What's the latest status of your research on these phenomena? Are you on the ground collecting the samples?

RP: Yes, we're on the ground, in the field trying to understand how the ecology of these systems works. How are the bats interacting with the environment? How is land use change and environmental change [altering] the way the bats behave, where they locate, what they eat, how they could potentially come in contact with humans, and how they're excreting these viruses?

We're collecting information on the bat ecology and how they're interacting with the environment. So the immune system of the bat is the nexus between the environmental stressors that they're experiencing and the viruses that they're harboring. So if the immune system is affected by the environment, then that can lead to the shedding of these viruses into the environment. We're really trying to understand that and we're doing that by collecting a lot of samples when bats are in good conditions and poor conditions. And by comparing those samples, we're trying to understand what's different and the different circumstances.



MF: Some researchers have proposed the idea of editing the genomes of bats as a way of preventing future coronavi-



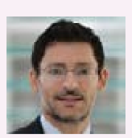
MF: rus pandemics. What would you say to those experts? It seems awfully risky to contemplate since no one knows how eliminating coronaviruses would affect bats.

RP: It's interesting how humanity always wants a technological fix to a problem, when sometimes the answer is actually really simple. So my answer is no, that would be silly and not feasible, not logistically possible with all sorts of potential unintended consequences. I think we can forget that one.

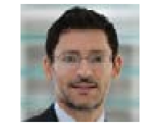
"I wish we could understand the ecology of all these systems before we destroy them."

– **RAINA PLOWRIGHT**, DISEASE ECOLOGIST AT CORNELL UNIVERSITY

What needs to be done is relatively simple, but the actual implementation of the solution is probably extraordinarily complex, because it would involve changing people's behavior. We think biology is complex, but human behavior is way more complex. What we're understanding is that land use change and environmental stress are the major drivers of these pathogens leaving animal communities and entering human communities. If you think back to the beginning of this pandemic, what are the processes that drove that virus out of the bat into humans? Well, anything that brings people into contact with bats, such as building roads that fragment landscapes. It's the constant encroachment on natural habitats by humanity that leads to situations like bats having to seek food in human environments. It's actually the biggest challenge of our times because the same kinds of things we need to do to stop spillover are also the things we need to do to preserve biodiversity.

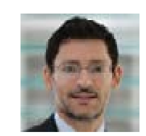


MF: Tyler Cowen, an economist at George Mason University, wrote a recent op-ed arguing that we need to be more willing to disrupt current animal habitats when developing infrastructure for wind or hydroelectrical power.



MF: Building wind turbines, for example, often leads to the death of many birds, but he says that's an acceptable loss in order to support the supply of green energy over the long-term, which would end up benefiting birds, humans and many other creatures. Is there any legitimacy to his thoughts on these tradeoffs?

RP: I certainly think there are going to be tradeoffs in any approach that we take. But I would hope that we really understand those tradeoffs. For example, if we're allowing a species of bird or bat to succumb to wind turbines, we should understand the implications. Maybe that bat is the only species that pollinates a type of tree, and that could affect the whole ecosystem in profound ways. I wish we could understand the ecology of all these systems before we destroy them. For pathogens, we often don't even know what the reservoir host is. [Reservoir hosts are species that maintain a pathogen and become a source for infecting other animals, including humans.] All we see is the pathogen in the human community. For example, we don't know which bat is the reservoir host for Ebola. We just know that we see deadly outbreaks in humans, and evidence suggests bats are the reservoir.



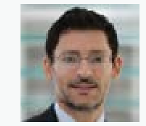
MF: In a paper published in *Nature* on May 19th, you and your co-authors focus on the incredibly important goal of preventing the spillovers that can result in human infections. How much success have you had in getting government, politicians and other influential actors to support research related to preventing infectious disease in the first place? These "steady state" prevention efforts seem almost invisible compared to efforts to respond to outbreaks, which get the limelight once a pandemic is in full swing.

RP: That is so true. If we prevent the spillover event, the entire outbreak wouldn't have occurred. But if nothing happens over many years, it becomes really hard to maintain the funding to keep that prevention going. Policymakers will say, “Why invest in this problem?” There's this fundamental shift that needs to happen in society: we need to become proactive and not reactive. Fantastic social scientists are probably thinking about this problem. It's extremely hard. And spillover is really forgotten. It's not studied. The beginnings of a pandemic are very poorly understood, possibly because they happen within an ecological context and involve huge complexity, including interactions with climate, land use, and human behavior. Few groups tackle these kinds of difficult problems. It takes big, well-coordinated, well-funded teams of scientists. Scientific funding bodies tend to value focused research in systems reduced to their simplest components like cells or knockout mice, not complex problems that require investigation at landscape scales.

There's not a lot of investment in trying to understand ecology, so it's often poorly understood. There is rarely a financial benefit from ecological research. There's no licensed vaccine or therapeutic as a result of the research. The research is purely for society's good. There isn't a drive or motivation in the biomedical community to focus on what's happening in the ecology of these systems. I think that needs to change.

“There's a lot we need to learn. There's this whole suite of processes that lead to the pathogen leaving the bat and entering the human population.”

– **RAINA PLOWRIGHT**, DISEASE ECOLOGIST AT CORNELL UNIVERSITY



MF: I wish you all the best with this critical research and with your recent move to Cornell. Thank you for sharing your thoughts and your work for the magazine.

RP: Thank you. It's been really fun talking with you.

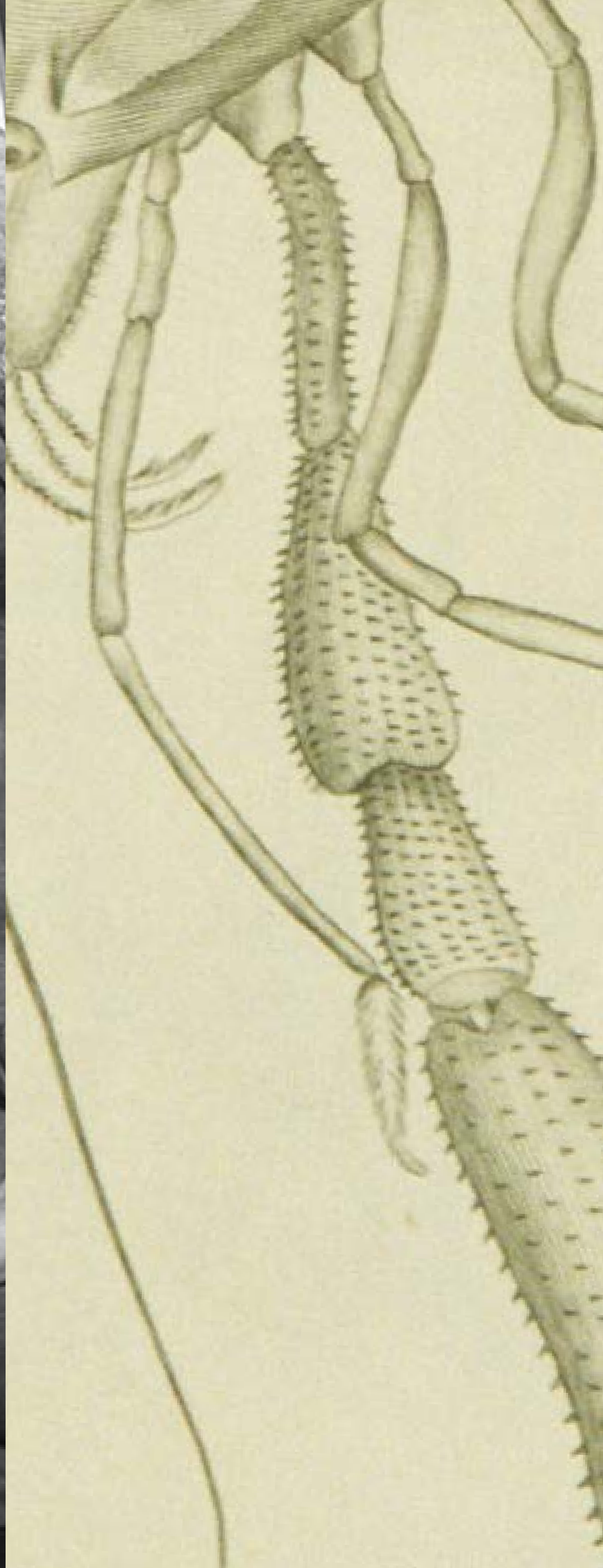
MATT FUCHS is the editor-in-chief of Leaps.org. He is also a contributing reporter for the Washington Post and a contributor to Time Magazine with other bylines in the New York Times, WIRED Magazine and the Washington Post Magazine. You can Follow him @FuchsWriter and Leaps.org @Making-SenseofScience

6. Animals, Plants & Crops:

Which Ones Will Survive in a Changing Climate?

By Temma Ehrenfeld

Along the west coast of South Florida and the Keys, Florida Bay is a nursery for young Caribbean spiny lobsters, a favorite local delicacy. Growing up in small shallow basins, they are especially vulnerable to warmer, more saline water. Climate change has brought tidal floods, bleached coral reefs and toxic algal blooms to the state, and since the 1990s, the population of the Caribbean spiny lobster has dropped some



20 percent, diminishing an important food for snapper, grouper, and herons, as well as people. In 1999, marine ecologist Donald Behringer discovered the first known virus among lobsters, *Panulirus argus virus*—about a quarter of juveniles die from it before they mature.

“When the water is warm PaV1 progresses much more quickly,” says Behringer, who is based at the Emerging Pathogens Institute at the University of Florida in Gainesville.

Caribbean spiny lobsters are only one example of many species that are struggling in the era of climate change, both at sea and on land. As the oceans heat up, absorbing greenhouse gases and growing more acidic, marine diseases are emerging at an accelerated rate. Marine creatures are migrating to new places, and carrying pathogens with them. The latest grim report in the journal *Science*, states that if global warming continues at the current rate, the extinction of marine species will rival the Permian–Triassic extinction, sometimes called the “Great Dying,” when volcanoes poisoned the air and wiped out as much as 90 percent of all marine life 252 million years ago.

Similarly, on land, climate change has exposed wildlife, trees and crops to new or more virulent pathogens. Warming environments allow fungi, bacteria, viruses and infectious worms to proliferate in new species and locations or become more virulent. One paper modeling records of nearly 1,400 wildlife species projects that parasites will double by 2070 in the far north and in high-altitude places. Right now, we are seeing the effects most clearly on the fringes—along the coasts, up north and high in the mountains—but as the climate continues changing, the ripples will reach everywhere.

Few species are spared

On the Hawaiian Islands, mosquitoes are killing more songbirds. The dusky gray akikiki of Kauai and the chartreuse-yellow kiwikiu of Maui could vanish in two years, under assault from mosquitoes bearing avian malaria, according to a University of Hawai'i 2022 report. Previously, the birds could escape infection by roosting high in the cold mountains, where the pests couldn’t thrive, but climate change expanded the range of the mosquito and narrowed theirs.

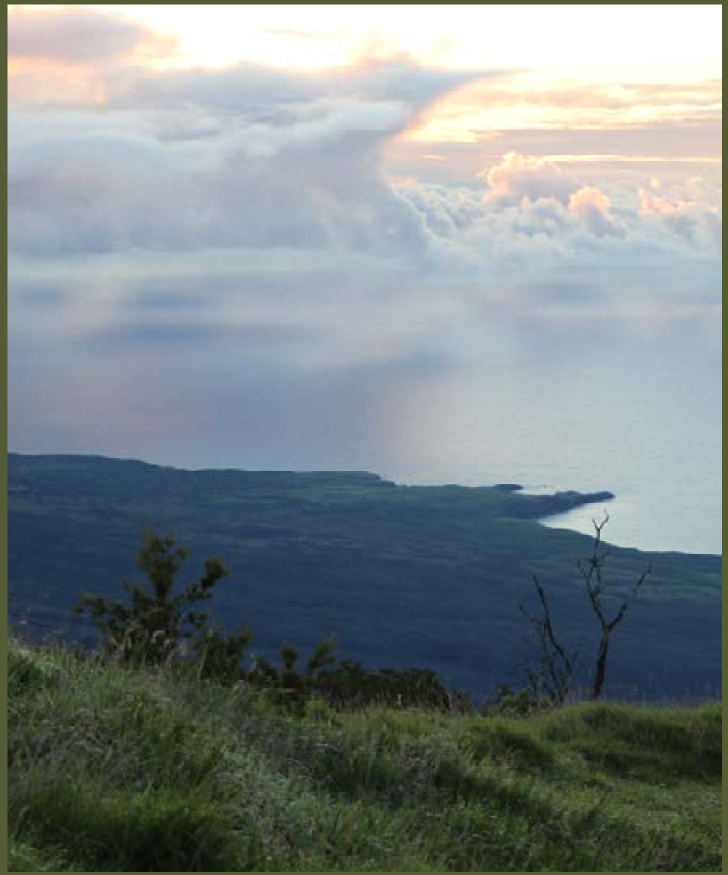
ABOVE: Hawaiian songbirds used to be able to escape mosquitoes carrying avian malaria by roosting high in the cold mountains. Warming weathers expanded the range of the mosquito and narrowed theirs, threatening survival. Credit: Government of Hawaiʻi.

Likewise, as more midge larvae survive over warm winters and breed better during drier summers, they bite more white-tailed deer, spreading often-fatal epizootic hemorrhagic disease. Especially in northern regions of the globe, climate change brings the threat of midges carrying blue tongue disease, a virus, to sheep and other animals. Tick-borne diseases like encephalitis and Lyme disease may become a greater threat to animals and perhaps humans.

In the “thermal mismatch” theory of wildlife disease, cold-adapted species are at greater risk when their habitats warm, and warm-adapted species suffer when their habitats cool. Mammals can adjust their body temperature to adapt to some extent. Amphibians, fish and insects that cannot regulate body temperatures may be at greater risk. Many scientists see amphibians, especially, as canaries in the coalmine, signaling toxicity.

Early melting ice can foster disease. Climate models predict that the spring thaw will come ever-earlier in the lakes of the French Pyrenees, for instance, which traditionally stayed frozen for up to half the year. The tadpoles of the midwife toad live under the ice, where they are often infected with amphibian chytrid fungus. When a seven-year study tracked the virus in three species of amphibians in Pyrenees's Lac Arlet, the research team found that, the earlier the spring thaw arrived, the more infection rates rose in common toads, while remaining high among the midwife toads. But the team made another sad discovery: with early thaws, the common frog, which was thought to be free of the disease in Europe, also became infected with the fungus and died in large numbers.

Changing habitats affect animal behavior. Normally, spiny lobsters rely on chemical cues to avoid predators and sick lobsters. New conditions may be hampering their ability to "social distance"—which may help PaV1 spread, Behringer's research suggests. Migration brings other risks. In April 2022, an international team led by scientists at Georgetown University announced the first comprehensive overview, published in the journal *Nature,* of how wild mammals under pressure from a changing climate may mingle with new populations and species—giving viruses a deadly opportunity to jump between hosts. Droughts, for example, will push animals to congregate at the few places where water remains.



ABOVE: Whitebark pine forests are facing a double threat, from white pine blister rust, a fungal disease, and multiplying pine beetles. Credit: Government of Hawaiʻi.

To identify new diseases and fine-tune crops for resistance, scientists are increasingly relying on genomic tools.

Plants face threats also. At the timberline of the cold, windy, snowy mountains of the U.S. west, whitebark pine forests are facing a double threat, from white pine blister rust, a fungal disease, and multiplying pine beetles. "If we do nothing, we will lose the species," says Robert Keane, a research ecologist for the U.S. Forest Service, based in Missoula, Montana. That would be a huge shift, he explains: "It's a keystone species. There are over 110 animals that depend on it, many insects, and hundreds of plants." In the past, beetle larvae would take two years to complete their lifecycle, and many died in frost. "With climate change, we're seeing more and more beetles survive, and sometimes the beetle can complete its lifecycle in one year," he says.

Quintessential crops are under threat too

As some pathogens move north and new ones develop, they pose novel threats to the crops humans depend upon. This is already happening to wheat, coffee, bananas and maize.

Breeding against wheat stem rust, a fungus long linked to famine, was a key success in the mid-20th century Green Revolution, which brought higher yields around the world. In 2013, wheat stem rust reemerged in Germany after decades of absence. It ravaged both bread and durum wheat in Sicily in 2016 and has spread as far as England and Ireland. Wheat blast disease, caused by a different fungus, appeared in Bangladesh in 2016, and spread to India, the world's second largest producer of wheat.

Insects, moths, worms, and coffee leaf rust—a fungus now found in all coffee-growing countries—threaten the livelihoods of millions of people who grow coffee, as well as everybody's cup of joe. More heat, more intense rain, and higher humidity have allowed coffee leaf rust to cycle more rapidly. It has grown exponentially, overcoming the agricultural chemicals that once kept it under control.

Tar spot, a fungus native to Latin America that can cut corn production in half, has emerged in highland areas of Central Mexico and parts of the U.S.. Meanwhile, maize lethal necrosis disease has spread to multiple countries in Africa, notes Mehrdad Ehsani, Managing Director for the Food Initiative in Africa of the Rockefeller Foundation. The Cavendish banana, which most people eat today, was bred to be resistant to the fungus Panama 1. Now a new fungus, Panama 4, has emerged on every continent–including areas of

Latin America that rely on the Cavendish for their income, reported a recent story in the Guardian. New threats are poised to emerge. Potato growers in the Andes Mountains have been shielded from disease because of colder weather at high altitude, but temperature fluxes and warming weather are expected to make this crop vulnerable to potato blight, found plant pathologist Erica Goss, at the Emerging Pathogens Institute.

Science seeks solutions

To protect food supplies in the era of climate change, scientists are calling for integrated global surveillance systems for crop disease outbreaks. “You can imagine that a new crop variety that is drought-tolerant could be susceptible to a pathogen that previous varieties had some resistance against,” Goss says. “Or a country suffers from a calamitous weather event, has to import seed from another country, and that seed is contaminated with a new pathogen or more virulent strain of an existing pathogen.” Researchers at the John Innes Center in Norwich and Aarhus University in Denmark have established ways to monitor wheat rust, for example.

Better data is essential, for both plants and animals. Historically, models of climate change predicted effects on plant pathogens based on mean temperatures, and scientists tracked plant responses to constant temperatures, explains Goss. “There is a need for more realistic tests of the effects of changing temperatures, particularly changes in daily high and low temperatures on pathogens,” she says.

To identify new diseases and fine-tune crops for resistance, scientists are increasingly relying on genomic tools. Goss suggests factoring the impact of climate change into those tools. Genomic efforts to select soft red winter wheat that is resistant to Fusarium head blight (FHB), a fungus that plagues farmers in the Southeastern U.S., have had early success. But temperature changes introduce a new factor.

A fundamental solution would be to bring back diversification in farming, says Ehsani. Thousands of plant species are edible, yet we rely on a handful. Wild relatives of domesticated crops are a store of possibly useful genes that may confer resistance to disease. The same is true for livestock. “If you put all your eggs in one basket and then a pest comes along, then you are more vulnerable to those risks. Research is needed on resilient, climate smart, regenerative agriculture,” Ehsani says.

Jonathan Sleeman, director of the U.S. Geological Survey National Wildlife Health Center, has called for data on wildlife health to be systematically collected and integrated with climate and other variables because more comprehensive data will result in better preventive action. “We have focused on detecting diseases,” he says, but a more holistic strategy would apply human public health concepts to assuring animal wellbeing. (For example, one study asked experts to draw a diagram of relationships of all the factors affecting the health of a particular group of caribou.) We must not take the health of plants and animals for granted, because their vulnerability inevitably affects us too, Sleeman says. “We need to improve the resilience of wildlife populations so they can withstand the impact of climate change.”

TEMMA EHRENFELD's science writing has appeared in Undark, Popular Science, Quartz, Salon, Newsweek, Psychology Today, *Leaps.org* and elsewhere.

“If you put all your eggs in one basket and then a pest comes along, then you are more vulnerable to those risks. Research is needed on resilient, climate smart, regenerative agriculture.”

– **MEHRDAD EHSANI**, MANAGING DIRECTOR FOR THE FOOD INITIATIVE IN AFRICA OF THE ROCKEFELLER FOUNDATION

7. Human Health:

Staying Well in the 21st Century is Like Playing Chess

By Lina Zeldovich

Illustrations by Juli Tudisco and Gabrielle Delabarre

On July 30, 1999, the Centers for Disease Control and Prevention published a report comparing data on the control of infectious disease from the beginning of the 20th century to the end. The data showed that deaths from infectious diseases declined markedly. In the early 1900s, pneumonia, tuberculosis and diarrheal diseases were the three leading killers, accounting for one-third of total deaths in the U.S.—with 40 percent being children under five. Mass vaccinations, the discovery of antibiot-

ics and overall sanitation and hygiene measures eventually eradicated smallpox, beat down polio, cured cholera, nearly rid the world of tuberculosis and extended the U.S. life expectancy by 25 years. By 1997, there was a shift in population health in the U.S. such that cancer, diabetes and heart disease were now the leading causes of death.

The control of infectious diseases is considered to be one of the "10 Great Public Health Achievements." Yet on the brink of the 21st century, new trouble was already brewing. Hospitals were seeing periodic cases of antibiotic-resistant infections. Novel viruses, or those that previously didn't afflict humans, began to emerge, causing outbreaks of West Nile, SARS, MERS or swine flu. In the years that followed, tuberculosis made a comeback, at least in certain parts of the world. What we didn't take into account was the very concept of evolution: as we built better protections, our enemies eventually boosted their attacking prowess, so soon enough we found ourselves on the defensive once again. At the same time, new, previously unknown or extremely rare disorders began to rise, such as autoimmune or genetic conditions. Two decades later, scientists began thinking about health differently—not as a static achievement guaranteed to last, but as something dynamic and constantly changing—and sometimes, for the worse.

What emerged since then is a different paradigm that makes our interactions with the microbial world more like a biological chess match, says Victoria McGovern, a biochemist and program officer for the Burroughs Wellcome Fund's Infectious Disease and Population Sciences Program. In this chess game, humans may make a clever strategic move, which could involve creating a new vaccine or a potent antibiotic, but that advantage is fleeting. At some point, the organisms we are up against could respond with a move of their own—such as developing resistance to medication or genetic mutations that attack our bodies. Simply eradicating the "opponent," or the pathogenic microbes, as efficiently as possible isn't enough to keep humans healthy long-term.

Instead, scientists should focus on studying the complexity of interactions between humans and their pathogens. "We need to better understand the lifestyles of things that afflict us," McGovern says. "The solutions are going to be in understanding various parts of their biology so we can influence how they behave around our systems."

What is being proposed will require a pivot to basic biology and other disciplines that have suffered from lack of research funding in recent years. Yet, according to McGovern, the research teams of funded proposals are answering bigger questions. "We look for people exploring questions about hosts and pathogens, and what happens when they touch, but we're also looking for people with big ideas," she says. For example, if one specific infection causes a chain of pathological events in the body, can other infections cause them too? And if we find a way to break that chain for one pathogen, can we play the same trick on another? "We really want to see people thinking of not just one experiment but about big implications of their work," McGovern says.

Jonah Cool, a cell biologist, geneticist and science officer at the Chan Zuckerberg Initiative, says that it's necessary to define what constitutes a healthy organism and how it overcomes infections or environmental assaults, such as pollution from forest fires or toxins from industrial smokestacks. An organism that catches a disease isn't necessarily an unhealthy one, as long as it fights it off successfully—an ability that arises from the complex interplay of its genes, the immune system, age, stress levels and other factors. Modern science allows many of these factors to be measured, recorded and compared. "We need a data-driven, deep-phenotyping approach to defining healthy biological systems and their responses to insults—which can be infectious disease or environmental exposures—and their ability to navigate their way through that space," Cool says.

Genetics and cell biology, combined with imaging techniques that allow one to see tissues and individual cells in action, will enable scientists to define and quantify what it means to be healthy at the molecular level. "As a geneticist and cell biologist, I believe in all these molecular underpinnings and how they arise in phenotypic differences in cells, genes, proteins—and how their combinations form complex cellular states," Cool says.

Julie Graves, a physician, public health consultant, former adjunct professor of management, policy and community health at the University of Texas Health Science Center in Houston, stresses the necessity of nutritious diets. According to the Rockefeller Food Initiative, "poor diet is the leading risk factor for disease, disability and premature death in the majority of countries around the world." Adequate nutrition is critical for maintaining human health and life. Yet, Western diets are often low in essential nutrients, high in calories and heavy on processed foods. Overconsumption of these foods has contributed to high rates of obesity and chronic disease in the U.S. In fact, more than half of American adults have at least one chronic disease, and 27 percent have more than one—which increases vulnerability to COVID-19 infections, according to the 2018 National Health Interview Survey.

Further, the contamination of our food supply with various agricultural and industrial toxins—petrochemicals, pesticides, PFAS and others—has implications for morbidity, mortality, and overall quality of life. "These chemicals are insidiously in everything, including our bodies," Graves says—and they are interfering with our normal biological functions. "We need to stop how we manufacture food," she adds, and rid our sustenance of these contaminants. According to the Humane Society of the United States, factory farms result in nearly 40 percent of emissions of methane. Concentrated animal feeding operations or CAFOs may serve as breeding grounds for pandemics, scientists warn, so humans should research better ways to raise and treat livestock. Diego Rose, a professor of food and nutrition policy at Tulane University School of Public Health & Tropical Medicine, and his colleagues found that "20 percent of Americans' diets account for about 45 percent of the environmental impacts [that come from food]." A subsequent study explored the impacts of specific foods and found that substituting chicken for beef lowers an individual's carbon footprint by nearly 50 percent, with water usage decreased by 30 percent. In addition, eating too much red meat has been associated with a variety of illnesses.

In some communities, the option to swap food types is limited or impossible. For example, "many populations live in relative food deserts where there's not a local grocery store that has any fresh produce," says Louis Muglia, the president and CEO of Burroughs Wellcome. Individuals in these communities suffer from an insufficient intake of beneficial macronutrients, and they're "probably being exposed to phenols and other toxins that are in the packaging." An equitable, sustainable and nutritious food supply will be vital to humanity's wellbeing in the era of climate change, unpredictable weather and spillover events.

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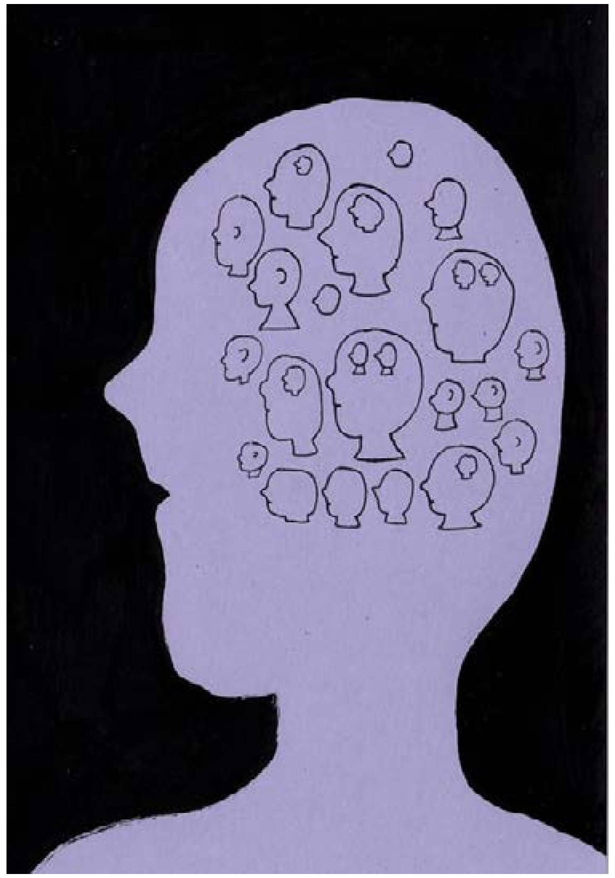
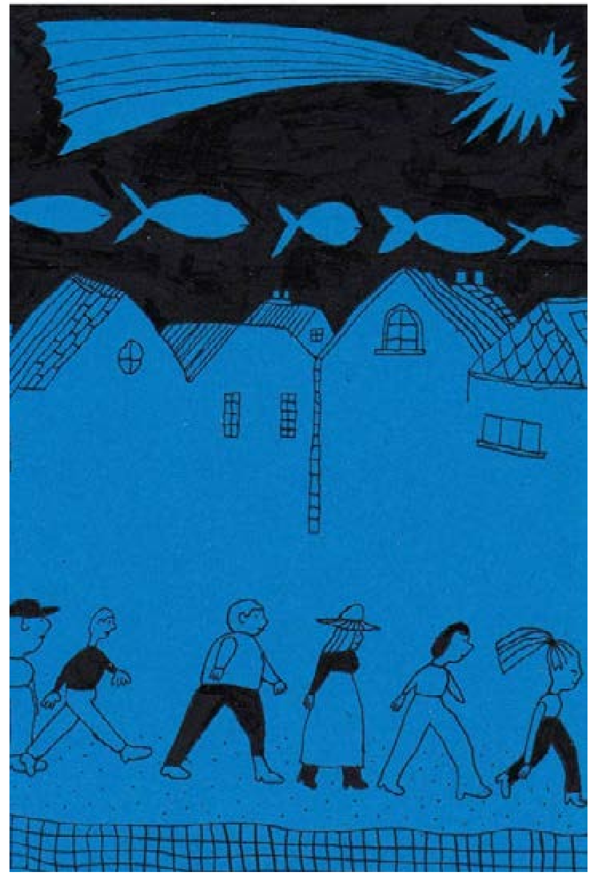
A recent report by See Change Institute and the Climate Mental Health Network showed that people who are experiencing socioeconomic inequalities, including many people of color, contribute the least to climate change, yet they are impacted the most. For example, people in low-income communities are disproportionately exposed to vehicle emissions, Muglia says. Through its Climate Change and Human Health Seed Grants program, Burroughs Wellcome funds research that aims to understand how various factors related to climate change and environmental chemicals contribute to premature births, associated with health vulnerabilities over the course of a person's life—and map such hot spots. "It's very complex, the combinations of socio-economic environment, race, ethnicity and environmental exposure, whether that's heat or toxic chemicals," he says. "Disentangling those things really requires a very sophisticated, multidisciplinary team. That's what we've put together to describe where these hotspots are and see how they correlate with different toxin exposure levels."





"Disentangling those things really requires a very sophisticated, multidisciplinary team. That's what we've put together to describe where these hotspots are and see how they correlate with different toxin exposure levels."

– **LOUIS MUGLIA**, PRESIDENT AND CEO OF BURROUGHS WELLCOME

In addition to mapping the risks, researchers are developing novel therapeutics that will be crucial to our armor arsenal, but we will have to be smarter at designing and using them. We will need more potent, better-working monoclonal antibodies. Instead of directly attacking a pathogen, we may have to learn to stimulate the immune system—training it to fight the disease-causing microbes on its own. And rather than indiscriminately killing all bacteria with broad-scope drugs, we would need more targeted medications. "Instead of wiping out the entire gut flora, we will need to come up with ways that kill harmful bacteria but not healthy ones," Graves says. Training our immune systems to recognize and react to pathogens by way of vaccination will keep us ahead of our biological opponents, too. "Continued development of vaccines against infectious diseases is critical," says Graves.

With all of the unpredictable events that lie ahead, it is difficult to foresee what achievements in public health will be reported at the end of the 21st century. Yet, technological advances, better modeling and pursuing bigger questions in science, along with education and working closely with communities will help overcome the challenges. The Chan Zuckerberg Initiative displays an optimistic message on its website: "Is it possible to cure, prevent, or manage all diseases by the end of this century? We think so." Cool shares the view of his employer—and believes that science can get us there. Just give it some time and a chance. "It's a big, bold statement," he says, "but the end of the century is a long way away."

LINA ZELDOVICH is an award-winning editor, journalist and book author focusing on the complex interactions between humans and their environment. Her work appeared in *Popular Science*, *Reader's Digest*, *Scientific American*, *Smithsonian* and *Leaps.org*, among other publications. You can visit her Amazon author page and follow her on Twitter @LinaZeldovich.

8. The Insect Apocalypse:

It Will Devastate Humans, but Science Can Keep Them Buzzing

By Susan Kreimer

Illustrations by Juli Tudisco

On a warm summer day, forests, meadows, and riverbanks should be abuzz with insects—from butterflies to beetles and bees. But bugs aren't as abundant as they used to be, and that's not a plus for people and the planet, scientists say. The declining numbers of insects, coupled with climate change, can have devastating effects for people in more ways than one. "Insects

have been around for a very long time and can live well without humans, but humans cannot live without insects and the many services they provide to us," says Philipp Lehmann, a researcher in the Department of Zoology at Stockholm University in Sweden. Their decline is not just bad, Lehmann adds. "It's devastating news for humans."

Insects and other invertebrates are the most diverse organisms on the planet. They fill most niches in terrestrial and aquatic environments and drive ecosystem functions. Many insects are also economically vital because they pollinate crops that humans depend on for food, including cereals, vegetables, fruits, and nuts. A paper published in PNAS notes that insects alone are worth more than $70 billion a year to the U.S. economy. In places where pollinators like honeybees are in decline, farmers now buy them from rearing facilities at steep prices rather than relying on "Mother Nature."

And because many insects serve as sustenance for other species—bats, birds and freshwater fish—they're an integral part of the ecosystem's food chain. "If you like to eat good food, you should thank an insect," says Scott Hoffman Black, an ecologist and executive director of the Xerces Society for Invertebrate Conservation in Portland, Oregon. "And if you like birds in your trees and fish in your streams, you should be concerned with insect conservation."

Deforestation, urbanization, and agricultural spread have eaten away at large swaths of insect habitat. The increasing poorly controlled use of insecticides, which harms unintended species, and the proliferation of invasive insect species that disrupt native ecosystems compound the problem.

"There is not a single reason why insects are in decline," says Jessica L. Ware, associate curator in the Division of Invertebrate Zoology at the American Museum of Natural History in New York, and president of the Entomological Society of America. "There are over one million described insect species, occupying different niches and responding to environmental stressors in different ways."

In addition to habitat loss fueling the decline in insect populations, the other "major drivers" Ware identified are invasive species, climate change, pollution, and fluctuating levels of nitrogen, which play a major role in the lifecycle of plants, some of which serve as insect habitats and others as their food. "The causes of world insect population declines are, unfortunately, very easy to link to human activities," Lehmann says.

ABOVE: Insects can live without humans, but humans can't live without insects. Credit: Juli Tudisco.

Climate change will undoubtedly make the problem worse. "As temperatures start to rise, it can essentially make it too hot for some insects to survive," says Emily McDermott, an assistant professor in the Department of Entomology and Plant Pathology at the University of Arkansas. "Conversely in other areas, it could potentially also allow other insects to expand their ranges."

Without pollinators humans will starve

We may not think much of our planet's getting warmer by only one degree Celsius, but it can spell catastrophe for many insects, plants, and animals, because it's often accompanied by less rainfall. "Changes in precipitation patterns will have cascading consequences across the tree of life," says David Wagner, a professor of ecology and evolutionary biology at the University of Connecticut. Insects, in particular, are "very vulnerable" because "they're small and susceptible to drying."

For instance, droughts have put the monarch butterfly at risk of being unable to find nectar to "recharge its engine" as it migrates from Canada and New England to Mexico for winter, where it enters a hibernation state until it journeys back in the spring. "The monarch is an iconic and a much-loved insect," whose migration "is imperiled by climate change," Wagner says.

Warming and drying trends in the Western United States are perhaps having an even more severe impact on insects than in the eastern region. As a result, "we are seeing fewer individual butterflies per year," says Matt Forister, a professor of insect ecology at the University of Nevada, Reno.

There are hundreds of butterfly species in the United States and thousands in the world. They are pollinators and can serve as good indicators of other species' health. "Although butterflies are only one group among many important pollinators, in general we assume that what's bad for butterflies is probably bad for other insects," says Forister, whose research focuses on butterflies. Climate change and habitat destruction are wreaking havoc on butterflies as well as plants, leading to a further indirect effect on caterpillars and butterflies.

Different insect species have different levels of sensitivity to environmental changes. For example, one-half of the bumble bee species in the United States are showing declines, whereas the other half are not, says Christina Grozinger, a professor of entomology at the Pennsylvania State University. Some species of bumble bees are even increasing in their range, seemingly resilient to environmental changes. But other pollinators are dwindling to the point that farmers have to buy from the rearing facilities, which is the case for the California almond industry. "This is a massive cost to the farmer, which could be provided for free, in case the local habitats supported these pollinators," says Lehman.

For bees and other insects, climate change can harm the plants they depend on for survival or have a negative impact on the insects directly. Overly rainy and hot conditions may limit flowering in plants or reduce the ability of a pollinator to forage and feed, which then decreases their reproductive success, resulting in dwindling populations, Grozinger explains.

"Nutritional deprivation can also make pollinators more sensitive to viruses and parasites, and therefore, cause disease spread," she says. "There are many ways that climate change can reduce our pollinator populations and make it more difficult to grow the many fruit, vegetable, and nut crops that depend on pollinators."

Disease-causing insects can bring more outbreaks

While some much-needed insects are declining, certain disease-causing species may be spreading and proliferating, which is another reason for human concern. Many mosquito types spread malaria, Zika virus, West Nile virus, and a brain infection called equine encephalitis, along with other diseases as well as heartworms in dogs, says Michael Sabourin, president of the Vermont Entomological Society. An animal health specialist for the state, Sabourin conducts vector surveys that identify ticks and mosquitoes.

Scientists refer to disease-carrying insects as vector species and, while there's a limited number of them, many of these infections can be deadly. Fleas were a well-known vector for the bubonic plague, while kissing bugs are a vector for Chagas disease, a potentially life-threatening parasitic illness in humans, dogs, and other mammals, Sabourin says.

As the planet heats up, some of the creepy crawlers are able to survive milder winters or move up north. Warmer temperatures and a shorter snow season have spawned an increasing abundance of ticks in Maine, including the blacklegged tick (*Ixodes scapularis*), known to transmit Lyme disease, says Sean Birkel, an assistant professor in the Climate Change Institute and Cooperative Extension at the University of Maine.

Coupled with more frequent and heavier precipitation, rising temperatures bring a longer warm season that can also lead to a longer period of mosquito activity. "While other factors may be at play, climate change affects important underlying conditions that can, in turn, facilitate the spread of vector-borne disease," Birkel says.

For example, if mosquitoes are finding fewer of their preferred food sources, they may bite humans more. Both male and female mosquitoes feed on sugar as part of their normal behavior, but if they aren't eating their fill, they may become more bloodthirsty. One recent paper found that sugar-deprived *Anopheles gambiae* females go for larger blood meals to stay in good health and lay eggs. "More blood meals equals

more chances to pick up and transmit a pathogen," McDermott says, He adds that climate change could reduce the number of available plants to feed on. And while most mosquitoes are "generalist sugar-feeders" meaning that they will likely find alternatives, losing their favorite plants can make them hungrier for blood.

Similar to the effect of losing plants, mosquitoes may get turned onto people if they lose their favorite animal species. For example, some studies found that *Culex pipiens* mosquitoes that transmit the West Nile virus feed primarily on birds in summer. But that changes in the fall, at least in some places. Because there are fewer birds around, *C. pipiens* switch to mammals, including humans. And if some disease-carrying insect species proliferate or increase their ranges, that boosts chances for human infection, says McDermott. "A larger concern is that climate change could increase vector population sizes, making it more likely that people or animals would be bitten by an infected insect."

Science can help bring back the buzz

To help friendly insects thrive and keep the foes in check, scientists need

ABOVE: Jessica Ware, an entomologist at the American Museum of Natural History, is using DNA methods to monitor insects. Listen to the new Leaps.org interview with Ware about her latest research. Credit:D.Finnin/AMNH.

> **"One day, something akin to Star Trek's tricorder will soon be on sale down at the local science store."**
>
> – **DAVID WAGNER**, PROFESSOR OF ECOLOGY AND EVOLUTIONARY BIOLOGY AT THE UNIVERSITY OF CONNECTICUT

better ways of trapping, counting, and monitoring insects. It's not an easy job, but artificial intelligence and molecular methods can help. Ware's lab uses various environmental DNA methods to monitor freshwater habitats and the species within them. For example, she is currently deploying these genomic tools to try to sequence each of the estimated 6,500 species of dragonflies across the globe. Molecular technologies hold much promise.

The so-called DNA barcodes, in which species are identified using a short string of their genes, can now be used to identify birds, bees, moths and other creatures, and should be used on a larger scale, says Wagner, the University of Connecticut professor. "One day, something akin to Star Trek's tricorder will soon be on sale down at the local science store."

Scientists are also deploying artificial intelligence, or AI, to identify insects in agricultural systems and north latitudes where there are fewer bugs, Wagner says. For instance, some automated traps already use the wingbeat frequencies of mosquitoes to distinguish the harmless ones from the disease-carriers. But new technology and software are needed to further expand detection based on vision, sound, and odors.

"Because of their ubiquity, enormity of numbers, and seemingly boundless diversity, we desperately need to develop molecular and AI technologies that will allow us to automate sampling and identification," says Wagner. "That would accelerate our ability to track insect populations, alert us to the presence of new disease vectors, exotic pest introductions, and unexpected declines."

"Once we have baseline data of what species exist, once we know the taxa and where they're found, we can start making predictions," says Ware. "We can start assessing changes and whether the impacts of particular phenomena or environmental catastrophes are impacting the species in an area."

She adds that most of our records on insect declines come from the Global North, even though other parts of the world are home to more biodiversity. "We have a lot of [research] gaps in the Global South," where warming temperatures may cause more disruption to insect populations, she says. "We need to work to support our colleagues who are most impacted by climate change."

SUSAN KREIMER is a New York-based freelance journalist who covers health, medicine, and science. Raised in the Chicago area, she earned a master's degree from the Columbia University Graduate School of Journalism and worked as a staff reporter for major daily newspapers.

9. Surveillance:

What Tools and Technologies are Needed to Monitor Zoonotic Spillovers and Optimize Disease Management?

By David Cox

Every year, the villages which lie in the so-called 'Nipah belt'— which stretches along the western border between Bangladesh and India, brace themselves for the latest outbreak. For since 1998, when Nipah virus—a form of hemorrhagic fever most common in Bangladesh—first spilled over into humans, it has been a grim annual visitor to the people of this region.

RIGHT:A team at the Catalan Institution for Research and Advanced Studies is utilizing drones and weather stations to collect data on how mosquito breeding patterns are changing in response to climate shifts. Credit: Gabriel Carrasco.

With a 70 percent fatality rate, no vaccine, and no known treatments, Nipah virus has been dubbed in the Western world as 'the worst disease no one has ever heard of.' Currently, outbreaks tend to be relatively contained because it is not very transmissible. The virus circulates throughout Asia in fruit eating bats, and only tends to be passed on to people who consume contaminated date palm sap, a sweet drink which is harvested across Bangladesh.

But as SARS-CoV-2 has shown the world, this can quickly change.

"Nipah virus is among what virologists call 'the Big 10,' along with things like Lassa fever and Crimean Congo hemorrhagic fever," says Noam Ross, a disease ecologist at New York-based non-profit EcoHealth Alliance. "These are pretty dangerous viruses from a lethality perspective, which don't currently have the capacity to spread into broader human populations. But that can evolve, and you could very well see a variant emerge that has human-human transmission capability."

That's not an overstatement. Surveys suggest that mammals harbour about 40,000 viruses, with roughly a quarter capable of infecting humans. The vast majority never get a chance to do so because we don't encounter them, but climate change can alter that. Recent studies have found that as animals relocate to new habitats due to shifting environmental conditions, the coming decades will bring around 300,000 first encounters between species which normally don't interact, especially in tropical Africa and southeast Asia. All these interactions will make it far more likely for hitherto unknown viruses to cross paths with humans.

ABOVE: A team at the Catalan Institution for Research and Advanced Studies is utilizing drones and weather stations to collect data on how mosquito breeding patterns are changing in response to climate shifts.
Credit: Gabriel Carrasco.

That's why for the last 16 years, EcoHealth Alliance has been conducting ongoing viral surveillance projects across Bangladesh. The goal is to understand why Nipah is so much more prevalent in the western part of the country, compared to the east, and keep a watchful eye out for new Nipah strains as well as other dangerous pathogens like Ebola.

Until very recently this kind of work has been hampered by the limitations of viral surveillance technology. The PREDICT project, a $200 million initiative funded by the United States Agency for International Development, which conducted surveillance across the Amazon Basin, Congo Basin and extensive parts of South and Southeast Asia, relied upon so-called nucleic acid assays which enabled scientists to search for the genetic material of viruses in animal samples.

However, it still wasn't the most efficient way of doing surveillance. "That approach requires a big sampling effort, because of the rarity of individual infections," says Ross. "Any particular animal may be infected for a couple of weeks, maybe once or twice in its lifetime. So if you sample thousands and thousands of animals, you'll eventually get one that has an Ebola virus infection right now."

Ross explains that there is now far more interest in serological sampling—the scientific term for the process of drawing blood for antibody testing. By searching for the presence of antibodies in the blood of humans and animals, scientists have a greater chance of detecting viruses which started circulating recently.

Despite controversy surrounding EcoHealth Alliance's involvement in so-called gain of function research—experiments that study whether viruses might mutate into deadlier strains, which have prompted concerns that they could escape the lab and lead to disease outbreaks—the organization's separate efforts to stay one step ahead of pathogen evolution are key to stopping the next pandemic.

“Having really cheap and fast surveillance is really important,” says Ross. “Particularly in a place where there's persistent, low level, moderate infections that potentially have the ability to develop into more epidemic or pandemic situations. It means there’s a pathway that something more dangerous can come through.”

In Bangladesh, EcoHealth Alliance is attempting to do this using a newer serological technology known as a multiplex Luminex assay, which tests samples against a panel of known antibodies against many different viruses. It collects what Ross describes as a ‘footprint of information,’ which allows scientists to tell whether the sample contains the presence of a known pathogen or something completely different and needs to be investigated further.

By using this technology to sample human and animal populations across the country, they hope to gain an idea of whether there are any novel Nipah virus variants or strains from the same family, as well as other deadly viral families like Ebola.

This is just one of several novel tools being used for viral discovery in surveillance projects around the globe. Multiple research groups are taking PREDICT’s approach of looking for novel viruses in animals in various hotspots. They collect environmental DNA (eDNA)—mucus, faeces or shed skin left behind in soil, sediment or water—which can then be genetically sequenced.

Five years ago, this would have been a painstaking work requiring bringing collected samples back to labs. Today, thanks to the vast amounts of money spent on new technologies during COVID-19, researchers now have portable sequencing tools they can take out into the field.

Christopher Jerde, a researcher at the UC Santa Barbara Marine Science Institute, points to the Oxford Nanopore MinION sequencer as one example. “I tried one of the early versions of it four years ago, and it was miserable,” he says. “But they’ve really improved, and what we’re going to be able to do in the next five to ten years will be amazing. Instead of having to carefully transport samples back to the lab, we're going to have cigar box-shaped sequencers that we take into the field, plug into a laptop,

ABOVE: By sampling human and animal populations in viral hotspots, scientists hope to identify novel variants or strains that are dangerous and deadly to humans, stopping the outbreaks before they happen. Credit: EcoHealth Alliance

“As climate patterns change on these big scales, we expect to see shifts in where people will be at risk for contracting these diseases.”

- **CAT LIPPI**, MEDICAL GEOGRAPHY RESEARCHER AT THE UNIVERSITY OF FLORIDA

ABOVE: Scientists are searching for the presence of antibodies in the blood of humans and animals in hopes to detect viruses that recently started circulating. Credit: EcoHealth Alliance

and do the whole sequencing of an organism.”

In the past, viral surveillance has had to be very targeted and focused on known families of viruses, potentially missing new, previously unknown zoonotic pathogens. Jerde says that the rise of portable sequencers will lead to what he describes as “true surveillance.”

“Before, this was just too complex,” he says. “It had to be very focused, for example, looking for SARS-type viruses. Now we’re able to say, ‘Tell us all the viruses that are here?’ And this will give us true surveillance – we’ll be able to see the diversity of all the pathogens which are in these spots and have an understanding of which ones are coming into the population and causing damage.”

But being able to discover more viruses also comes with certain challenges. Some scientists fear that the speed of viral discovery will soon outpace the human capacity to analyze them all and assess the threat that they pose to us.

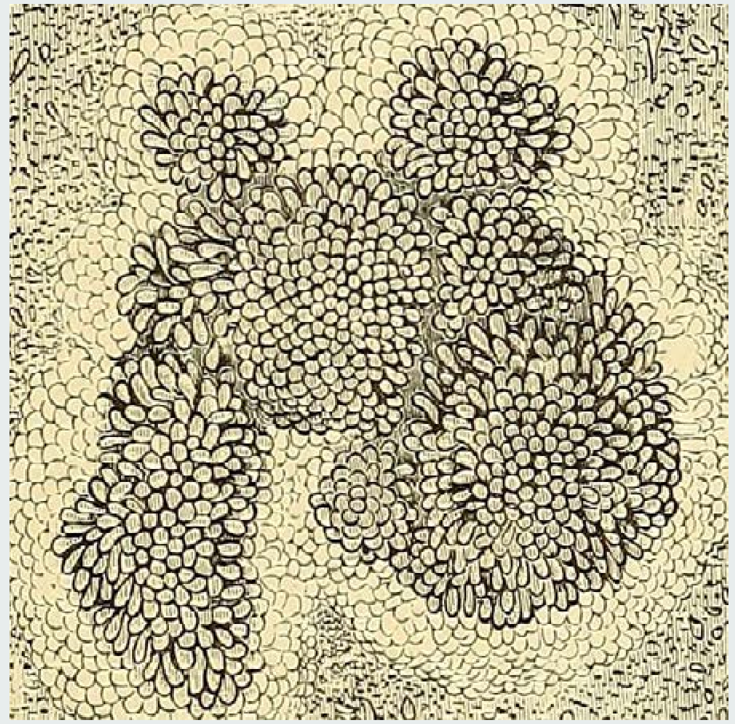
“I think we're already there,” says Jason Ladner, assistant professor at Northern Arizona University’s Pathogen and Microbiome Institute. “If you look at all the papers on the expanding RNA virus sphere, there are all of these deposited partial or complete viral sequences in groups that we just don't know anything really about yet.” Bats, for example, carry a myriad of viruses, whose ability to infect human cells we understand very poorly.

Cultivating these viruses under laboratory conditions and testing them on organoids— miniature, simplified versions of organs created from stem cells—can help with these assessments, but it is a slow and painstaking work. One hope is that in the future, machine learning could help automate this process. The new SpillOver Viral Risk Ranking platform aims to assess the risk level of a given virus based on 31 different metrics, while other computer models have tried to do the same based on the similarity of a virus’s genomic sequence to known zoonotic threats.

However, Ladner says that these types of comparisons are still overly simplistic. For one thing, scientists are still only aware of a few hundred zoonotic viruses, which is a very limited data sample for accurately assessing a novel pathogen. Instead, he says that there is a need for virologists to develop models which can determine viral compatibility with human cells, based on genomic data.

“One thing which is really useful, but can be challenging to do, is understand the cell surface receptors that a given virus might use,” he says. “Understanding whether a virus is likely to be able to use proteins on the surface of human cells to gain entry can be very informative.”

As the Earth’s climate heats up, scientists also need to better model the so-called vector borne diseases such as dengue, Zika, chikungunya and yellow fever. Transmitted by the *Aedes* mosquito residing in humid climates, these blights currently disproportionally affect people in low-income nations. But predictions suggest that as the planet warms and the pests find new homes, an estimated one billion people who currently don’t encounter them might be threatened by their bites by 2080. “When it comes to mosquito-borne diseases we have to worry about shifts in suitable habitat,” says Cat Lippi, a medical geography researcher at the University of Florida. “As climate patterns change on these big scales, we expect to see shifts in where people will be at risk for contracting these diseases.”



“There are a lot of different infectious agents that are sensitive to climate change that don’t have these sorts of software tools being developed for them.”

- **CAT LIPPI**, MEDICAL GEOGRAPHY RESEARCHER AT THE UNIVERSITY OF FLORIDA

Public health practitioners and government decision-makers need tools to make climate-informed decisions about the evolving threat of different infectious diseases. Some projects are already underway. An ongoing collaboration between the Catalan Institution for Research and Advanced Studies and researchers in Brazil and Peru is utilizing drones and weather stations to collect data on how mosquitoes change their breeding patterns in response to climate shifts. This information will then be fed into computer algorithms to predict the impact of mosquito-borne illnesses on different regions.

Lippi says that similar models are urgently needed to predict how changing climate patterns affect respiratory, foodborne, waterborne and soilborne illnesses. The UK-based Wellcome has allocated significant assets to fund such projects, which should allow scientists to monitor the impact of climate on a much broader range of infections. “There are a lot of different infectious agents that are sensitive to climate change that don't have these sorts of software tools being developed for them,” she says.

COVID-19’s havoc boosted funding for infectious disease research, but as its threats begin to fade from policymakers’ focus, the money may dry up. Meanwhile, scientists warn that another major infectious disease outbreak is inevitable, potentially within the next decade, so combing the planet for pathogens is vital. “Surveillance is ultimately a really boring thing that a lot of people don't want to put money into, until we have a wide scale pandemic,” Jerde says, but that vigilance is key to thwarting the next deadly horror. “It takes a lot of patience and perseverance to keep looking.”

DAVID COX is a freelance health journalist and former neuroscientist. He is a regular contributor to Leaps.org as well as WIRED, TIME, Guardian, BBC and many others.

10. Changing Habitats:

For Solutions to Climate Change and Infectious Disease, Researchers Go Back to the First Domino

Humans have altered approximately 75 percent of the planet's terrestrial surface over the past thousand years—and almost a third of these changes have occurred since 1960. It's a process known as land use change, in which people transform the structure and function of ecosystems. This happens when, for example, forests are cleared for agricultural production.

RIGHT: A research team associated with Drew Harvell, Cornell professor of ecology and evolutionary biology, conducts fieldwork on the health of eelgrass meadows on a misty morning at Fourth of July Beach on the San Juan Islands in Washington state. Credit: David O. Brown.

By David L. Levine

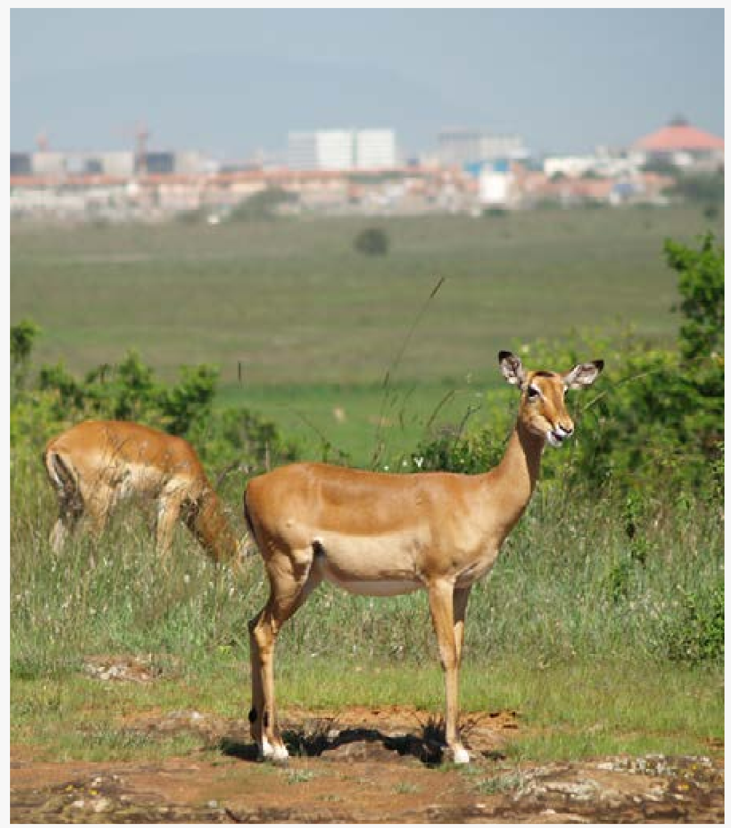
Human-made changes both on land and in our oceans and rivers are accelerating conditions that can cause illnesses and even pandemics. Combined with the direct stresses of global-scale climate change, these transformations are forcing some species to move northward and to higher elevations to survive, producing novel opportunities for sharing disease-causing organisms, or pathogens, among species of life that hadn't previously mixed.

For example, a parasite known to infect oysters has recently roamed from the Chesapeake to Maine, a distance of over 300 miles, which scientists attribute to warming temperatures. "Climate change will become the biggest risk factor for disease emergence, exceeding deforestation, wildlife trade and industrial agriculture," said Colin Carlson, a global change biologist at Georgetown University, at a press conference for his research paper on these issues published in *Nature* late last month.

The concept that land use change and disease risk are linked has long been recognized by the scientific community, dating at least as far back as the groundbreaking research of Edward Jenner and Louis Pasteur in the 1800s and articulated more comprehensively by Laurie Garrett in *The Coming Plague*. But people are altering natural environments at an unprecedented pace and scale—for instance, we're losing our forests at a faster clip, which could lead to more cases of animals transmitting pathogens to humans, a process called spillover. "If you care about preventing pandemics, it's time to start caring about saving trees," said physician Neil Vora, a fellow who leads the efforts of Conservation International on pandemic prevention.

"The ideal goal is to prevent the first domino from falling. To do that, we need to focus on ecological integrity—the health of ecological systems."

- **JAMIE K. REASER**, AFFILIATE FACULTY MEMBER IN ENVIRONMENTAL SCIENCE AND POLICY AT GEORGE MASON UNIVERSITY



ABOVE: Wildlife in Nairobi National Park, Kenya, graze all too close to an urban area. Jamie Reaser, an affiliate faculty member at George Mason University says that we need to better understand interactions between wildlife and people - and project how these interactions will change. Credit: Jamie Reaser.

The connections between climate change, land use and infectious disease are complex, involving interrelationships between aquatic and terrestrial ecosystems, urbanization and, of course, a rapidly changing climate. But scientists are identifying promising avenues of research that could, with greater effort, address this cluster of problems. We can mitigate the risk of future pandemics through research to learn more about the best strategies for reducing stressors on animals—by, for example, protecting our natural environments and reintroducing displaced populations—and implementing nature-based solutions that counter the effects of changing habitats.

A complex problem starts with the first domino

Protecting and restoring ecological systems is fundamental to preventing future pandemics, said Jamie K. Reaser, an affiliate faculty member in environmental science and policy at George Mason University. "The process by which diseases emerge in wildlife populations and later infect large numbers of humans proceeds like a series of dominos, one hitting the other until we have a pandemic," she said. "The ideal goal is to prevent the first domino from falling. To do that, we need to focus on ecological integrity—the health of ecological systems."

Reaser develops ecological strategies and policies for preventing disease outbreaks from wildlife to humans, known as zoonoses. "Ecosystem health directly affects human health," she said. "The protection of human health by high-functioning ecosystems is one of many ecological services—as important as provisioning clean air and water."

These strategies should focus on nature-based solutions, such as removal of invasive species and the conservation or reintroduction of native plants.

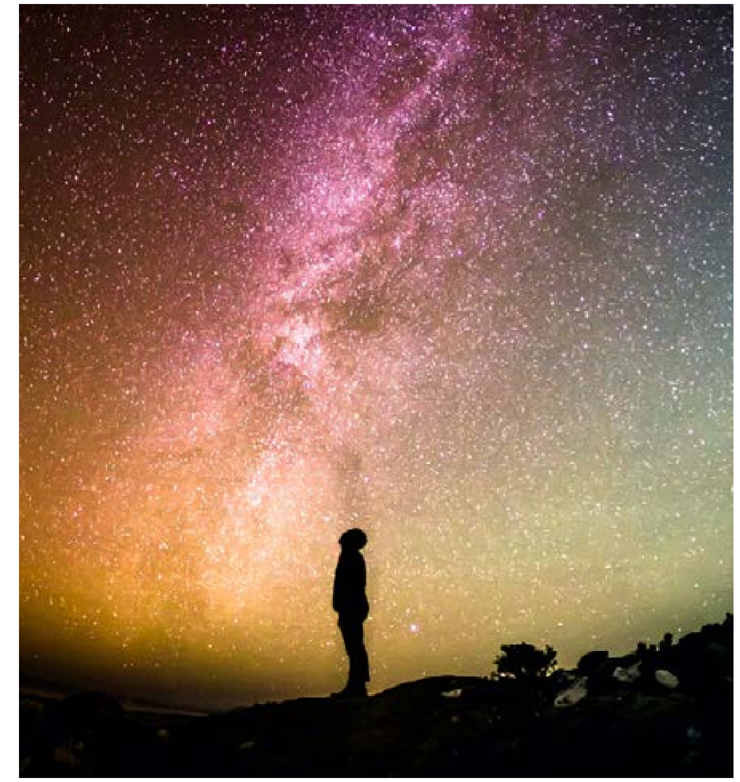
A recent study found that controlling non-native plants can help with reducing the risk of malaria. In another example, the building of dams in the Senegal River Basin in Africa had obstructed yearly migrations of river prawn that are indigenous to the African west coast. Once they were returned, the prawn helped control populations of aquatic snails that can host parasitic flatworms, which had previously led to disease outbreaks causing bladder cancer and other serious health problems among 250 million people worldwide. Nature-based solutions, such as restoring wetlands, also play essential roles in absorbing flood water and coastal surges of tropical storms that are becoming more common as the planet warms.

According to Reaser, more research is needed to maximize the potential of nature-based solutions and learn how to best manage invasive plants and their relationships with disease vectors. Scientists must work more closely across fields such as landscape ecology, wildlife immunology, and disease ecology to inform policy and management measures, said Reaser, adding that One Health paradigm was formed to accomplish precisely these goals.

Sea change

Although many people think of pandemic events happening on land, they are also occurring more frequently in our oceans, according to Drew Harvell, professor of ecology and evolutionary biology at Cornell University.

Harvell first warned about the dangers to our ecosystems in 2002, noting that infectious diseases can cause rapid population declines or species extinctions. Marine species are just as sensitive as those on land to variations in temperature, rainfall, and humidity, and these vulnerabilities can harm biodiversity. "Climate warming can increase pathogen development and survival rates, disease transmission, and host susceptibility," Harvell said. The impacts of marine diseases can be lessened by reducing coastal pollution resulting from poor sewage management, habitat loss, and overharvesting. Harvell proposes nature-based solutions for pathogen reduction in her book, *Ocean Outbreak: Confronting the Rising Tide of Marine Disease*, citing her team's work with the impressive powers of native ocean plants like seagrasses to reduce these troublesome microbes.



Credit: Greg Rakozy.

"Understanding how urbanization and agricultural development forces out wild species and brings in other species that can cause pathogen spillover in humans and wildlife is important."

- **DANIEL BECKER**, PROFESSOR OF BIOLOGY AT THE UNIVERSITY OF OKLAHOMA

In Ocean Outbreak, Harvell also explains that, in some areas, warming ocean temperatures may be contributing to marine epidemics that cause mass die-offs of corals, oysters and other wildlife from the bottom to the top of food chains. Since 2013, sea star wasting disease has brought about massive mortality in sea stars from Mexico to Alaska to Asia. Harvell and her colleagues found evidence of a viral-sized microbe bacteria that could be the culprit, while continuing the hunt to pinpoint the exact species. The precipitous, disease-driven decline of the once-common sunflower sea stars, newly listed as endangered species, has resulted in massive blooms of sea urchins that threaten the kelp forests that are key to supporting biodiversity and fisheries.

Spreading cities – and travelers

In the last few decades, infectious disease specialists have been sounding alarms as emerging infections have been jumping from one species to another, including Ebola, SARS, Monkeypox and, most experts believe, COVID-19. Urbanization is a key factor, said Daniel Becker, assistant professor of biology at University of Oklahoma. He studies vampire bats in Latin America, which thrive by feeding on the blood of abundant livestock. “Understanding how urbanization and agricultural development forces out wild species and brings in other species that can cause pathogen spillover in humans and wildlife is important,” said Becker. "We know that bats and birds can move over long distances and spread diseases to wider areas. Combined with climate change, which forces species to move around due to being too hot or cold, it causes new opportunities for overlap for wildlife and humans."

Both climate change and land use changes are redefining the interface between people, animals, and disease, said Jay Varma, an epidemiologist at Weill Cornell Medical College. "The factors responsible for these changes are well-known and include deforestation, which allows human encroachment; trade in wildlife and consumption of animal proteins which increases trade in animals; urbanization; travel; and climate change. Humans become infected by animals directly or by an intermediary which feeds on animals such as a tick or mosquito."

ABOVE: Land use change-such as this illegal land clearing for charcoal production near Iquitos, Peru-stresses wild animals, potentially making them more susceptible to zoonotic infections and releasing pathogens.
Credit: Jamie Reaser.

Just as bats and birds can fly long distances and spread illnesses, humans are traveling farther and faster than they used to. Case in point: SARS-CoV-2 came to New York via Europe in early 2020, leading to the city becoming an epicenter of the COVID-19 outbreak in the U.S. "We live in a world where people are more in contact with one another than ever before,” said Varma.

Ebola, monkeypox and Zika are examples of diseases that were spread by travelers from their countries of origin. Monkeypox is found mostly in Africa, but cases have now been found in the U.S. and U.K. For decades, Zika had been confined to forests in East Africa, but somehow got transplanted to the South Pacific and then South America and the US. The only plausible explanation is air travel, said Varma.

International travel and the impacts of climate change are here for the foreseeable future. Facing that new reality, the most promising areas of research to pursue point back to the problem of changing habitats—and how to restore them. According to the International Union for Conservation of Nature, restorations of tropical forests are especially important as the loss of these ecosystems accounts for as much as 19 percent of greenhouse-gas emissions resulting from activities by humans.

One way to repair these ecosystems is by sustainable harvesting—an approach that provides a constant supply of wood while allowing the forest to regenerate enough that future yields are unaffected or even improved. Becker said that more research must focus on how to facilitate these conservation efforts. "This can help both local economics as well as result in less sickness due to spillover events," he said.

DAVID LEVINE is co-chair of Science Writers in New York. He has written for The New York Times, Scientific American and Nature Medicine.

11. Modeling:

Scientists Recommend a Multidisciplinary Approach to Predicting Outbreaks

A mosquito under the microscope. Credit: Joacim Rocklov

Two years, six million deaths and still counting, scientists are searching for answers to prevent another COVID-19-like tragedy from ever occurring again. And it's a gargantuan task.

By Eve Glicksman

Our disturbed ecosystems are creating more favorable conditions for the spread of infectious disease. Global warming, deforestation, rising sea levels and flooding have contributed to a rise in mosquito-borne infections and longer tick seasons. Disease-carrying animals are in closer range to other species and humans as they migrate to escape the heat. Bats

are thought to have carried the SARS-CoV-2 virus to Wuhan, either directly or through another host animal, but thousands of novel viruses are lurking within other wild creatures.

Understanding how climate change contributes to the spread of disease is critical in predicting and thwarting future calamities. But the problem is that predictive models aren't yet where they need to be for forecasting with certainty beyond the next year, as we could for weather, for instance.

The association between climate and infectious disease is poorly understood, says Irina Tezaur, a computational scientist at Sandia National Laboratories. "Correlations have been observed but it's not known if these correlations translate to causal relationships."

To make accurate longer-term predictions, scientists need more empirical data, multiple datasets specific to locations and diseases, and the ability to calculate risks that depend on unpredictable nature and human behavior. Another obstacle is that climate scientists and epidemiologists are not collaborating effectively, so some researchers are calling for a multidisciplinary approach, a new field called Outbreak Science.

Credit: Vinicius Amnx Amano.

Disease forecasting will require a significant investment into the infrastructure needed to collect data about the environment, vectors, and hosts at all spatial and temporal resolutions.

Climate scientists are far ahead of epidemiologists in gathering essential data.

Earth System Models—combining the interactions of atmosphere, ocean, land, ice and biosphere—have been in place for two decades to monitor the effects of global climate change. These models must be combined with epidemiological and human model research, areas that are easily skewed by unpredictable elements, from extreme weather events to public environmental policy shifts.

"There is never just one driver in tracking the impact of climate on infectious disease," says Joacim Rocklöv, a professor at the Heidelberg Institute of Global Health & Heidelberg Interdisciplinary Centre for Scientific Computing in Germany. Rocklöv has studied how climate affects vector-borne diseases—those transmitted to humans by mosquitoes, ticks or fleas. "You need to disentangle the variables to find out how much difference climate makes to the outcome and how much is other factors." Determinants from deforestation to population density to lack of healthcare access influence the spread of disease.

Even though climate change is not the primary driver of infectious disease today, it poses a major threat to public health in the future, says Rocklöv.

The promise of predictive modeling

"Models are simplifications of a system we're trying to understand," says Jeremy Hess, who directs the Center for Health and the Global Environment at University of Washington in Seattle. "They're tools for learning that improve over time with new observations."

Accurate predictions depend on high-quality, long-term observational data but models must start with assumptions. "It's not possible to apply an evidence-based approach for the next 40 years," says Rocklöv. "Using models to experiment and learn is the only way to figure out what climate means for infectious disease. We collect data and analyze what already happened. What we do today will not make a difference for several decades."

To improve accuracy, scientists develop and draw on thousands of models to cover as many scenarios as possible. One model may capture the dynamics of disease transmission while another focuses on immunity data or ocean influences or seasonal components of a virus. Further, each model needs to be disease-specific and often location-specific to be useful.

"All models have biases so it's important to use a suite of models," Tezaur stresses.

The modeling scientist chooses the drivers of change and parameters based on the question explored. The drivers could be increased precipitation, poverty or mosquito prevalence, for instance. Later, the scientist may need to isolate the effect of one driver so that will require another model.

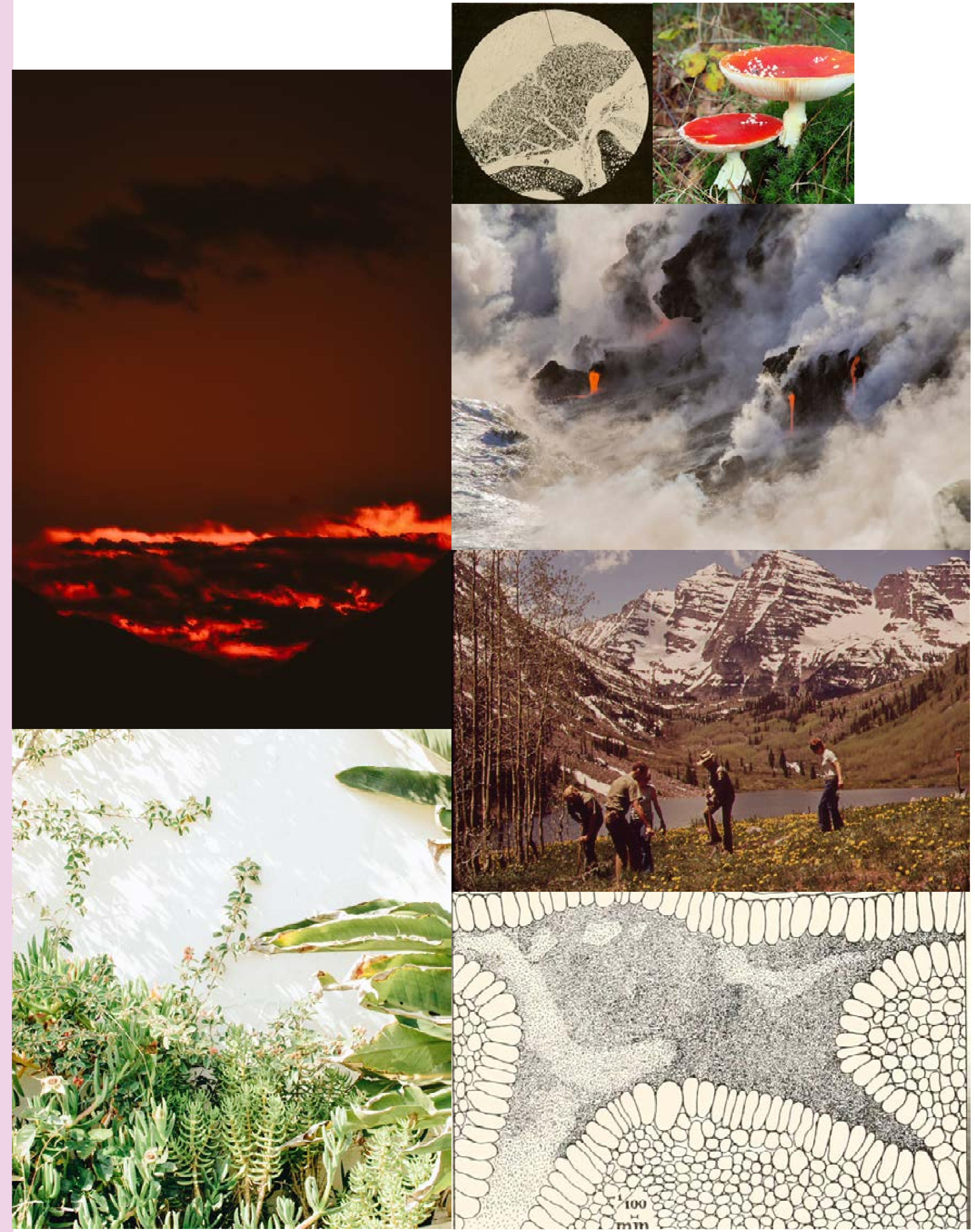
There have been some related successes, such as the latest models for mosquito-borne diseases like Dengue, Zika and malaria as well as those for flu and tick-borne diseases, says Hess.

Rocklöv was part of a research team that used test data from 2018 and 2019 to identify regions at risk for West Nile virus outbreaks. Using AI, scientists were able to forecast outbreaks of the virus for the entire transmission season in Europe. "In the end, we want data-driven models; that's what AI can accomplish," says Rocklöv. Other researchers are making an important headway in creating a framework to predict novel host–parasite interactions.

Modeling studies can run months, years or decades. "The scientist is working with layers of data. The challenge is how to transform and couple different models together on a planetary scale," says Jeanne Fair, a scientist at Los Alamos National Laboratory, Biosecurity and Public Health, in New Mexico.

And it's a constantly changing picture. A modeling study in an April 2022 issue of *Nature* predicted that thousands of animals will migrate to cooler locales as temperatures rise. This means that various species will come into closer contact with people and other mammals for the first time. This is likely to increase the risk of emerging infectious disease transmitted from animals to humans, especially in Africa and Asia.

Other things can happen too. Global warming could precipitate viral mutations or new infectious diseases that don't respond to antimicrobial treatments. Insecticide-resistant mosquitoes could evolve. Weather-related food insecurity could increase malnutrition



ABOVE: Predicting outbreaks will require a multi-disciplinary approach. Scientists will have to merge epidemiological data with climatic, biological, environmental, ecological and demographic data, so joining forces is the only way to solve the formidable challenges ahead. Credit: Dr. Jeanne Fair.

and weaken people's immune systems. And the impact of an epidemic will be worse if it co-occurs during a heatwave, flood, or drought,
says Hess.

The devil is in the climate variables

Solid predictions about the future of climate and disease are not possible with so many uncertainties. Difficult-to-measure drivers must be added to the empirical model mix, such as land and water use, ecosystem changes or the public's willingness to accept a vaccine or practice social distancing. Nor is there any precedent for calculating the effect of climate changes that are accelerating at a faster speed than ever before.

The most critical climate variables thought to influence disease spread are temperature, precipitation, humidity, sunshine and wind, according to Tezaur's research. And then there are variables within variables. Influenza scientists, for example, found that warm winters were predictors of the most severe flu seasons in the following year.

The human factor may be the most challenging determinant. To what degree will people curtail greenhouse gas emissions, if at all? The swift development of effective COVID-19 vaccines was a game-changer, but will scientists be able to repeat it during the next pandemic? Plus, no model could predict the amount of internet-fueled COVID-19 misinformation, Fair noted. To tackle this issue, infectious disease teams are looking to include more sociologists and political scientists in their modeling.

Addressing the gaps

Currently, researchers are focusing on the near future, predicting for next year, says Fair. “When it comes to long-term, that's where we have the most work to do.” While scientists cannot foresee how political influences and misinformation spread will affect models, they are positioned to make headway in collecting and assessing new data streams that have never been merged.

Disease forecasting will require a significant investment into the infrastructure needed to collect data about the environment, vectors, and hosts at all spatial and temporal resolutions, Fair

The human factor may be the most challenging determinant.

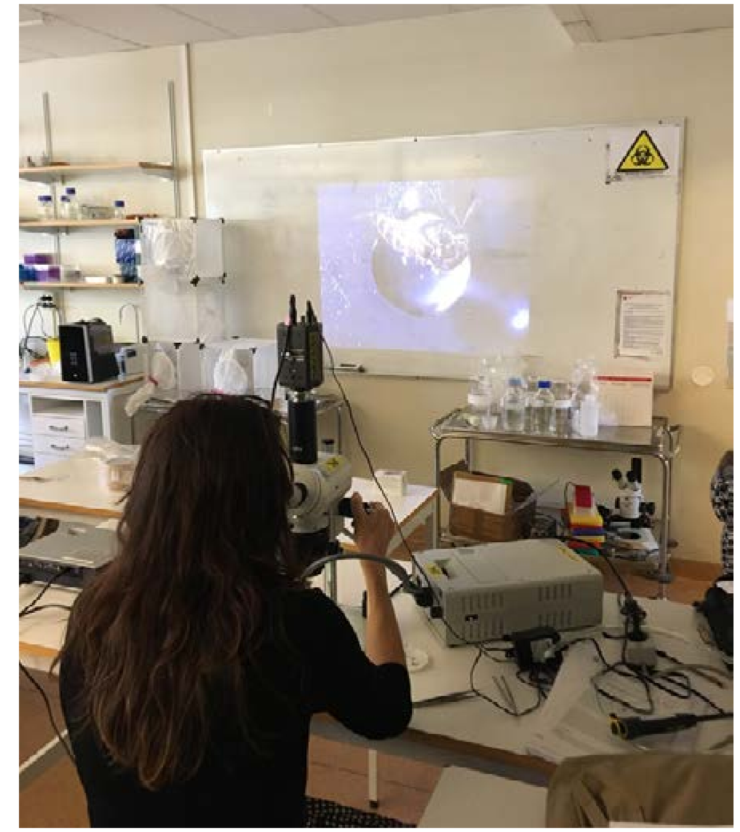
To what degree will people curtail greenhouse gas emissions, if at all?

and her co-authors stated in their recent study. For example real-time data on mosquito prevalence and diversity in various settings and times is limited or non-existent. Fair also would like to see standards set in mosquito data collection in every country. "Standardizing across the US would be a huge accomplishment," she says.

Hess points to a dearth of data in local and regional datasets about how extreme weather events play out in different geographic locations. His research indicates that Africa and the Middle East experienced substantial climate shifts, for example, but are unrepresented in the evidentiary database, which limits conclusions. "A model for dengue may be good in Singapore but not necessarily in Port-au-Prince," Hess explains. And, he adds, scientists need a way of evaluating models for how effective they are.

The hope, Rocklöv says, is that in the future we will have data-driven models rather than theoretical ones. In turn, sharper statistical analyses can inform resource allocation and intervention strategies to prevent outbreaks.

Most of all, experts emphasize that epidemiologists and climate scientists must stop working in silos. If scientists can successfully merge epidemiological data with climatic, biological, environmental, ecological and demographic data, they will make better predictions about complex disease patterns. A lack of modeling "cross talk" among scientific disciplines and nations is hindering discovery and advances, as well as countries refusing to release data.



ABOVE: Understanding how climate change contributes to the spread of disease is critical for thwarting future calamities. Credit: Dr. Jeanne Fair.

It's time for bold transdisciplinary action, says Hess. He points to initiatives that need funding in disease surveillance and control; developing and testing interventions; community education and social mobilization; decision-support analytics to predict when and where infections will emerge; advanced methodologies to improve modeling; training scientists in data management and integrated surveillance.

Establishing a new field of Outbreak Science to coordinate collaboration would accelerate progress. Investment in decision-support modeling tools for public health teams, policy makers, and other long-term planning stakeholders is imperative, too. We need to invest in programs that encourage people from climate modeling and epidemiology to work together in a cohesive fashion, says Tezaur. Joining forces is the only way to solve the formidable challenges ahead.

EVE GLICKSMAN is a freelance journalist in the Washington, DC, area. She has written for the Washington Post, WebMD, Leaps.org, US News & World Report, AAMCNews, and the Monitor on Psychology, among many others.