11-5-2022

The DAMA Protocol, an Introduction: Finding Pathogens before They Find Us

Eric P. Hoberg

Walter A. Boeger

Orsolya Molnár

Gábor Földvári

Scott Gardner

See next page for additional authors

Authors

Eric P. Hoberg, Walter A. Boeger, Orsolya Molnár, Gábor Földvári, Scott Gardner, Alicia Juarrero, Vitaliy A. Kharchenko, Eloy Ortiz, Valeria Trivellone, and Daniel R. Brooks

MANTER: Journal of Parasite Biodiversity (ISSN 2470-8224)
Occasional Papers, Number 21, November 3, 2022
doi: 10.32873/unl.dc.manter21
https://digitalcommons.unl.edu/manter/

This article has been produced in support of and with appreciation for the efforts by Gábor Földvári of the Institute of Evolution, Centre for Ecological Research, and the Centre for Eco-Epidemiology, National Laboratory for Health Security (both located at 1121 Budapest, Konkoly-Thege Miklós út 29-33, Hungary). Through his untiring efforts, team building, and leadership, he has secured the first EU-wide team research grant. This work was supported by the National Research, Development and Innovation Office in Hungary (RRF-2.3.1-21-2022-00006) and the COST Action CA21170 "Prevention, anticipation and mitigation of tick-borne disease risk applying the DAMA protocol (PRAGMATICK)," which represent the first funded efforts to apply the principles of the DAMA protocol.

The DAMA Protocol, an Introduction: Finding Pathogens before They Find Us

Eric P. Hoberg,[1] Walter A. Boeger,[2] Orsolya Molnár,[3] Gábor Földvári,[4] Scott L. Gardner,[5] Alicia Juarrero,[6] Vitaliy Kharchenko,[7] Eloy Ortiz,[8] Valeria Trivellone,[9] and Daniel R. Brooks[10]

1 Museum of Southwestern Biology, Department of Biology, University of New Mexico, MSC03 2020, Albuquerque, New Mexico, USA, 87138, and Department of Pathobiological Sciences, School of Veterinary Medicine, University of Wisconsin–Madison, Madison, Wisconsin, USA, 53716
2 Biological Interactions, Universidade Federal do Paraná, Curitiba, Paraná, Brazil
3 Konrad Lorenz Institute for Evolution and Cognition Research, Martinstrasse 12, Klosterneuburg, Austria, 3400, and Institute of Evolution, Centre for Ecological Research, 1121 Budapest, Konkoly-Thege Miklós út 29-33, Hungary
4 Institute of Evolution, Centre for Ecological Research, and the Centre for Eco-Epidemiology, National Laboratory for Health Security, 1121 Budapest, Konkoly-Thege Miklós út 29-33, Hungary.
5 Harold W. Manter Laboratory of Parasitology, W-529 Nebraska Hall, University of Nebraska State Museum and School of Biological Sciences, University of Nebraska–Lincoln, Lincoln, Nebraska, USA, 68588-0514
6 VectorAnalytica, Inc., Washington, DC, USA, 20007
7 I. I. Schmalhausen Institute of Zoology, vul. B. Khmelnyts'kogo, 15 Kyiv, 01054, Ukraine
8 VectorAnalytica, Inc., 6904 N. Kendall Drive, Apt. F302, Miami, Florida, USA, 33156
9 Illinois Natural History Survey, Prairie Research Institute, University of Illinois at Urbana-Champaign, Champaign, Illinois, USA, 61820
10 Institute of Evolution, Centre for Ecological Research, 1121 Budapest, Konkoly-Thege Miklós út 29-33, Hungary; Stellenbosch Institute for Advanced Study, Stellenbosch, South Africa; Harold W. Manter Laboratory of Parasitology, University of Nebraska State Museum, University of Nebraska–Lincoln, Lincoln, Nebraska, USA, 68588-0514; and Department of Ecology and Evolutionary Biology, University of Toronto, Toronto, Ontario, Canada, M5S3B2

Corresponding author – Eric P. Hoberg, email geocolonizer@gmail.com

ORCID:
Walter A. Boeger https://orcid.org/0000-0002-6004-2822
Daniel R. Brooks https://orcid.org/0000-0002-7891-9821
Gábor Földvári https://orcid.org/0000-0001-5297-9036
Scott L. Gardner https://orcid.org/0000-0003-3133-740X
Eric P. Hoberg https://orcid.org/0000-0003-0819-7437
Orsolya Molnár https://orcid.org/0000-0002-2458-4659
Valeria Trivellone https://orcid.org/0000-0003-1415-4097

Abstract
Globally, humanity is coming to recognize the magnitude of the interactive crisis for emerging infectious disease (EID). Strategies for coping with EID have been largely in the form of reactive measures for crisis response. The DAMA protocol (Document, Assess, Monitor, Act), the operational policy extension of the Stockholm paradigm, constitutes a preventive/proactive dimension to those efforts. DAMA is aimed at focusing and extending human and material resources devoted to coping with the accelerating wave of EID. DAMA is integrative, combining efforts to strategically document the distribution of complex pathogen and host assemblages in the biosphere in the context of dynamic environmental interfaces that provide the opportunities for pathogen exchange and emergence. Movement of habitats and animals (a breakdown in ecological isolation) catalyzed by climate change and broader anthropogenic trajectories of environmental disruption provide the landscape of opportunity for emergence. Evolutionarily and ecologically conserved capacities for exploitation of host-based resources allow pathogens to persist in one place or among a particular spectrum of hosts and provide insights to predict outcomes of persistence and emergence in novel conditions and across changing ecological interfaces. DAMA trajectories combine "boots on the ground" contributions of citizen scientists working with field biologists in development and application of sophisticated archival repositories, bioinformatics, molecular biology, and satellite surveillance. DAMA is a focus for anticipation, mitigation, and prevention of EID through knowledge of pathogens present in the environment and actions necessary to diminish risk space for their emergence. DAMA can be an effective strategy for buying time in the arena of accelerating environmental and socioeconomic disturbance and expanding EID linked to a future of climate change. Information + action = prediction and lives saved in a realm of EID.

Keywords: DAMA protocol (Document, Assess, Monitor, Act); Stockholm paradigm; emerging pathogens and disease; anticipation, prevention, and mitigation of emerging infectious disease (EID)

A Conceptual Arena for DAMA

An old adage says "an ounce of prevention is worth a pound of cure." Public and agricultural health specialists have made great progress in the area of those diseases, primarily with metabolic and behavioral etiology, deemed to be "preventable." Among people, preventive measures have proven to provide health and longevity benefits, which in turn have reduced the cost of crisis response to life-threatening acute episodes. Effective prevention depends on individual and societal capabilities which enable us to *anticipate* and *predict* the outcomes of certain behaviors—for example, too much sugar in a diet leads to increased risk of diabetes and too much red meat leads to risk of cardiovascular disease associated with elevated cholesterol levels. Until the formulation of the Stockholm paradigm (SP), infectious diseases were not considered preventable on a broad scale, a contention that remains dominant in current discourse about the nature of emerging infectious disease (EID) (Brooks et al., 2019; Agosta, 2022). The traditional assumption has embodied the idea that we must wait for a pathogen to evolve the capacity to colonize a new host, and we cannot predict when or where that will happen. Our responses over the past century have met with sporadic islands of success, signifying that effectively we have had few options beyond waiting for an EID to emerge and then trying to cope after the fact through eradication, vaccination, and palliation (Molnár, Hoberg, et al., 2022).

Once an EID was recognized and we came to understand its transmission dynamics, it was possible to think about mitigating new and extended outbreaks in a local sense on restricted landscape scales. The assumption that particular mutations must arise in order for a pathogen to move into a new host, however, gave us a false sense of security because we embraced the idea of an evolutionary or coevolutionary bulwark that would limit infections and disease. Such misconceptions continue to be propagated even in the most current explorations of emergence of infectious disease (e.g.,Tan et al., 2022). Given that EIDs were expected to be rare, there was often little incentive for thinking broadly and proactively about prevention or preventive measures. As a consequence, an accelerating EID crisis has caught medical, veterinary, agricultural, and wildlife health specialists often siloed and certainly unprepared (Brooks and Hoberg, 2013; Irving and Welburn, 2021; Trivellone et al., 2021; Wilcox et al., 2021; Wille et al., 2021; Harvey and Holmes, 2022; Trivellone, Cao, et al., 2022; Trivellone, Hoberg, et al., 2022). Concurrently, an effective proactive

stance has been hampered by adherence to concepts with limited explanatory power in the evolutionary and ecological arenas (Brooks et al., 2019; Agosta and Brooks, 2020; Wilcox et al., 2021; Agosta, 2022; Brooks, Boeger, et al., 2022).

The SP recognizes that the risk space for EIDs is far larger than many recent estimates (e.g., Carlson, Albery, et al., 2022; Harvey and Holmes, 2022). Concurrently, the SP explains how environmental perturbations, such as climate change or anthropogenic impacts, play a critical role in setting the stage through breakdown in ecological isolation, providing the opportunity for EIDs (Agosta, 2022; Brooks, Boeger, et al., 2022). The danger is great, time is short, and we remain largely complacent and often without focused purpose (Hoberg, Trivellone, et al., 2022). The SP provides a pathway for elucidating and understanding the broadening risk space of EIDs, leading to the possibility of proactive approaches for prevention and mitigation (Brooks et al., 2014, 2019; Molnár, Hoberg, et al., 2022; Trivellone, Hoberg, et al., 2022).

The SP suggests that colonizing a new host is based on preexisting capacities, especially with respect to transmission dynamics and microhabitat preferences (Araujo et al., 2015; Hoberg and Brooks, 2015; Brooks et al., 2019; Agosta, 2022; Brooks, Boeger, et al., 2022). Both the host resources needed for colonization and the modes of transmission from host to host are highly specific but phylogenetically conservative; a capacity for colonization is less about hosts than it is about the distribution of vital host-based resources. We can thus anticipate how those pathogens and their close relatives might operate in new circumstances when exposed to susceptible hosts they have not encountered in the past. Consequently, we can largely predict, within an evolutionary/ecological arena of capacity and opportunity, how a given known pathogen, or a previously unknown close relative of a known pathogen, might behave when it enters a new ecosystem or encounters a susceptible host for the first time (Brooks et al., 2019; Brooks, Boeger, et al., 2022; Boeger et al., 2022; Hoberg, Boeger, et al., 2022). A real expectation is apparent, and it becomes clear that with this knowledge we can begin to prevent at least some EIDs and mitigate the impacts of most on the horizon.

Definitions of biological diversity and distribution are windows to understand the realm of pathogens and their circulation among assemblages of hosts within and across environments; with knowledge, we can buy time while searching for long-term solutions. We can buy time because we can anticipate what pathogens are going to do as they come toward us, our crops, and our livestock. We can act to mitigate their advance and their impacts as they approach. This requires information about pathogens that might cause, but are not currently causing, disease in hosts that are infected, so we can assess their level of threat before a crisis emerges. In theory and practice, we should be able to *anticipate* to *mitigate* and *prevent* at least some of the potential disease risk for pathogens that have not yet—but shortly will have—emerged.

Increasing the geographic or host range of a pathogen may not always cause disease. Some host populations are less tolerant than others, some pathogen variants are inherently more pathogenic than others, and some pathogen variants are more or less pathogenic in different hosts (e.g., Brooks et al., 2019; Brooks, Boeger, et al., 2022). Collectively, such components of transmission dynamics may be subtly different in changing conditions or novel circumstances, either dampening or accelerating pathogen emergence (e.g., consider San Francisco and the history of introduction of bubonic plague to North America—Anderson, 1978; Randall, 2019). This means there may be a lag between the arrival of a pathogen in a host population or a geographic area and a subsequent disease outbreak. Shifting mosaics of pathogen presence and disease—emergence, quiescence, and reemergence—may be apparent, but pathogens seldom, if ever, disappear (Audy, 1958). If we can find these pathogens before they find us, we might be able to avert or at least mitigate disease outbreaks (Brooks et al., 2014; Vora et al., 2022).

Biodiversity knowledge is the essential foundation in recognizing and limiting potential outcomes of rapidly changing patterns of geographic and host associations among pathogens and the interfaces that establish boundaries across environments (Wille et al., 2021; Hoberg, Trivellone, et al., 2022). In order to be effective, we must have a fuller accounting of the geographic distribution, the fundamental fitness space, including actual and potential host range and the full dimensions of genetic variation—especially of the rare genotypes—for all pathogens known to cause disease. We need to know diversity and patterns of circulation for an array of pathogens when they are not infecting us or species of economic or societal importance across environments and food chains.

These interactions define the proactive aspect of the Stockholm paradigm. Once recognized, it becomes clear that putting the SP to work on the EID crisis requires a comprehensive policy extension to build a forward-scanning capacity to understand, anticipate, and respond to emerging disease. That policy proposal is the DAMA protocol—Document, Assess, Monitor, Act (Brooks et al., 2014, 2019; Brooks, Hoberg, et al. 2022; Trivellone, Hoberg, et al., 2022).

In our manuscript, and through a series of interconnected dialogues and perspectives in the current series of

papers on the subject of SP and DAMA in *MANTER: Journal of Parasite Biodiversity*, we introduce and consider the operational foundations of DAMA and its conceptual connections to the SP (Agosta, 2022; Brooks, Boeger, et al., 2022; Trivellone, 2022, and references therein). Components of DAMA receive attention in extended discussions of (1) *documentation* and the critical nature of biorepositories, archives, specimens, and information (Hoberg, Trivellone, et al., 2022; Trivellone, 2022); (2) *assessment*, with development of comparative phylogenetic methods and triage to define diversity and the dimensions of risk space (Trivellone and Panassiti, 2022) and the outcomes and insights of modeling the dynamics of colonization and emergence in complex host-pathogen systems (Souza et al., 2022); (3) *monitoring* with essential contributions from strategic field-based inventory, survey, and resurvey to recognize change, environmental interfaces, and risk (Hoberg, Trivellone, et al., 2022; Trivellone, 2022), and applications of novel and powerful electronic platforms for rapid surveillance and information exchange (Ortiz and Juarrero, 2022); and (4) *actions* considered in the arena of citizen science and integrative, real-time information on landscape scales to demonstrate risk space (Ortiz and Juarrero, 2022) and inclusion of evolutionary concepts and the essential role of information translation, dissemination, and communication networks in public policy and prevention (Molnár, Knickel, et al., 2022; Trivellone, 2022).

Defining the Components of DAMA

Document

We cannot make policy for species whose existence we know nothing about. We have increasingly fine-scale and sophisticated technology capable of documenting the diversity and distribution of potentially pathogenic micro- and macro-parasites before they announce themselves in disease outbreaks (Brooks et al., 2014, 2019; Hoberg and Brooks, 2015; Colella et al., 2021; Wille et al., 2021; Harvey and Holmes, 2022). The technological/empirical toolkit must be expanded with applications through strategic inventories and development of field-based biological collections guided by the SP (Colella et al., 2021; Hoberg, Trivellone, et al., 2022).

Documentation of diversity linked to phylogeny and natural history establishes ecological context for EIDs spatially and temporally, focusing on potential reservoirs and environmental interfaces that facilitate persistence and transmission. Pathogens are not a special subset of organisms that circulate under special evolutionary and ecological pathways. Pathogens are components of the larger biosphere and logically require understanding under a substantially broader umbrella of global diversity, which establishes environmental and biological context (Agosta, 2022; Brooks, Boeger, et al., 2022). DNA and RNA technology can facilitate this task, allowing us to prospect for potentially dangerous pathogens in and among animal or plant assemblages associated with urban, peri-urban, and natural habitats and the agrosphere extending beyond the usual focus of socioeconomic importance (Colella et al., 2021; Wille et al., 2021; Trivellone et al., 2021; Albery et al., 2022; Hoberg, Trivellone, et al., 2022; Trivellone, 2022; Trivellone, Cao, et al., 2022). Despite recommendations, documenting potentially zoonotic pathogens should be performed in their original (reservoir) hosts, prior to colonization of humans as a process of field-based discovery (Brooks, Boeger, et al., 2022). Contrary to recent comments summarized by E.C. Holmes (2022), documenting pathogens only after emergence is, in our view, profoundly dangerous and perpetuates a long-standing reactive stance toward pathogens and disease.

Those critical of a proactive stance (for zoonoses) advocate instead, or mainly, for surveillance to identify early human cases in conjunction with rapid response (Holmes et al., 2018; Gray et al., 2021). As counterarguments, (1) it is usually too late then for effective response and containment; (2) these measures may not be feasible, especially given that primary emergence events often occur in poor areas hugely lacking in healthcare infrastructure (for example, for West Nile virus and monkeypox—we have learned/will learn more about these pathogens in 2 years in the USA and Europe than in 70 years of endemism in Africa); and (3) once the "horse has bolted," costs explode and, as we have suggested, become unsustainable (Zinsstag et al., 2020; Bernstein et al., 2022; Trivellone, Hoberg, et al., 2022). Once colonization occurs, the emerging pathogen can rapidly exploit and spread through human populations and can often "evade" response-based attempts for containment and eradication in a globalized world that facilitates rapid expansion.

Proper assessment of biodiversity on scales from local to global begins with, and is dependent on, information derived from systematics (Hoberg, Trivellone, et al., 2022). Biologists implicitly acknowledge that systematics is the underpinning of all life sciences whenever they attach a species name to the organism they are studying. Systematics is the branch of biology charged with the responsibility of making certain that every biologist who uses a particular name refers to "the same thing." Assigning a specific epithet to a group of organisms is the proposal of a hypothesis that those organisms belong to what Darwin termed "communities of descent." That is, they are members of a diagnosable inclusive and exclusive hereditary

information system. When we name a species, we provide a key to valuable information about its origins and history, its location, and how it interacts with its surroundings, including other species (Brooks and McLennan, 2002; Hoberg, Trivellone, et al., 2022). Some of that information is embodied in the species itself, but most of it is embodied in the species' histories.

We cannot anticipate anything about the chances of expanding host range or disease, nor about the means of mitigation, for pathogens we have never documented. We do not have robust or approximate estimates of the diversity of pathogens in circulation on the planet because most of this micro- and macro-biota cause no problems or cause transient problems for a small minority of hosts or infect hosts that we rarely encounter. Despite efforts to the contrary, we continue to be limited and incomplete in evaluating the structure of the biosphere (Brooks and Hoberg, 2000, 2013; Carlson et al., 2020; Wille et al., 2021; Hoberg, Trivellone, et al., 2022). It is only when pathogens begin exploring new hosts that we notice their presence because that is when they are exploring a new fitness space, often becoming apparent through the disease outbreaks they trigger (e.g., Wei et al., 2021; Boeger et al., 2022; Brooks, Boeger, et al., 2022; Hoberg, Boeger, et al., 2022). If we focus only on symptoms and a socioeconomic context, we are likely missing both the true diversity of pathogens and the dimensions of risk space.

We live in a veritable sea of pathogens, and we have been blissfully unaware of most of them and their essential functions in the biosphere (e.g., Brooks and Ferrao, 2005; White, 2021; Wille et al., 2021). We do not, however, have to remain ignorant. Best estimates are that we have documented less than 10% of the pathogens on this planet. For example, an estimated 1.7 million viruses occur in mammals and waterbirds (the vertebrate hosts most commonly identified in the origins of novel zoonoses), while the current catalogued viral diversity from these hosts is less than 2,000 (Carroll et al., 2018; Carlson et al., 2019). A generation ago, compiling a comprehensive inventory of species of pathogens was a daunting challenge, hugely expensive in time, money, and personnel; for the most part, the challenge was not taken up. Technological advances made in the intervening years have allowed us to generate large amounts of data about the presence of micro- and macro-parasites in any given site for relatively little money and in a short time (e.g., Dunnum et al., 2017; Colella et al., 2021; Wille et al., 2021). Over the past decade, this capability has contributed to a kind of "basic field biology on steroids" in our accelerating view of pathogens in the global biosphere (USAID, 2014, 2016; Joly et al., 2016; Cook et al., 2017).

When we discuss documentation, we are immediately talking about systematists. Systematists are the biologists best trained to expect the unexpected. In fact, they are often preoccupied to the point of obsession with finding species no one has ever seen before. Poor attention paid to taxonomy can have significant repercussions in coping with disease (Dunnum et al., 2017; Cook et al., 2020; Hoberg, Trivellone, et al., 2022). We must continuously and strategically explore the interfaces of managed agricultural and wildlands ecosystems, where the biological complexity of viruses, bacteria, plants, fungi, animals (including humans), and environments are in frequent contact. We must have rapid and accurate identification from taxonomy and systematics to create the risk matrix to predict the impact of pathogens. Disease emergence and substantial economic impacts can be averted when taxonomic principles—knowing what you actually have—are applied in practice (Hoberg, Trivellone, et al., 2022).

Expanding technology in hand can further change the game by creating possibilities for searching for pathogens in ways that do not injure or kill the host; a caveat is definitive identification of host specimens and deposition of vouchers remain absolutely essential (Colella et al., 2021; Hoberg, Trivellone, et al., 2022). If we examine feces left by large and mobile animals, however, that were not in the vicinity when we arrived, preexisting nucleotide sequence databases (if these are sufficiently robust, validated, and comprehensive) allow us to identify the host species as well as the pathogens and to link those data to information about geographic ranges and host population structure. We can do this with blood, urine, and tissues of animals as well, greatly enhancing the possibility of microbial discovery (Curry, 2014; Kutz et al., 2015; Forde et al., 2016; Cook et al., 2017; Galbreath et al., 2019; Colella et al., 2020). Further, the discovery of plant pathogens is immediately enhanced through sampling of fluids from the hemocoel of arthropod vectors and molecular characterization of associated microparasites (Trivellone et al., 2021; Trivellone, Cao, et al., 2022).

At the metagenomics frontier, there is now the possibility of increasingly rapid to real-time identification of microparasites (viruses, bacteria, fungi, and protozoa) and macroparasites (worms and arthropods) through noninvasive sampling (Colella et al., 2020, 2021; Wille et al., 2021). Noninvasive sampling provides a trajectory for near-simultaneous evaluations of distribution that are both geographically extensive and site intensive and can be a logistically powerful alternative in remote environments for tracking diversity and change in space and time when based on authoritative identification (Kutz et al., 2007; Forde et al., 2016; Kafle et al., 2020). A capacity for noninvasive survey,

however, does not eliminate the continuing necessity for strategic field-based biological collections and development of archival resources for host species, tissues, pathogen specimens, and information (e.g., Dunnum et al., 2017; Cook et al., 2020; Colella et al., 2020, 2021; Hoberg, Trivellone, et al., 2022). In the absence of archives and vouchers with authoritative identifications, biodiversity information cannot be confirmed, and baselines are suspect; access to original materials from the field for extended analyses in the realm of the "holistic specimen" with the advent of new tools and technologies is not possible (Hoberg, Trivellone, et al., 2022).

In short, taxonomic inventories are a necessity for humanity. As a pathogen-centric process, documentation and expanding inventories linked directly to archives should be focused around the tasks of providing the following information: (1) pathogen diversity and species identity; (2) host identity (and tissue tropism); (3) geographic (geo-referenced) locality; (4) an eventual phylogenetic history and context; and (5) documentation of interface conditions, ecological circumstances, natural history, and epidemiological information. These efforts require a fusion of modern technology with old-fashioned sweat equity–based natural history, taxonomy, ecology, and behavior. As a result of technological advances in the past 25 years, inventories for documenting diversity have been transformed from clawing a manageable number of data points out of the wildlands to being overwhelmed by mountains of data obtained from large-scale field collections.

Coordination of large-scale inventories may remain a top-down, science-driven trajectory with a dispersed capacity across landscapes. For example, consider the temporal/spatial scales for survey across the continuum apparent from the PREDICT program that explores viral pathogen diversity in putative geographic hotspots (Jones et al., 2008) primarily in the tropics (e.g., USAID, 2014, 2016; Young and Olival, 2016; Olival et al., 2017; Grange et al., 2021) to synoptic surveying that explores diversity and connectivity across major biogeographic zones at high latitudes (e.g., Cook et al., 2017; Colella et al., 2020) and landscape-level elucidation of reservoir hosts and pathogens at the immediate human-environment interface (e.g., Földvári et al., 2011, 2014; Szekeres et al., 2019). Effective documentation is ultimately dependent on grassroots training and cooperation from citizen scientists to parataxonomists across local networks on the ground (e.g., Kutz and Tomaselli, 2019; Földvári et al., 2022). In the arena of biorepositories and archives, with authoritative identification and documentation, everything else downstream becomes possible.

Assess

Assessment is the process of establishing or estimating risk relative to observed diversity for micro- and macro-parasites. In the course of any effort to document pathogen diversity, we will encounter an enormous number of species that are not recognized as pathogens. Some of these may be of potential use to humanity, possibly even of help in treating disease. If we had time, we would document every single species we discover and painstakingly study it to determine just how it might affect humanity, for better or worse. Given the immediacy and magnitude of the EID threat, we cannot afford that luxury.

We must make rapid decisions, in the face of massive amounts of data, about which species need our immediate attention. The documentation phase of the DAMA protocol advocates inventories that are strategic, with the goal of revealing potentially dangerous pathogens before they become a problem. As a consequence, the focus of the DAMA protocol is not on accumulating synoptic snapshots of biodiversity but on assessing a burgeoning foundation of basic information acquired strategically in the context of environmental boundaries and disease risk.

The speed with which EID crises are unfolding and their global extent make methods for rapid sampling of large numbers of potential hosts a priority. Historically, quests to find pathogens involved laborious and detailed examinations of single hosts; often, when necessary, intricate protocols for culturing; and challenging methods for diagnostics. Fusion of classical methods with emergent molecular technologies for identification is driving a dramatic transformation. Pathogen diversity among animals or plants can be assessed and characterized through direct subsampling, amplification, and targeted sequencing from tissues and fluids derived from reservoir hosts and arthropod vectors (Trivellone et al., 2021; Trivellone, Cao, et al., 2022). A component of this methodological shift evolved from original concepts of genetic barcoding (having definitive molecular markers for identification of each species) and has begun to intensify our capabilities. Importantly, these original and new extensions of barcoding always need to be grounded in what we call authoritative identification based on an actual archived specimen, highlighting the critical relevance of museums, taxonomists, databases, and informatics (Colella et al., 2021).

Inventories will document more micro- and macro-parasites than we can hope to analyze in a timely manner (Carlson et al., 2020; Harvey and Holmes, 2022). For example, although current estimates vary (Wille et al., 2021; Carlson, Albery, et al., 2022; Gibb et al., 2022), approximately 320,000 species of viruses in 9 families circulate among mammals (Anthony et al., 2013). Most of the viruses

documented will not pose imminent threats. We need to rapidly and effectively assess the apparent risk for suites of potential pathogens discovered through inventory. In the absence of assessment based on principles of the SP, there is no simple path to such prioritization. Further, current attempts for documentation and monitoring that emanate from assessment have to an extent been based on previously known limits for diversity. Effective assessment is a 3-part process combining phylogenetic and ecological components.

1 Phylogenetic Triage

Of the myriad pathogens documented, which ones should be the focus of special attention? As a result of the phylogenetics revolution, systematics has become a multifaceted science capable of providing a wide range of essential biological information in an explicitly evolutionary framework. If we first place each documented pathogen in its phylogenetic context (Young and Olival, 2016; Brooks et al., 2019; Temmam et al., 2022), we can quickly focus our research beam by asking two questions. First, is this a known pathogen? Second, is this a close relative of a known pathogen? If the answer to both questions is "no," the pathogen is deemed to be of low risk at that time and accorded the status of "defer focused study but archive," recognizing that initial risk designations may change. If the answer to question 1 is "yes," and the pathogen has been found in a host known to be susceptible to disease when infected, relevant health authorities should be alerted and their plans for dealing with the pathogen activated. If the known pathogen is found in a novel host, or if the answer to question 1 is "no" but "yes" to question 2, the pathogen is targeted for further scrutiny in the DAMA context (Figure 1).

As a current and timely example, operationally we would anticipate that *Betacoronavirus* (including *Sarbecovirus* which contains SARS-CoV and SARS-CoV-2) and

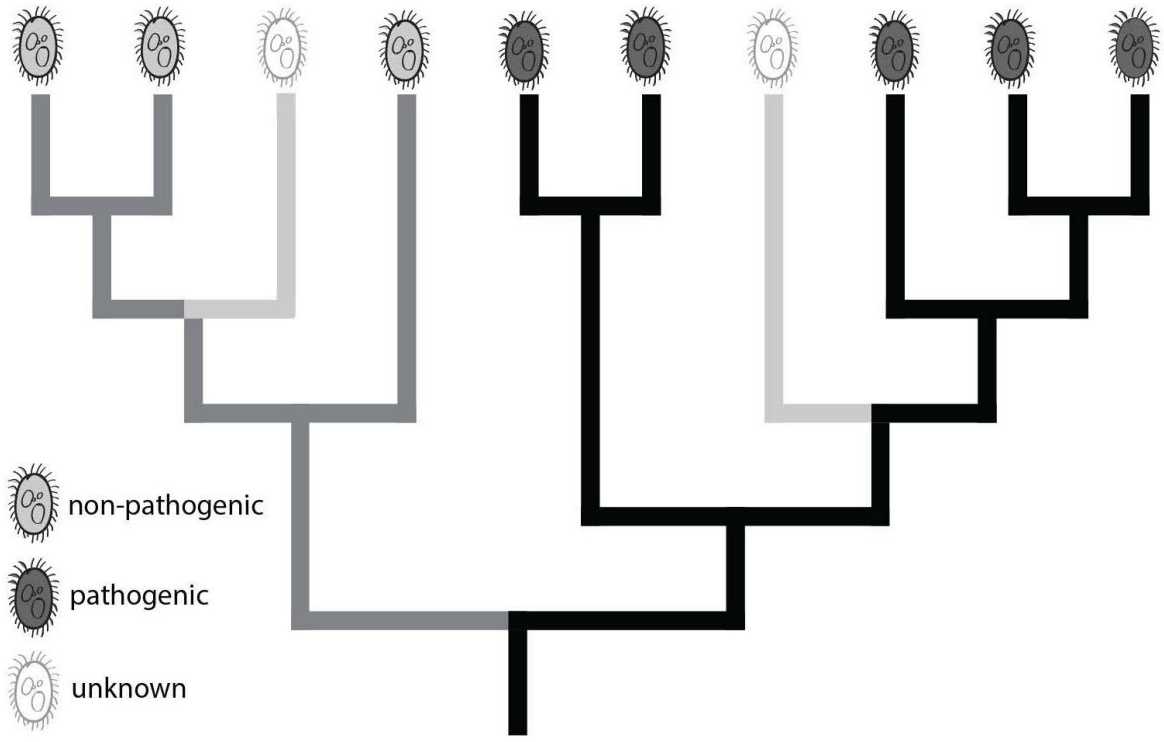

Figure 1. Diagrammatic representation of how we use phylogenetic relationships to assess the threat that an unknown, newly discovered pathogen might cause disease. In this case, we have a group of ciliated microbes of some sort, two of which are "unknowns." The one on the left is closely related to a group of 3 other species, none of which cause disease. The one on the right is also a member of a group of 3 other species, but in this case, all of them are disease-causing pathogens. All other things being equal, we would assess the threat level for the unknown on the left as "low" and for the one on the right as "high." (From Brooks et al., 2019)

some *Alphacoronavirus* species pose a high risk for emergence and reemergence (Boni et al., 2020; Damas et al., 2020; Latinne et al., 2020; Cai and Cai, 2021; Lin et al., 2021; Mallapaty, 2021; Rochman et al., 2021; Boeger et al., 2022; Hoberg, Boeger, et al., 2022; Sun et al., 2022). Documentation thus would focus initially, in this scenario, on the isolated assemblages of chiropterans in Southeast Asia where a considerable diversity of SARS-like viruses has been recognized (Latinne et al., 2020; Temmam et al., 2022); inventory should extend to an array of sympatric and synchronic mammalian species in adjacent landscapes. Assessment involves phylogeny with the recognition that capacity for infection in mammals is widespread and that ecological factors (opportunity) are critical in posing particular limits on realized host distribution and linkages to human infection through stepping-stone pathways (e.g., Boeger et al., 2022; Brooks, Boeger, et al., 2022; Hoberg, Boeger, et al., 2022). Stepping-stone dynamics and pathways are critical given the limited potential for direct colonization from chiropterans to humans (e.g., Zhao et al., 2022). Consequently, phylogenetic assessment and triage provides the initial foundation for defining capacity within the broader limits of ecological opportunity.

2 Phylogenetic Assessment and Context = Capacity

Comparative phylogenetic studies of pathogens, identified with high threat potential, allow us to infer their likely places of origin, hosts of origin, likely transmission modes, and likely microhabitat preferences (host resource specificity); examples across a diversity of micro- and macro-parasites have been summarized elsewhere (Brooks and McLennan, 2002; Brooks et al., 2019). It is at this point that the SP becomes essential. These pathogen-host associations demonstrated a fundamental insight from the SP which signifies the generality of processes for colonization (the interaction of capacity and opportunity) in the biosphere and applicability in managed and wild systems involved in human and animal health, agricultural production, and food security (e.g., Brooks, Hoberg, et al., 2022; Trivellone, Hoberg, et al., 2022).

The dimensions of diversity in a historical-phylogenetic context for pathogens and hosts that defines the distribution of critical and conserved host-based resources is essential in understanding capacity and the limits of risk space. As a hypothetical example from SARS-like viruses, 5,400 species of mammals all may possess functional ACE2 receptors which define the fundamental fitness space for viral transmission and persistence; as understood, essentially all mammals on the planet are susceptible. In a thought experiment, let's assume conservatively a minimum of 50 species of *Sarbecovirus* that are specialized on ACE2—this suggests 270,000 potential EIDs in mammals from sarbecoviruses alone (without considering potential environmental-ecological drivers influencing opportunity). Carlson, Albery, et al. (2022) suggested that the risk from climate change is only about 1,200 EIDs in mammals across the currently 320,000 species of viruses in 9 families known to circulate among this class of vertebrates. If each of those 320,000 species is as specialized as SARS-CoV-2, however, the potential risk space for viral EID in mammals from viruses infecting other mammals alone is considerably greater—representing 1,728,000,000 potential events of colonization and expansion. An ongoing demonstration of this risk space is indicated by global resurgence of infections attributed to monkeypox virus (Brooks et al., 2019; Howard and Nedelman, 2022). Additionally, such an estimate excludes a broader array of pathogens, for example, West Nile virus and avian influenza expanding their host ranges from birds to mammals (Chen et al., 2022). Of course, major caveats are linked to such estimates that depend directly on the accuracy of inventory and the dimensions of documented viral diversity (Wille et al., 2021; Gibb et al., 2022). Capacity for exploitation of host-based resources, in a phylogenetic context, however, is central and is tempered by changing opportunity in dynamic ecological associations and across interfaces in space and time.

As well, we should expect that the disease syndromes associated with closely related pathogen species should be quite similar. As a consequence, some EIDs may be misdiagnosed early in an outbreak, with potentially disastrous consequences (e.g., Randall, 2019; Hoberg, Trivellone, et al., 2022).

3 Ecological Assessment and Context = Opportunity

Understanding the population genetics and ecology of a potential pathogen is explored through matching fitness profiles within a modeling platform (Araujo et al., 2015; Braga et al., 2018; Brooks et al., 2019; D'Bastiani et al., 2020; ; Feronato et al., 2022; Souza et al., 2022) to identify likely reservoir hosts. Secondarily, ecological niche modeling can refine insights or determine likely habitat interfaces for transmission (Peterson, 2006). Ecological assessment reveals information about the nature of changing environments and where to anticipate focal points for high-risk pathogens and the environmental interfaces that drive pathways for contact. Defining potential gateways for circulation and transmission is fundamental before the onset of an outbreak rather than waiting for pathogens to announce themselves with the expansion of disease among wildlife, livestock, crops, or people (e.g., Hoberg, Trivellone, et al., 2022; Trivellone, 2022; Trivellone, Hoberg, et al., 2022).

Although complex and sophisticated, activities that produce data necessary for assessment decisions are straightforward. They involve molecular taxonomy to identify known pathogens before they trigger disease outbreaks *and* phylogenetic analyses to identify relatives of known pathogens. A phylogenetic comparative framework, as shown in explorations of viral diversity among mammals, facilitates historical ecological comparisons of those close relatives to assess the risk potential of an unknown pathogen (Anthony et al., 2013; Young and Olival, 2016; Latinne et al., 2020; Mollentze and Streicker, 2020; Wille et al., 2021; Zhou et al., 2021; Temmam et al., 2022; Harvey and Holmes, 2022). Consequently, phylogeny is the foundation for assessment and provides the basis for definitions of risk space and the need for downstream monitoring to identify the outcomes of changing opportunity and fluid environmental boundaries.

Monitor

Monitoring activities reinforce assessment where targeted and strategic time series for resurvey regularly sample assemblages of pathogens and hosts across the landscapes or regions where they have been discovered. Environmental sloshing under climate warming and habitat perturbations can modify or shift the distribution of "vulnerable or permissive areas" that are essential for persistence of pathogens and which influence the dynamics of EIDs (Hoberg and Brooks, 2015; Kafle et al., 2020). Monitoring reveals movement, invasion, and biotic mixing coinciding with environmental forcing, resulting in floral and faunal mosaics, signifying new opportunities concurrent with temporal and spatial expansion (or contraction) of risk space over time (Hoberg, 2010). Integral to monitoring are the cumulative pictures and baselines of pathogen and host diversity that are assembled and summarized in archival biorepositories of specimens and information (Dunnum et al., 2017; Colella et al., 2021; Hoberg, Trivellone, et al., 2022).

Monitoring efforts should focus on discovery of reservoir hosts that are infected but not diseased (Audy, 1958), along with the dynamics for pathogen transmission within core habitats and across boundaries and interfaces on the margins of urban/peri-urban, wildlands, and agroscape environments (Figure 2). Connectivity within those spaces is fluid, with pathways influencing pathogen and disease distribution. As J.R. Audy (1958) noted more than half a century ago, pathogen distribution is not homogenous, and the geographic and host range of a pathogen always exceeds that of the disease caused by it. Audy's insights, coupled with the SP, suggest that many disease outbreaks are the result of "silent spreading" in asymptomatic hosts or in hosts that are not known to be competent hosts for a given pathogen and as a consequence are not being monitored (also see comments in Hoberg, Trivellone, et al., 2022). In addition, early in an outbreak, clinicians not trained to expect novel disease emergence may misdiagnose the pathogen as something previously known that causes similar signs and symptoms. The COVID pandemic and the secondary emergence of Omicron (Boeger et al., 2022; Hoberg, Boeger, et al., 2022) were associated with all three shortcomings.

Field-based biological collections, as a component of monitoring, drive continuing reassessment of diversity and ecological circumstances in conjunction with modeling platforms to alert us to changes in pathogen populations. Monitoring and surveillance generate actionable information about expanding risk space (e.g., the extent and outcomes of anthropogenic and environmental disruption across habitat interfaces). These events emphasize monitoring as a critical capability.

We have limited understanding of the geographic distribution and natural history of pathogens during those times when they are not engaging our attention. Nor do we always understand well the biotic/abiotic factors that catalyze shifts from quiescence to disease. Now that there is an emerging popular awareness of the role of climate change in EID (Carlson, Albery, et al., 2022), it is possible there will be more attention and support for this aspect of DAMA activities. As a consequence, we must monitor and model anthropogenic climate forcing, indicated by long-term progressive and short-term fluctuating changes in many variables, particularly temperature and precipitation (Brooks et al., 2019). We must also monitor host and geographic ranges for pathogens of elevated threat, paying particular attention to new biotic mosaics emerging from geographic and host range expansion under the ultimate and proximate drivers and often subtle outcomes of climate forcing (Hoberg et al., 2017).

Monitoring networks can combine geographically extensive and site-intensive sampling information across thousands of kilometers into series of snapshots of pathogen distribution. Linking those snapshots into time sequences (metaphorical videos) would allow us to observe changes in pathogen distribution and behavior, such as those driven by subtle climate shifts, in near real time. The ultimate goals are to recognize previously unoccupied fitness space before the pathogen finds it (anticipation) and to recognize in real time when the pathogen enters it (mitigation). As indicated previously, ecological niche modeling should play a critical role in these efforts.

The need to coordinate on multiple levels of human society becomes apparent in monitoring activities. On the one hand, we will take advantage of ongoing

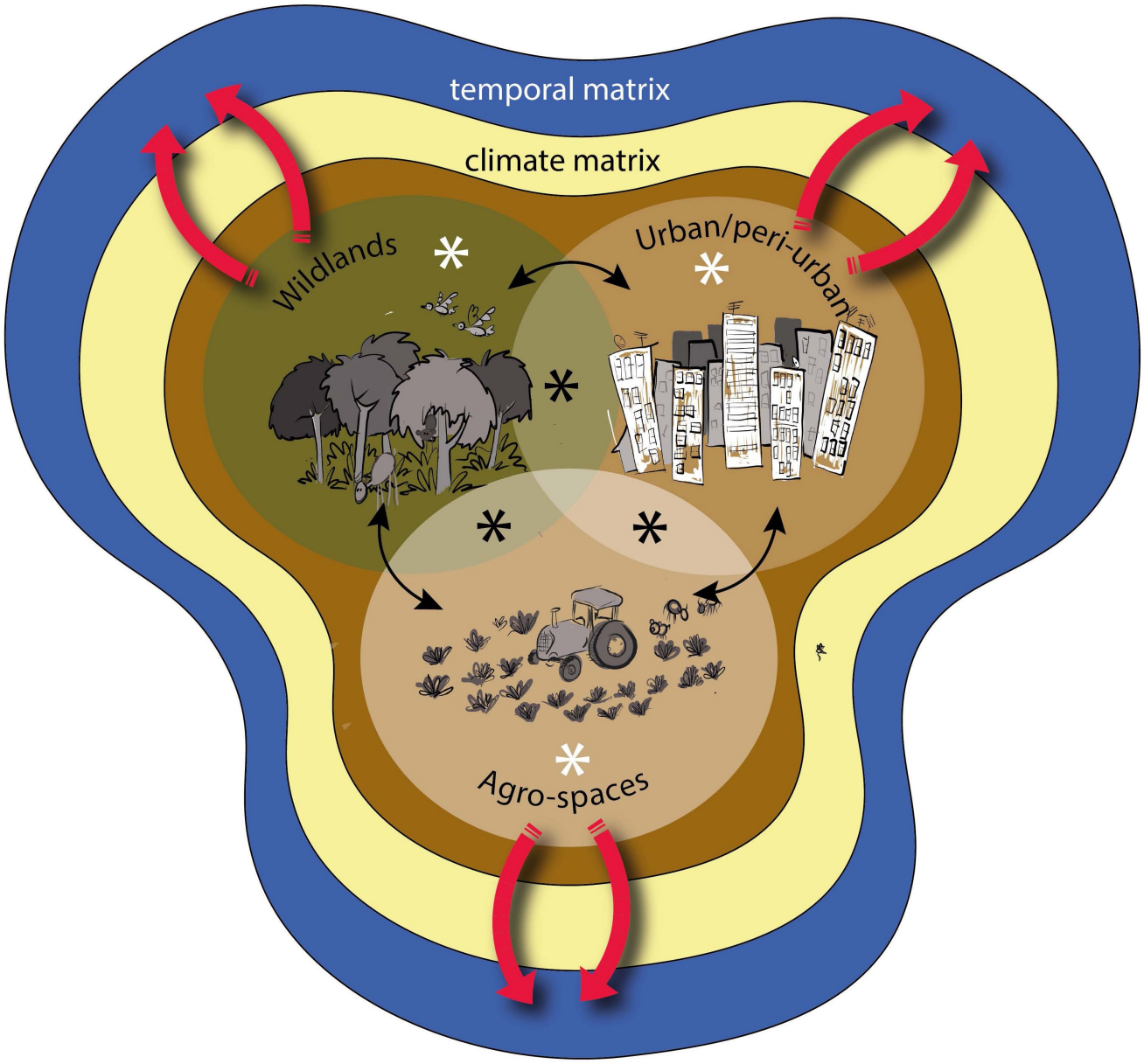

Figure 2. The arena for DAMA, showing a strategic focus for documentation and action regions with the potential for intervention within a matrix that links space, climate, and time. Three major landscapes—Wildlands, Urban/peri-urban, and Agro-spaces—and diverse habitat interfaces (black asterisks) represent risk spaces for occurrence of EIDs (bidirectional black arrows). Connectivity within and among the landscapes (red arrows) is dynamic (temporal matrix) and includes passive (e.g., climate responses) and active pathways (e.g., globalization, land use). In a proactive capacity, interventions are most appropriate and effective within landscapes (white asterisks) and among interfaces (black asterisks), which we define as *intervention space*, in order to prevent triggers for pathogen expansion. In this way, the scientific community can identify and communicate specific targets for actions to be undertaken. Taking action, however, requires cooperation among an often-siloed scientific community, public institutions, and governmental and nongovernmental organizations and agencies that develop, receive, and translate knowledge and insights for global humanity. (Modified from Trivellone et al., 2022a)

documentation activities and personnel to begin the essential process of getting "buy-in" from local citizens. Sharing local or indigenous insights and observations—what is often called traditional ecological knowledge—is critical. For example, in boreal hamlets and communities, hunters on the tundra and sea ice hold special knowledge and experience and are often among the few that regularly venture across remote regions (Kutz and Tomaselli, 2019). Tapping this kind of human capacity, from the poles to the tropics, will produce regular observations by people with great sensitivity to changes in their local ecosystems that might enhance pathogen transmission. Observations, sent to coordinating data centers using specially designed cell phone applications, can provide the essential information for specialists exploring the interactions of population genetics, population ecology, and phylogeography (Ortiz and Juarrero, 2022). Further, their results will also allow modelers to produce projections for various temporal and spatial scales (how fast is it moving, how far is it going?) (e.g., Kafle et al., 2020). And those results will disseminate to those people and organizations in the broader surveillance community. The goal is to create a flow of "observation to data to analysis to projection to decision," a loop operating as close to real time as possible, beginning with those who are most at risk, directly for human disease and indirectly through food chains and security (Brooks et al., 2014; Colella et al., 2021; Ortiz and Juarrero, 2022; Trivellone, Hoberg, et al., 2022).

Specimens and data assembled through resurvey and monitoring activities feed into assessment, providing a path to refine basic information about diversity and expand insights derived from phylogeny and ecology (e.g., Colella et al., 2021; Hoberg, Trivellone, et al., 2022). Results of ongoing monitoring and reassessment form the basis for alerting public officials and the general public to environmental and biological changes that could indicate an emerging threat. Information from monitoring programs can determine which potential or known pathogens of high risk are already present but not yet causing disease and which are likely to be approaching (and the array of vectors and reservoirs). The goal is to prevent as many outbreaks as possible and to mitigate the impact of those we cannot prevent.

Act

Once pathogen/disease threats have been identified, there must be action. And it must be prompt and decisive. The activities of health practitioners of all kinds are based on a simple, straightforward, ancient, and honorable philosophy known as "Do No Harm." Lamentably, "Do No Harm" has become a prescription for conservative thinking and for waiting until an epidemic or pandemic occurs, initially rushing to build uncoordinated responses for containment while hoping this will be the last one. A passive complacency seems to follow, as each emergent event fades or burns out into the pathogen background. Priorities and urgency shift with time. That recurrent model, played out on local to regional and global scales, has proven to be less effective than we would wish—and economically unsustainable.

As the world becomes increasingly urbanized, the challenge of EID will grow, exacerbated by climate displacement, food and water insecurity, and inequality (e.g., Whitmee et al., 2015; Brooks et al., 2019; Trivellone, Hoberg, et al., 2022). High population density in urban settings makes it difficult to know who you can count on in an emergency. Not knowing who to cooperate with puts people at risk of not being able to mobilize effectively. A lack of trust is generally compensated for by government services, assumed to be neutral and objective with respect to all citizens. Even this assumption is regularly doubted, especially in the largest urban centers, where services seem to be delivered in a nonuniform manner; again, consider the history of plague and responses in San Francisco more than a century ago (e.g., Randall, 2019).

Operational Action—Education and Infrastructure

Two components of activities are associated with "Act." The first emphasizes public outreach and jobs training. Public health means public education. People need reliable information that provides choices for behavioral change to accommodate EID. Simply knowing what to look for—the signs and symptoms of emergent disease—is fundamental. Knowing your local environment—for example, checking your children for ticks, emptying a bird bath, altering dawn and dusk activity patterns, and maintaining access to clean water and unspoiled food—can limit chains of exposure and infection. A cost-effective way to do this is through the science-based curriculum of local schools and public natural history museums, where knowledge is power.

Everyone should be educated to make a contribution. Adult education through government-funded outreach programs as well as informal outreach is also essential. Not only will this communication provide critical information, it will reinforce to the average citizen that EID prevention is a national security priority. Then there can be a partnership in which the average citizen understands that there is a crisis; although the government-supported scientists deal with existing problems and try to anticipate new threats, actions by the public are essential.

The EID crisis is a global concern for security and human well-being such that "act" recommendations must be shared with relevant governmental and nongovernmental

organizations (NGOs) that can spread an alert as widely as is necessary and take appropriate action. In return, those organizations bear the responsibility of getting DAMA projects off the ground. "Do No Harm" must be replaced with the "Precautionary Principle," which admonishes researchers that incomplete knowledge is no reason not to act when faced with a crisis. In the case of the EID crisis, the *precautionary principle* gives us a mandate to investigate pathogens that represent a risk of disease before they become the agents of an outbreak.

Information must circulate easily, and DAMA can link components of translated data to effective action. In the Information Age, barriers to accessibility for critical insights and actions for EIDs must be eliminated. DAMA initiatives can function effectively when information is shared freely among all concerned parties. Anticipate

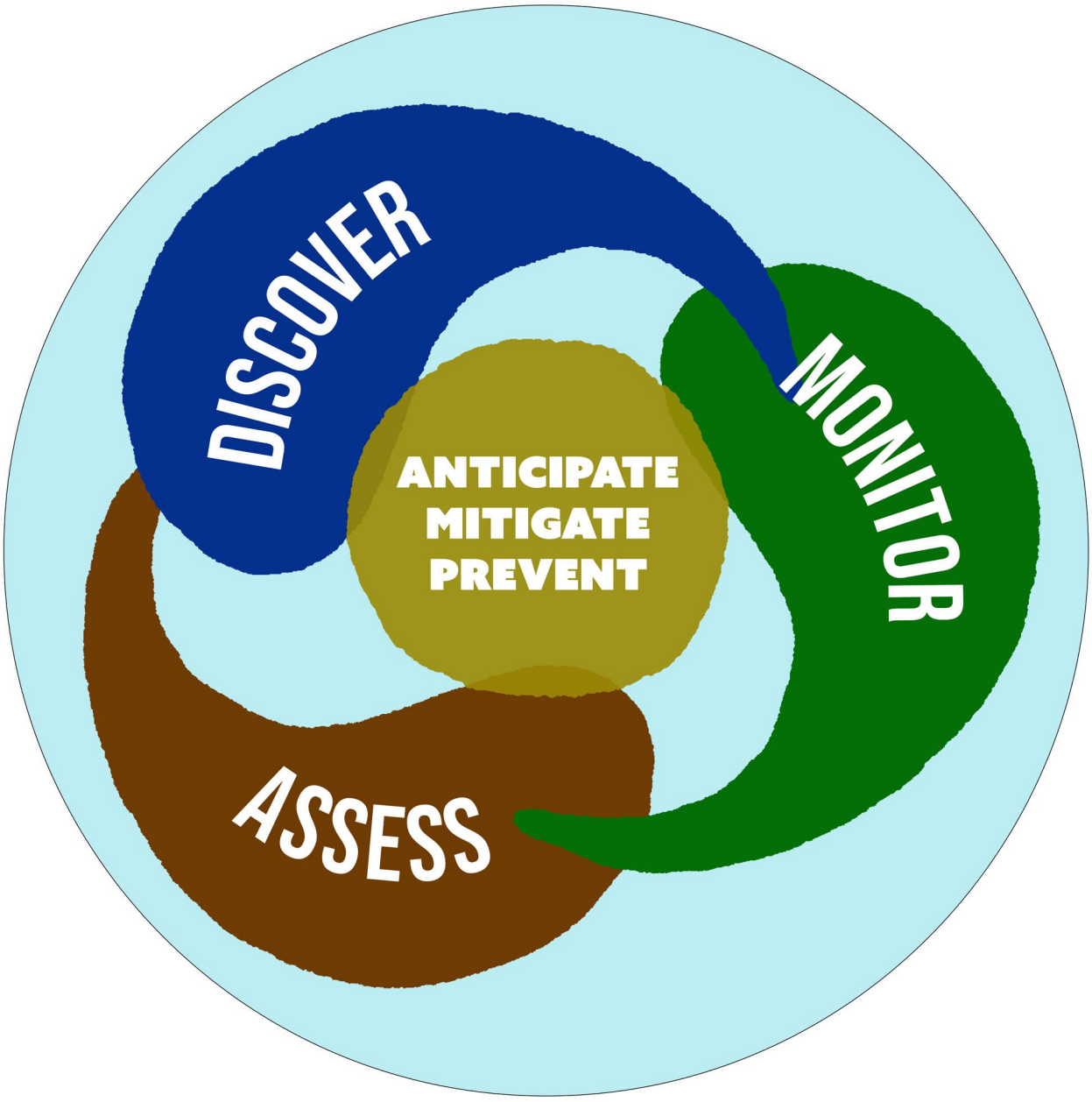

Figure 3. Interconnected DAMA pathways showing the scheme for information flow across Discover, Assess, Monitor as the primary interacting focus for actions that support prevention through anticipation and mitigation. (Modified from Trivellone, Hoberg, et al., 2022)

to prevent is the rationale for producing time-sensitive recommendations that can avert outbreaks of diseases (Ortiz and Juarrero, 2022; Trivellone, Hoberg, et al., 2022) (Figure 3).

One of the best "proof of concept" studies that we know of for DAMA has been done by the Hungarian disease ecologist Gábor Földvári and his associates working with urban hedgehogs and their pathogens in a Budapest city park. Margaret Island sits in the middle of the Danube River just upstream from the Hungarian Parliament Building. It is a place of history, natural beauty, and intense human recreational use. Among the wildlife species on the island are the incredibly cute hedgehogs. They, in turn, host an array of ticks, some of which may attach themselves to humans, given the opportunity. Földvári and his research group investigated hedgehogs of the island for three consecutive years (Földvári et al., 2011, 2014). While documenting basic ecological parameters of the animals, they made several important observations. First, these hedgehogs, as one of the most successful mammals adapted to an urban environment, reach several times higher densities in the urban park than in rural areas. Second, they maintain an exceptionally high intensity of tick infestation. The intensive fieldwork that enabled the researchers to study more than 400 individual hedgehogs was possible only with substantial involvement from citizen science. Sometimes over 40 enthusiastic volunteers, students, family members, and friends of scientists helped in collecting, transporting, and releasing the hedgehogs during the late-night hours. The bulk of the nearly 10,000 ticks removed and identified was the sheep tick, *Ixodes ricinus*, for which the most important host seemed to be the hedgehog itself. However, the exotic species *Hyalomma marginatum* (vector of the Crimean-Congo haemorrhagic fever virus) was also identified, highlighting the importance of monitoring these ectoparasites even within our closest neighborhoods. They also discovered that although they had no symptoms, hedgehogs carry an array of bacteria like *Borrelia burgdorferi sensu lato*, *Anaplasma phagocytophilum*, *Neoehrlichia mikurensis*, and *Rickettsia* species, which are potentially pathogenic in humans (Földvári et al., 2014; Szekeres, Majláthová, et al., 2016; Szekeres, van Leeuwen, et al., 2016). Further, they revealed that very few humans actually found ticks on themselves when they returned from a day at the island. And they discovered two additional pieces of information. First, no one who spent the day lying on grass that was regularly mowed by city personnel ever reported finding a tick on themselves. Evidently, the mown grass is too short for maintaining humidity, the limiting environmental factor for the ticks. Second, a significantly higher density of ticks occurred in the shrubberies and "hidden" parts of the island where the dense vegetation favored tick survival. As a consequence, all those people who reported finding ticks on themselves had one thing in common: finding that the island had only two public toilets, which were not always open, they had availed themselves of the underbrush beside the areas of mowed grass. As those people using the bushes as latrines are at highest risk, a relatively cheap and effective way of significantly reducing disease risk is the installation of additional public toilets on the island (G. Földvári et al., unpublished data). Scalable from landscapes to regions, DAMA provides insights and access to critical information that can limit pathogen exposures and potential for emergent disease.

A Sense of Urgency—The Proof of Concept

DAMA projects integrate across geographic and temporal scales. To date there have been no complete initiatives, although global programs exemplified under One Health, Eco-Health, Planetary Health, and the PREDICT project have incorporated or embody some basic elements consistent with a DAMA framework (e.g., King et al., 2008; Horton and Lo, 2015; Whitmee et al., 2015; Daszak, Olival, et al., 2020; Kelly et al., 2020; Alimi et al., 2021; Chatterjee et al., 2021; Ellwanger et al., 2021). International initiatives, including those with intergovernmental bodies and the World Health Organization, reflect a similar and incomplete or fragmented trajectory (Daszak, Amuasi, et al., 2020; Carlson, Boyce, et al., 2022). *Risk management* for EID requires having actionable information before a crisis appears. Strategic protocols that would obtain such information have been largely missing in PREDICT and One Health proposals. Having actionable information obtained in advance of disease emergence can be achieved only if we think we can prevent EIDs or greatly mitigate their impact.

Critical space for risk management occurs at environmental interfaces (Figure 2) (Brooks et al., 2014, 2019; Trivellone, Hoberg, et al., 2022; echoed by Vora et al., 2022). Most importantly, natural history collections must be recognized and utilized as the critical hubs for data gathering and informatics synthesis (Cook et al., 2020; Colella et al., 2021; Hoberg, Trivellone, et al., 2022). Synthesis requires dedicated databases and personnel trained to translate data into actionable information. Resources and expertise must be maintained, expanded, and used in action plans. A global action is realized when shared comprehensive DAMA programs within and specific to each country or region are established and interconnected.

Current insights about the abiotic and biotic factors of disease emergence have been developed by combining field observations with different aspects of mathematical

modeling. A general understanding of the "landscape" and conditions for EID have been outlined. The results were not surprising: landscape modification, encroachment, and habitat disruption along with mobility encompassing transportation and trade, and climate, with variation on seasonal cycles and long-term incremental change, are among the primary drivers associated with disease emergence (Suzán et al., 2015; Brierley et al., 2016; Faust et al., 2018; Dobson et al., 2020; Gibb et al., 2020; Glidden et al., 2021; Keesing and Ostfeld, 2021; Plowright et al., 2021; Baker et al., 2022; Carlson, Albery, et al., 2022; Reaser et al., 2022). Pathogen diversity has also been directly related to host species richness and climate, and transmission risk was correlated with population density, bush meat consumption, and the proximity to livestock (Brierley et al., 2016). Climate forcing and the downstream influence on diversity, biotic movement, and dynamics at interfaces remain the overall determinant for the environmental opportunity and the potential for EIDs (Hoberg et al., 2017; Brooks et al., 2019). Missing from these initiatives is an integrative process across field-based collections, archives, and actionable information to establish insights that reflect a historical and contemporary context for EID which is at the core of DAMA and the basis for cultural transformation in the disease-ecology community (Brooks et al., 2014; Brooks, Hoberg, et al., 2022; Hoberg, Trivellone, et al., 2022). Like the blind men with the elephant, each recognizes a component of the larger challenge but remains incomplete in defining the problem, often with overlapping and seemingly competing explanations bordering on single explanations for EID and with limited proposals for solutions and a pathway forward beyond rapid response (Brooks et al., 2019).

We endorse a broader perspective with increasingly transboundary and interdisciplinary cooperation that brings ecology, biodiversity, environmental health, and medicine to the forefront in addressing complex challenges for humanity and the global landscape (Whitmee et al., 2015; Brooks et al., 2019; Trivellone, Hoberg, et al., 2022). In order to cope with the onrushing multiple threats associated with climate change—of which EID is only one—we must integrate diverse human activities on multiple scales, and everyone must contribute (Brooks and Hoberg, 2013; Brooks et al., 2019; Mora et al., 2022). This integration calls for truly long-term planning—beyond the event horizon of most politicians. We have to assume these changes will be permanent. Coping with changes of this magnitude requires the cooperation of many people within and among countries and on an unprecedented scale.

Irrespective of the interface and boundaries, DAMA can be the foundation for revealing the interconnected components of diversity, an evolutionary and ecological arena of pathogen circulation and exchange, and the complex dimensions of risk space for EID. Ultimately, EID is movement with faunal/floral mixing at interfaces—of habitats, reservoirs, other animals and pathogens, and complexity facilitated by disruption over space and time, which determines the interaction of capacity and opportunity (Brooks, Boeger, et al., 2022) (Figure 3).

> *It is never just one thing, and it always depends.*
> Juarrero, 1999

Taking a cue from the SP, Carlson, Albery, et al. (2022) attempted to estimate how many viral EIDs could be expected in mammals due to climate change–induced movement of hosts and pathogens and the resulting exposure of viruses to susceptible but previously unexposed hosts. Ecological fitting and sloppy fitness space were absent in their model, and as a consequence their estimates of the risk space fell far short of that predicted by the modeling platform derived from the SP (e.g., Araujo et al., 2015; Feronato et al., 2022; Souza et al., 2022). Notably, guidelines for anticipation were not outlined nor summarized as a basis for prevention and mitigation of the predicted increase in viral EIDs among mammals (Carlson, Albery, et al., 2022). As a result, these and prior efforts to limit the unfolding impact of EIDs have met with limited success (Brooks et al., 2014, 2019; echoed by Vora et al., 2022). We spend time identifying the postulated drivers in the absence of proposals for proactive solutions.

> *Despite intensive, high-quality research efforts globally, we are still not able to predict which viruses will become pathogenic to people; which will cause new epidemics in animals; nor where and under what circumstances disease will emerge.*
> Carlson, Albery, et al., 2022

An array of international and regional proposals embody this standard model for pathogen-host interactions and EID (Agosta, 2022; Brooks, Boeger, et al., 2022). The power of the SP, to the contrary, shows how easily EIDs can occur in a biosphere affected by global climate change, anthropogenic perturbation, and modification. The SP explains why pre- and post-pandemic expansion dynamics differ (Audy, 1958; Wei et al., 2021; Hoberg, Boeger, et al., 2022). New hosts are colonized by pathogens based on preexisting—and thus predictable—capacities. New variants arise after a novel host is infected, and they are unpredictable. We live in a world in which emerging infectious diseases will be increasingly common in crops, livestock,

and humans as the cascades of accelerating climate warming—in conjunction with globalized trade and travel, displacement, and conflict—catalyzes movements of hosts and pathogens across rapidly changing and fluid interfaces (Brooks and Hoberg, 2007; Brouqui, 2011; Baker et al., 2022; Mora et al., 2022). Disruption and movements in biological systems fundamentally are the source of increasing contacts between pathogens and susceptible but previously un-exposed assemblages of potential hosts. As we have noted, climate warming is the ultimate driver of disruption across complex biological systems, and anthropogenic release of greenhouse gases must be limited and controlled (Brooks et al., 2019). We disagree with Mora et al. (2022), however, in their contention that the complex pathways leading to EIDs exceed our capacity for effective interventions.

> *The sheer number of pathogenic diseases and transmission pathways aggravated by climatic hazards reveals the magnitude of the human health threat posed by climate change and the urgent need for aggressive actions to mitigate GHG emissions.*
>
> Mora et al., 2022

The DAMA protocol is a proposal within a broader framework for buying time in an arena of accelerating change and must be at the forefront of policies aimed at reducing the socioeconomic impact of EIDs (Brooks, 2022; Vasbinder and Sim, 2022). The best chance we have for mitigating EIDs is through anticipation and protocols that enhance our abilities to find them before they find us. Implementing the DAMA protocol will be expensive, but projected costs of the interminable cycles of emergence, reaction, and crisis response are unsustainable (Brooks et al., 2019; Brooks, Hoberg, et al., 2022; Trivellone, Hoberg, et al., 2022; Vora et al., 2022). Humanity is vulnerable; not implementing the DAMA protocol will be catastrophic.

> *There must be a sense of urgency and purpose. But our protocols must be evolvable; there is no static solution for problems involving an evolving Earth and an evolving biosphere.*
>
> Brooks, Hoberg, and Boeger, 2019

Acknowledgments – Concepts for DAMA, integrative inventories, and archival specimen biorepositories for pathogens and hosts were in part developed with support from the National Science Foundation (NSF) grants to SLG (DEB-0717214, DBI-1458139, DBI-1756397). Funding was provided to J.A. Cook, EPH, and the Museum of Southwestern Biology, University of New Mexico for collaborative research: RUI-Integrated Inventory of Biomes of the Arctic through NSF Division of Environmental Biology, DEB 1258010. WAB received support from the Conselho Nacional de Desen-volvimento Científico e Tecnológico (CNPq), Brazil. DRB expresses appreciation to the Hungarian Academy of Sciences Distinguished Guest Scientist Fellowship Program during March–May 2022. This work was further supported through grants to GF by the National Laboratory for Health Security, RRF-2.3.1-21-2022-00006 and the COST Action CA21170 "Prevention, anticipation and mitigation of tick-borne disease risk applying the DAMA protocol (PRAGMATICK)." All authors express recognition of their parent academic centers for facilities, infrastructure, and continuing support during the preparation of our manuscript.

References

Agosta, S.J. 2022. The Stockholm Paradigm explains the dynamics of Darwin's Entangled Bank, including emerging infectious disease. MANTER: Journal of Parasite Biodiversity 27. https://doi.org/10.32873/unl.dc.manter27

Agosta, S.J.; Brooks, D.R. 2020. The major metaphors of evolution: Darwinism then and now. Springer International Publishers, Cham, Switzerland. 273 pp. https://doi.org/10.1007/978-3-030-52086-1

Albery, G.F.; Carlson, C.J.; Cohen, L.E.; Eskew, E.A.; Gibb, R.; Ryan, S.J.; Sweeny, A.R.; Becker, D.J. 2022. Urban-adapted mammal species have more known pathogens. Nature Ecology and Evolution 6: 794–801. https://doi.org/10.1038/s41559-022-01723-0

Alimi, Y.; Bernstein, A.; Epstein, J.; Espinal, M.; Kakkar, M.; Kochevar, D.; Werneck, G. 2021. Report of the Scientific Task Force on Preventing Pandemics. Harvard Global Health Institute and the Center for Climate, Health, and the Global Environment at the Harvard T.H. Chan School of Public Health. 36 pp.

Anderson, E.T. 1978. Plague in the continental United States, 1900–76. Public Health Reports 93: 297–301.

Anthony, S.J.; Epstein, J.H.; Murray, K.A.; Navarrete-Macias, I.; Zambrana-Torrelio, C.M.; Solovyov, A.; et al. 2013. A strategy to estimate unknown viral diversity in mammals. mBio 4: e00598-13. https://doi.org/10.1128/mBio.00598-13

Araujo, S.B.L.; Braga, M.P.; Brooks, D.R.; Agosta, S.J.; Hoberg, E.P.; von Hartenthal, F.W.; Boeger, W.A. 2015. Understanding host-switching by ecological fitting. PloS ONE 10: e0139225. https://doi.org/10.1371/journal.pone.0139225

Audy, J.R. 1958. The localization of disease with special reference to the zoonoses. Transactions of the Royal Society of Tropical Medicine and Hygiene 52: 308–334. https://doi.org/10.1016/0035-9203(58)90045-2

Baker, R.E.; Mahmud, A.S.; Miller, I.F.; Rajeev, M.; Rasambainarivo, F.; Rice, B.L.; et al. 2022. Infectious disease in an era of global change. Nature Reviews Microbiology 20: 193–205. https://doi.org/10.1038/s41579-021-00639-z

Bernstein, A.S.; Ando, A.W.; Loch-Temzelides, T.; Vale, M.M.; Li, B.V.; Li, H.; et al. 2022. The costs and benefits of primary prevention of zoonotic pandemics. Science Advances 8: eabl4183. https://doi.org/10.1126/sciadv.abl4183

Boeger, W.A.; Brooks, D.R.; Trivellone, V.; Agosta, S.J.; Hoberg, E.P. 2022. Ecological super-spreaders drive host-range oscillations: Omicron and risk space for emerging infectious disease. Transboundary and Emerging Diseases 69: e1280–e1288. https://doi.org/10.1111/tbed.14557

Boni, M.F.; Lemey, P.; Jiang, X.; Lam, T.T.-Y.; Perry, B.W.; Castoe, T.A.; et al. 2020. Evolutionary origins of the SARS-CoV-2 sarbecovirus lineage responsible for the COVID-19 pandemic. Nature Microbiology 5: 1408–1417. https://doi.org/10.1038/s41564-020-0771-4

Braga, M.P.; Araujo, S.B.L.; Agosta, S.; Brooks, D.R.; Hoberg, E.P.; Nylin, S.; Janz, N.; Boeger, W.A. 2018. Host use dynamics in a heterogeneous fitness landscape generates oscillations and diversification. Evolution 72: 1773–1783. https://doi.org/10.1111/evo.13557

Brierley, L.; Maarten, J.V.; Olival, K.J.; Daszak, P.; Jones, K.E. 2016. Quantifying global drivers of zoonotic bat viruses: A process-based perspective. American Naturalist 187: E53–E64. https://doi.org/10.1086/684391

Brooks, D.R. 2022. What are emerging infections diseases? In: Buying Time for Climate Action: Exploring Ways around Stumbling Blocks. J.W. Vasbinder and J.Y.H. Sim (eds.). World Scientific Publishing, Singapore. 43–49 p.

Brooks, D.R.; Boeger, W.A.; Hoberg, E.P. 2022. The Stockholm paradigm: lessons for the emerging infectious disease crisis. MANTER: Journal of Parasite Biodiversity 22. https://doi.org/10.10.32873/unl.dc.manter22

Brooks, D.R.; Ferrao, A. 2005. The historical biogeography of co-evolution: emerging infectious diseases are evolutionary accidents waiting to happen. Journal of Biogeography 32: 1291–1299. https://doi:10.1111/j.1365-2699.2005.01315.x

Brooks, D.R.; Hoberg, E.P. 2000. Triage for the biosphere: the need and rationale for taxonomic inventories and phylogenetic studies of parasites. Comparative Parasitology 67: 1–25.

Brooks, D.R.; Hoberg, E.P. 2007. How will global climate change affect parasite-host assemblages? Trends in Parasitology 23: 571–574. https://doi.org/10.1016/j.pt.2007.08.016

Brooks, D.R.; Hoberg, E.P. 2013. The emerging infectious diseases crisis and pathogen pollution: a question of ecology and evolution. In: The Balance of Nature and Human Impact. K. Rhode (ed.). Cambridge University Press, Cambridge, UK. 215–229 p. https://doi.org/10.1017/CBO9781139095075

Brooks, D.R.; Hoberg, E.P.; Boeger, W.A. 2019. The Stockholm Paradigm: Climate Change and Emerging Disease. University of Chicago Press, Chicago. 423 pp.

Brooks, D.R.; Hoberg, E.P.; Boeger, W.; Gardner, S.L.; Galbreath, K.E.; Herczeg, D.; et al. 2014. Finding them before they find us: informatics, parasites, and environments in accelerating climate change. Comparative Parasitology 81: 155–164. https://doi.org/10.1654/4724b.1

Brooks, D.R.; Hoberg, E.P.; Boeger, W.A.; Trivellone, V. 2022. Emerging infectious disease: an underappreciated area of strategic concern for food security. Transboundary and Emerging Diseases 69: 254–267. https://doi.org/10.1111/tbed.14009

Brooks, D.R.; McLennan, D.A. 2002. The Nature of Diversity: An Evolutionary Voyage of Discovery. University of Chicago Press, Chicago. 684 pp.

Brouqui, P. 2011. Arthropod-borne diseases associated with political and social disorder. Annual Review Entomology 56: 357–374. https://doi.org/10.1146/annurev-ento-120709-144739

Cai, H.Y.; Cai, A. 2021. SARS-CoV-2 spike protein variants with N501T and G142D mutation-dominated infections in mink in the United States. Journal of Veterinary Diagnostic Investigation 33: 939–942. https://doi.org/10.1177/10406387211023

Carlson, C.J.; Albery, G.F.; Merow, C.; Trisos, C.H.; Zipfel, C.M.; Eskew, E.A.; et al. 2022. Climate change increases cross-species viral transmission risk. Nature 607: 555–562. https://doi.org/10.1038/s41586-022-04788-w

Carlson, C.J.; Boyce, M.R.; Dunne, M.; Graeden, E.; Lin, J.; Abdellatif, Y.O.; et al. 2022. The World Health Organization's disease outbreak news: a retrospective database. Preprint version posted March 23, 2022, in medRxiv. https://doi.org/10.1101/2022.03.22.22272790

Carlson, C.J.; Dallas, T.A.; Alexander, L.W.; Phelan, A.L.; Phillips, A.J. 2020. What would it take to describe the global diversity of parasites? Proceedings of the Royal Society B 287: 20201841. http://dx.doi.org/10.1098/rspb.2020.1841

Carlson, C.J.; Zipfel, C.M.; Garnier, R.; Bansal, S. 2019. Global estimates of mammalian viral diversity accounting for host sharing. Nature Ecology and Evolution 3: 1070–1075. https://doi.org/10.1038/s41559-019-0910-6

Carroll, D.; Daszak, P.; Wolfe N.D.; Gao, G.F.; Morel, C.M.; Morzaria, S.; et al. 2018. The Global Virome Project. Science 359: 872–874. https://doi.org/10.1126/science.aap7463

Chatterjee, P.; Nair, P.; Chersich, M.; Terefe, Y.; Chauhan, A.S.; Quesada, F.; Simpson, G. 2021. One Health, "disease X" and the challenge of "unknown" unknowns. Indian Journal of Medical Research 153: 264–271. https://doi.org/10.4103/ijmr.IJMR_601_21

Chen, Y.; Bai, T.; Shu, Y. 2022. Poultry to human passport: cross-species transmission of zoonotic H7N9 avian influenza virus to humans. Zoonoses 2. https://doi.org/10.15212/ZOONOSES-2021-0026

Colella, J.P.; Bates, J.; Burneo, S.F.; Camacho, M.A.; Carrion Bonilla, C.; Constable, I.; et al. 2021. Leveraging natural history biorepositories as a global, decentralized, pathogen surveillance network. PloS Pathogens 17: e1009583. https://doi.org/10.1371/journal.ppat.1009583

Colella, J.P.; Talbot, S.L.; Brochmann, C.; Taylor, E.B.; Hoberg, E.P.; Cook, J.A. 2020. Conservation genomics in a changing Arctic. Trends in Ecology and Evolution 35: 149–162. https://doi.org/10.1016/j.tree.2019.09.008

Cook, J.; Arai, S.; Armién, B.; Bates, J.; Carrion Bonilla, C.A.; de Souza Cortez, M.B.; et al. 2020. Integrating biodiversity infrastructure into pathogen discovery and mitigation of emerging infectious diseases. BioScience 70: 531–534. https://doi.org/10.1093/biosci/biaa064

Cook, J.A.; Galbreath, K.E.; Bell, K.C.; Campbell, M.L.; Carrière, S.; Colella, J.P.; et al. 2017. The Beringian Coevolution Project: holistic collections of mammals and associated parasites reveal novel perspectives on evolutionary and environmental change in the North. Arctic Science 3: 585–617. https://doi.org/10.1139/as-2016-0042

Curry, P.S.; Ribble, C.; Sears, W.C.; Hutchins, W.; Orsel, K.; Godson, D.; et al. 2014. Blood collected on filter paper for wildlife serology: detecting antibodies to *Neospora caninum*, West Nile virus, and five bovine viruses in reindeer. Journal of Wildlife Diseases 50: 297–307. https://doi.org/10.7598/2012-02-047

Damas, J.; Hughes, G.M.; Keough, K.C.; Painter, C.A.; Persky, N.S.; Corbo, M.; et al. 2020. Broad host range of SARS-CoV-2 predicted by comparative and structural analysis of ACE2 in vertebrates. Proceedings of the National Academy of Sciences USA 117: 22311–22322. https://doi.org/10.1073/pnas.2010146117

Daszak, P.; Amuasi, J.; das Neves, C.G.; Hayman, D.; Kuiken, T.; Roche, B.; et al. 2020. IPBES Workshop on Biodiversity and Pandemics: Workshop Report. Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services, Bonn, Germany. Retrieved from https://ipbes.net/pandemics

Daszak, P.; Olival, K.J.; Li, H. 2020. A strategy to prevent future epidemics similar to the 2019-nCoV outbreak. Biosafety and Health 2: 6–8. https://doi.org/10.1016/j.bsheal.2020.01.003

D'Bastiani, E.; Campião, K.M.; Boeger, W.A.; Araújo, S.B.L. 2020. The role of ecological opportunity in shaping host-parasite networks. Parasitology 147: 1452–1460. https://doi.org/10.1017/S003118202000133X

Dobson, A.P.; Pimm, S.L.; Hannah, L.; Kaufman, L.; Ahumada, J.A.; Ando, A.W.; et al. 2020. Ecology and economics for pandemic prevention. Science 369: 379–381. https://doi.org/10.1126/science.abc3189

Dunnum, J. L.; Yanagihara, R.; Johnson, K. M.; Armien, B.; Batsaikhan, N.; Morgan, L.; Cook, J. A. 2017. Biospecimen repositories and integrated databases as critical infrastructure for pathogen discovery and pathobiology research. PLoS Neglected Tropical Diseases 11: e0005133. https://doi.org/10.1371/journal.pntd.0005133

Ellwanger, J.H.; da Veiga, A.B.G.; Kaminski, V.D.L.; Valverde-Villegas, J.M.; de Freitas, A.W.Q.; Chies, J.A.B. 2021. Control and prevention of infectious diseases from a One Health perspective. Genetics and Molecular Biology 44: e20200256. https://doi.org/10.1590/1678-4685-GMB-2020-0256

Faust, C.L.; McCallum, H.I.; Bloomfield, L.S.P.; Gottdenker, N.L.; Gillespie, T.R.; Torney, C.J.; et al. 2018. Pathogen spillover during land conversion. Ecology Letters 21: 471–483. https://doi.org/10.1111/ele.12904

Feronato, S.G.; Araujo, S.; Boeger, W.A. 2022. "Accidents waiting to happen"—insights from a simple model on the emergence of infectious agents in new hosts. Transboundary and Emerging Diseases 69: 1727–1738. https://doi.org/10.1111/tbed.14146

Földvári, G.; Jahfari, S.; Rigó, K.; Jablonszky, M.; Szekeres, S.; Majoros, G.; et al. 2014. *Candidatus* Neoehrlichia mikurensis and *Anaplasma phagocytophilum* in urban hedgehogs. Emerging Infectious Diseases 20: 496–498. https://doi.org/10.3201/eid2003.130935

Földvári, G.; Rigó, K.; Jablonszky, M.; Biró, N.; Majoros, G.; Molnár, V.; Tóth, M. 2011. Ticks and the city: ectoparasites of the northern white-breasted hedgehog (*Erinaceus roumanicus*) in an urban park. Ticks and Tick-borne Diseases 2: 231–234. https://doi.org/10.1016/j.ttbdis.2011.09.001

Földvári, G.; Szabó, É.; Tóth, G.E.; Lanszki, Z.; Zana, B.; Varga, Z.; Kemenesi, G. 2022. Emergence of *Hyalomma marginatum* and *Hyalomma rufipes* adults revealed by citizen science tick monitoring in Hungary. Transboundary and Emerging Diseases 69: 1–9. https://doi.org/10.1111/tbed.14563

Forde, T.L.; Orsel, K.; Zadoks, R.N.; Biek, R.; Adams, L.G.; Checkley, S.L.; et al. 2016. Bacterial genomics reveal the complex epidemiology of an emerging pathogen in Arctic and boreal ungulates. Frontiers in Microbiology 7: 1759. https://doi.org/10.3389/fmicb.2016.01759

Galbreath, K.E.; Hoberg, E.P.; Cook, J.A.; Armién, B.; Bell, K.C.; Campbell, M.L.; et al. 2019. Building an integrated infrastructure for exploring biodiversity: field collections and archives of mammals and parasites. Journal of Mammalogy 100: 382–393, plus supplemental material: "Field Methods for Collection and Preservation of Mammalian Parasites" (36 p.). https://doi.org/10.1093/jmammal/gyz048

Gibb, R.; Albery, G.F.; Mollentze, N.; Eskew, E.A.; Brierley, L.; Ryan, S.J.; et al. 2022. Mammal virus diversity estimates

are unstable due to accelerating discovery effort. Biology Letters 18: 20210427. https://doi.org/10.1098/rsbl.2021.0427

Gibb, R.; Redding, D.W.; Chin, K.Q.; Donnelly, C.A.; Blackburn, T.M.; Newbold, T.; Jones, K.E. 2020. Zoonotic host diversity increases in human-dominated ecosystems. Nature 584: 398–402. https://doi.org/10.1038/s41586-020-2562-8

Glidden, C.K.; Nova, N.; Kain, M.P.; Lagerstrom, K.M.; Skinner, E.B.; Mandle, L.; et al. 2021. Human-mediated impacts on biodiversity and the consequences for zoonotic disease spillover. Current Biology 31: R1342–R1361. https://doi.org/10.1016/j.cub.2021.08.070

Grange, Z.L.; Goldstein, T.; Johnson, C.K.; Anthony, S.; Gilardi, K.; Daszak, P.; et al. 2021. Ranking the risk of animal-to-human spillover for newly discovered viruses. Proceedings of the National Academy of Sciences USA 118: e2002324118. https://doi.org/10.1073/pnas.2002324118

Gray, G.C.; Robie, E.R.; Studstill, C.J.; Nunn, C.L. 2021. Mitigating future respiratory virus pandemics: new threats and approaches to consider. Viruses 13: 637. https://doi.org/10.3390/v13040637

Harvey, E.; Holmes, E.C. 2022. Diversity and evolution of the animal virome. Nature Reviews Microbiology 20: 321–334. https://doi.org/10.1038/s41579-021-00665-x

Hoberg, E.P. 2010. Invasive processes, mosaics and the structure of helminth parasite faunas. Revue Scientifique et Technique (Office International des Épizooties) 29: 255–272. http://dx.doi.org/10.20506/rst.29.2.1972

Hoberg, E.P.; Boeger, W.A.; Brooks, D.R.; Trivellone, V.; Agosta, S.J. 2022. Stepping-stones and mediators of pandemic expansion—a context for humans as ecological superspreaders. MANTER: Journal of Parasite Biodiversity 18. https://doi.org/10.32873/unl.dc.manter18

Hoberg, E.P.; Brooks D.R. 2015. Evolution in action: climate change, biodiversity dynamics and emerging infectious disease. Philosophical Transactions of the Royal Society B 370: 20130553. https://doi.org/10.1098/rstb.2013.0553

Hoberg, E.P.; Cook, J.A.; Agosta, S.J.; Boeger, W.; Galbreath, K.E.; Laaksonen, S.; et al. 2017. Arctic systems in the Quaternary: ecological collision, faunal mosaics and the consequences of a wobbling climate. Journal of Helminthology 91: 409–421. https://doi.org/10.1017/S0022149X17000347

Hoberg, E.P.; Trivellone, V.; Cook, J.A.; Dunnum, J.L.; Boeger, W.A.; et al. 2022. Knowing the biosphere: documentation, specimens, archives, and names reveal environmental change and emerging pathogens. MANTER: Journal of Parasite Biodiversity 26. https://doi.org/10.10.32873/unl.dc.manter26

Holmes, E.C. 2022. COVID-19—lessons for zoonotic disease. Science 375: 1114–1115. https://doi.org/10.1126/science.abn2222

Holmes, E.C.; Rambaut, A.; Andersen, K.G. 2018. Pandemics: spend on surveillance, not prediction. Nature 558: 180–182. https://doi.org/10.1038/d41586-018-05373-w

Horton, R.; Lo, S. 2015. Planetary health: a new science for exceptional action. Lancet 386: 1921–1922. https://doi.org/10-1016/S0140-6736(15)61038-8

Howard, J.; Nedelman, M. 2022. Silent spread of monkeypox may be a wakeup call for the world. CNN. Thursday, June 2, 2022, 4:25 p.m. EDT. https://www.cnn.com/2022/06/02/health/monkeypox-endemic-silent-spread/index.html

Irving, A.T.; Welburn, S.C. 2021. SARS-CoV-2 and zoonotic preparedness: unknown knowns? Infectious Microbes and Diseases 3: 30–31. https://doi.org/10.1097/IM9.0000000000000051

Joly, D.; Kreuder Johnson, C.; Goldstein, T.; Anthony, S.J.; Karesh, W.; Daszak, P.; et al. 2016. The first phase of PREDICT: surveillance for emerging infectious zoonotic diseases of wildlife origin (2009–2014). International Journal of Infectious Diseases 53: 31–32. https://doi.org/10.1016/j.ijid.2016.11.086

Jones, K.E.; Patel, N.G.; Levy, M.A.; Storeygard, A.; Balk, D.; Gittleman, J.L.; Daszak, P. 2008. Global trends in emerging infectious diseases. Nature 451: 990–993. https://doi.org/10.1038/nature06536

Juarrero, A. 1999. Dynamics in Action: Intentional Behavior as a Complex System. MIT Press, Boston.

Kafle, P.; Peller, P.; Massolo, A.; Hoberg, E.; Leclerc, L.-M.; Tomaselli, M.; Kutz, S. 2020. Range expansion of muskox lungworms track rapid Arctic warming: implications for geographic colonization under climate forcing. Scientific Reports 10: 17323. https://doi.org/10.1038/s41598-020-74358-5

Keesing, F.; Ostfeld, R.S. 2021. Impacts of biodiversity and biodiversity loss on zoonotic diseases. Proceedings of the National Academy of Sciences USA 118: e2023540118. https://doi.org/10.1073/pnas.2023540118

Kelly, T.R.; Machalaba, C.; Karesh, W.B.; Crook, P.Z.; Gilardi, K.; Nziza, J.; et al. 2020. Implementing One Health approaches to confront emerging and re-emerging zoonotic disease threats: lessons from PREDICT. One Health Outlook 2: 1. https://doi.org/10.1186/s42522-019-0007-9

King, L.J.; Anderson, L.R.; Blackmore, C.G.; Blackwell, M.J.; Lautner, E.A.; Marcus, L.C.; et al. 2008. Executive summary of the AVMA One Health Initiative Task Force report. Journal of the American Veterinary Medical Association 233: 259–261. https://doi.org/10.2460/javma.233.2.259

Kutz, S.J.; Asmundsson, I.; Hoberg, E.P.; Appleyard, G.D.; Jenkins, E.J.; Beckmen, K.; et al. 2007. Serendipitous

discovery of a novel protostrongylid (Nematoda: Metastrongyloidea) in caribou, muskoxen, and moose from high latitudes of North America based on DNA sequence comparisons. Canadian Journal of Zoology 85: 1143–1156. https://doi.org/10.1139/Z07-091

Kutz, S.; Bollinger, T.; Branigan, M.; Checkley, S.; Davison, T.; Dumond, M.; et al. 2015. *Erysipelothrix rhusiopathiae* associated with recent widespread muskox mortalities in the Canadian Arctic. Canadian Veterinary Journal 56: 560–563.

Kutz, S.J.; Tomaselli, M. 2019. "Two-eyed seeing" supports wildlife health. Science 364: 1135–1137. https://doi.org/10.1126/science.aau6170

Latinne, A.; Hu, B.; Olival, K.J.; Zhu, G.; Zhang, L.; Li, H.; et al. 2020. Origin and cross-species transmission of bat coronaviruses in China. Nature Communications 11: 4235. https://doi.org/10.1038/s41467-020-17687-3

Lin, C.-N.; Chan, K.R.; Ooi, E.E.; Chiou, M.-T.; Hoang, M.; Hsueh, P.-R.; Ooi, P.T. 2021. Animal coronavirus diseases: parallels with COVID-19 in humans. Viruses 13: 1507. https://doi.org/10.3390/v13081507

Mallapaty, S. 2021. Laos bats host closest known relatives of virus behind COVID. Nature 597: 603.

Mollentze, N.; Streicker, D.G. 2020. Viral zoonotic risk is homogenous among taxonomic orders of mammalian and avian reservoir hosts. Proceedings of the National Academy of Sciences USA 117: 9423–9430. https://doi.org/10.1073/pnas.1919176117

Molnár, O.; Hoberg, E.; Trivellone, V.; Földvári, G.; Brooks, D.R. 2022. The 3P framework: a comprehensive approach to coping with the emerging infectious disease crisis. MANTER: Journal of Parasite Biodiversity 23. https://doi.org/10.10.32873/unl.dc.manter23

Molnár, O.; Knickel, M.; Marizzi, C. 2022.Taking action: turning evolutionary theory into preventive policies. MANTER: Journal of Parasite Biodiversity 28. https://doi.org/10.32873/unl.dc.manter28

Mora, C.; McKenzie, T.; Gaw, I.M.; Dean, J.M.; von Hammerstein, H.; Knudson, T.A.; et al. 2022. Over half of known human pathogenic diseases can be aggravated by climate change. Nature Climate Change 12: 869–875. https://doi.org/10.1038/s41558-022-01426-1

Olival, K.J.; Hosseini, P.R.; Zambrana-Torrelio, C.; Ross, N.; Bogich, T.L.; Daszak, P. 2017. Host and viral traits predict zoonotic spillover from mammals. Nature 546: 646–650. https://doi.org/10.1038/nature22975

Ortiz, E.; Juarrero, A. 2022. An emerging infectious disease surveillance platform for the 21st century. MANTER: Journal of Parasite Biodiversity 29. https://doi.org/10.32873/unl.dc.manter29

Peterson, A.T. 2006. Ecologic niche modeling and spatial patterns of disease transmission. Emerging Infectious Diseases 12: 1822–1826. https://doi.org/10.3201/eid1212.060373

Plowright, R.K.; Reaser, J.K.; Locke, H.; Woodley, S.J.; Patz, J.A.; Becker, D.J.; et al. 2021. Land use–induced spillover: a call to action to safeguard environmental, animal, and human health. Lancet Planetary Health 5, E237–E245. https://doi.org/10.1016/S2542-5196(21)00031-0

Randall, D.K. 2019. Black Death at the Golden Gate: The Race to Save America from the Bubonic Plague. W.W. Norton, New York. 273 pp.

Reaser, J.K.; Hunt, B.E.; Ruiz-Aravena, M.; Tabor, G.M.; Patz, J.A.; Becker, D.J.; et al. 2022. Fostering landscape immunity to protect human health: a science-based rationale for shifting conservation policy paradigms. Conservation Letters 15: e12869. https://doi.org/10.1111/conl.12869

Rochman, N.D.; Wolf, Y.I.; Faure, G.; Mutz, P.; Zhang, F.; Koonin, E.V. 2021. Ongoing global and regional adaptive evolution of SARS-CoV-2. Proceedings of the National Academy of Sciences USA 118: e2104241118. https://doi.org/10.1073/pnas.2104241118

Souza, A.T.C.; Araujo, S.B.L.; Boeger, W.A. 2022. The evolutionary dynamics of infectious diseases on an unstable planet: insights from modeling the Stockholm paradigm. MANTER: Journal of Parasite Biodiversity 25. https://doi.org/10.10.32873/unl.dc.manter25

Sun, Y.; Lin, W.; Dong, W.; Xu, J. 2022. Origin and evolutionary analysis of the SARS-CoV-2 Omicron variant. Journal of Biosafety and Biosecurity 4: 33–37. https://doi.org/10.1016/j.jobb.2021.12.001

Suzán, G.; García-Peña, G.E.; Castro-Arellano, I.; Rico, O.; Rubio, A.V.; Tolsá, M.J.; et al. 2015. Metacommunity and phylogenetic structure determine wildlife and zoonotic infectious disease patterns in time and space. Ecology and Evolution 5: 865–873. https://doi.org/10.1002/ece3.1404

Szekeres, S.; Majláthová, V.; Majláth, I.; Földvári, G. 2016. Neglected hosts: The role of lacertid lizards and medium-sized mammals in the ecoepidemiology of Lyme borreliosis. In: Ecology and Prevention of Lyme Borreliosis (Ecology and Control of Vector-borne Diseases, Vol. 4). M.A.H. Braks, S.E. van Wieren, W. Takken, and H. Sprong (eds.). Wageningen Academic Publishers, Wageningen, the Netherlands. 103–126 p.

Szekeres, S.; van Leeuwen, A.D.; Rigó, K.; Jablonszky, M.; Majoros, G.; Sprong, H.; Földvári, G. 2016. Prevalence and diversity of human pathogenic rickettsiae in urban versus rural habitats, Hungary. Experimental and Applied Acarology 68: 223–226. https://doi.org/10.1007/s10493-015-9989-x

Szekeres, S.; van Leeuwen, A.D.; Tóth, E.; Majoros, G.; Sprong, H.; Földvári, G. 2019. Road-killed mammals provide insight into tick-borne bacterial pathogen communities within urban habitats. Transboundary and Emerging Diseases 66: 277–286. https://doi.org/10.1111/tbed.13019

Tan, C.C.S.; Lam, S.D.; Richard, D.; Owen C.J.; Berchtold, D.; Orengo, C.; et al. 2022. Transmission of SARS-Cov-2 from humans to animals and potential host adaptation. Nature Communications 13: 2988. https://doi.org/10.1038/s41467-022-30698-6

Temmam, S.; Vongphayloth, K.; Baquero, E.; Munier, S.; Bonomi, M.; Regnault, B.; et al. 2022. Bat coronaviruses related to SARS-CoV-2 and infectious for human cells. Nature 604: 330–336. https://doi.org/10.1038/s41586-022-04532-4

Trivellone, V. 2022. Let emerging plant disease be predictable. MANTER: Journal of Parasite Biodiversity 30. https://doi.org/10.32873/unl.dc.manter30

Trivellone, V.; Cao, Y.; Dietrich, C.H. 2022. Comparison of traditional and next-generation approaches for uncovering phytoplasma diversity, with discovery of new groups, subgroups and potential vectors. Biology 11: 977. https://doi.org/10.3390/biology11070977

Trivellone, V.; Hoberg, E.P.; Boeger, W.A.; Brooks, D.R. 2022. Food security and emerging infectious disease: risk assessment and risk management. Royal Society Open Science 9: 211687. https://doi.org/10.1098/rsos.211687

Trivellone, V.; Panassiti, B. 2022. A field synopsis, systematic review, and meta-analyses of cophylogenetic studies: what is affecting congruence between phylogenies? MANTER: Journal of Parasite Biodiversity 24. https://doi.org/10.10.32873/unl.dc.manter24

Trivellone, V.; Wei, W.; Filippin, L.; Dietrich, C.H. 2021. Screening potential insect vectors in a museum biorepository reveals undiscovered diversity of plant pathogens in natural areas. Ecology and Evolution 11: 6493–6503. https://doi.org/10.1002/ece3.7502

USAID [United States Agency for International Development]. 2014. Reducing Pandemic Risk, Promoting Global Health. PREDICT 1 (2009–2014) Final Report.

USAID. [United States Agency for International Development]. 2016. Reducing Pandemic Risk, Promoting Global Health, Supporting the Global Health Security Agenda. PREDICT Annual Report. Washington, DC.

Vasbinder, J.W.; Sim, J.Y.H. (eds.). 2022. Buying Time for Climate Action: Exploring Ways around Stumbling Blocks. Exploring Complexity series, vol. 8. World Scientific, Singapore. 222 pp.

Vora, N.M.; Hannah, L.; Lieberman, S.; Vale, M.M.; Plowright, R.K.; Bernstein, A.S. 2022. Want to prevent pandemic? Stop spillovers. Nature 605: 419–422. https://doi.org/10.1038/d41586-022-01312-y

Wei, C.; Shan, K.-J.; Wang, W.; Zhang, S.; Huan, Q.; Qian, W. 2021. Evidence for a mouse origin of the SARS-CoV-2 Omicron variant. Journal of Genetics and Genomics 48: 1111–1121. https://doi.org/10.1016/j.jgg.2021.12.003

White, R.A., III. 2021. The future of virology is synthetic. mSystems 6: e00770-21. https://doi.org/10.1128/mSystems.00770-21

Whitmee, S.; Haines, A.; Beyrer, C.; Boltz, F.; Capon, A.G.; de Souza Dias, B.F.; et al. 2015. Safeguarding human health in the Anthropocene epoch: report of the Rockefeller Foundation–Lancet Commission on planetary health. Lancet 386: 1973–2028. https://doi.org/10.1016/S0140-6736(15)60901-1

Wilcox, J.J.S.; Lopez-Cotto, J.J.; Hollocher, H. 2021. Historical contingency, geography and anthropogenic patterns of exposure drive the evolution of host switching in the *Blastocystis* species-complex. Parasitology 148: 985–993 https://doi.org/10.1017/S003118202100055X

Wille, M.; Geoghegan, J.L.; Holmes, E.C. 2021. How accurately can we assess zoonotic risk? PLoS Biology 19: e3001135. https://doi.org/10.1371/journal.pbio.3001135

Young, C.C.W.; Olival, K.J. 2016. Optimizing viral discovery in bats. PLoS ONE 11: e0149237. https://doi.org/10.1371/journal.pone.0149237

Zhao, K.; Zhang, W.; Li, B.; Xie, S-Z.; Yi, F.; Jang, R-D.; Luo, Y.; He, X-Y.; Zhang, Y-Z.; Shi, Z-L.; Zhang, L-B.; Yang, X-L. 2022. Ecological study of cave nectar bats reveals low risk of direct transmission of bat viruses to humans. Zoological Research. 43: 514-522. https://doi.org/10.24272/j.issn.2095-8137.2021.480

Zhou, H.; Ji, J.; Chen, X.; Bi, Y.; Li, J.; Wang, Q.; et al. 2021. Identification of novel bat coronaviruses sheds light on the evolutionary origins of SARS-CoV-2 and related viruses. Cell 184: 4380–4391.E14. https://doi.org/10.1016/j.cell.2021.06.008

Zinsstag, J.; Utzinger, J.; Probst-Hensch, N.; Shan, L.; Zhou, X.-N. 2020. Towards integrated surveillance-response systems for the prevention of future pandemics. Infectious Diseases of Poverty 9: 140. https://doi.org/10.1186/s40249-020-00757-5