Trends in Parasitology

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Forum

Convergence Research for Emerging Zoonoses

Benoit Talbot [1,*] Manisha A. Kulkarni,[1] and Robert I. Colautti[2]

Global emergence of vector-borne and zoonotic diseases presents a rapidly growing 'wicked' problem. We outline the need for a transdisciplinary research program that is grounded in ecological and evolutionary theory but integrates fundamentally with research perspectives spanning the health, social, and natural sciences.

Problem-Solving in the Face of Emerging Zoonotic Diseases

Among the many consequences of globalization and global change is an increasing exposure of world populations to emerging and re-emerging vector-borne and zoonotic diseases. These diseases are caused by a broad range of pathogens, including respiratory influenza and coronaviruses, tropical arboviruses like Zika and dengue, and tick-borne pathogens like *Borrelia* spirochetes (the agent of Lyme disease) and *Babesia* parasites.

Addressing the health impacts of zoonoses is complicated by challenges with surveillance, imprecise diagnostic tools, and variable symptomology. Vector-borne zoonoses present a 'wicked' problem in that a deep integration across disciplines is needed to advance beyond the conflicting points of view and incomplete solutions that characterize many vector-borne diseases [1]. Intellectually, 'wicked' problems also present opportunities to alter the momentum of established disciplines by integrating the latest intellectual and technological advances. A recent example of this is the application of evolutionary biology and high-throughput sequencing to track the spread of influenza and coronavirus pandemics [2].

Here, we outline a transdisciplinary approach to address emerging zoonoses, using the recent emergence of Lyme disease in Canada as a model (Box 1). We outline three key facets of the Lyme disease problem and explain how a transdisciplinary research program could improve health outcomes (Figure 1).

Ecological Evidence

Ecological processes and human activity jointly determine the population dynamics and spread of arthropod vectors, their hosts, and the pathogens that both carry. Ecological niche models have improved predictions of range expansion of *Ixodes* ticks to inform risk assessment across Canada [3]. In addition, variability in host competence for *Borrelia burgdorferi* infections [4], combined with population dynamics of competent hosts and vectors [5], have been fundamental to understanding spatial heterogeneity in disease dynamics. Ecological research, particularly in the context of global change, can help to prioritize management resources based on climate and landscape elements associated with host populations.

Molecular Evidence

Different strains and species of *Borrelia* have been identified in North America and Europe [6]. However, establishing a clear link between pathogen diversity and pathogenicity requires the use of model systems, particularly for identifying specific virulence loci. In addition, molecular studies of serological progression help to identify the breadth of potential Lyme disease manifestations [7] and the variable accuracy of diagnostic tests [8]. This is especially important for *B. burgdorferi sensu stricto*, which can have wide-ranging effects in the human body due to an immunological cascade from initial infection to late-onset symptoms.

Human Health and Sociological Evidence

Research shows that human behavior affects exposure and disease risk. Education of health practitioners can affect disease progression because Lyme disease can be mistaken for other pathologies [9]. This

Box 1. The Emergence of Lyme Disease in Canada

Lyme disease is a tick-borne illness which, if untreated, can cause complex neurological and musculoskeletal manifestations months after initial infection. Found across Europe, Asia, and North America, Lyme disease is caused by several genospecies within the *Borrelia burgdorferi sensu lato* complex, transmitted by ticks of the genus *Ixodes* [15]. Multiple challenges currently prevent efficient management of the disease in Canada and elsewhere, including:

Research Challenges

- Geographic decoupling of tick, host, and pathogen populations amplifies heterogeneity in pathogen prevalence, epidemiology, and health practitioner experience.
- Human and pathogen diversity reduce sensitivity of diagnostic tests and broaden disease natural history.
- Lived experiences are valuable but overlooked as data for hypothesis generation and testing; patient engagement requires strong communication and empathy skills.

Systemic Challenges

- Academic training tends to focus on specialization, reinforced by specialized peer reviewers and funding systems that favor productivity over risk, creativity, novelty, and impact.
- Funding for convergence research is increasing but remains highly competitive and represents a tiny fraction of research budgets compared to traditional research silos.
- Diverse teams that span research silos are difficult to establish and manage, spanning cultural norms, specialized jargon, and research philosophies.

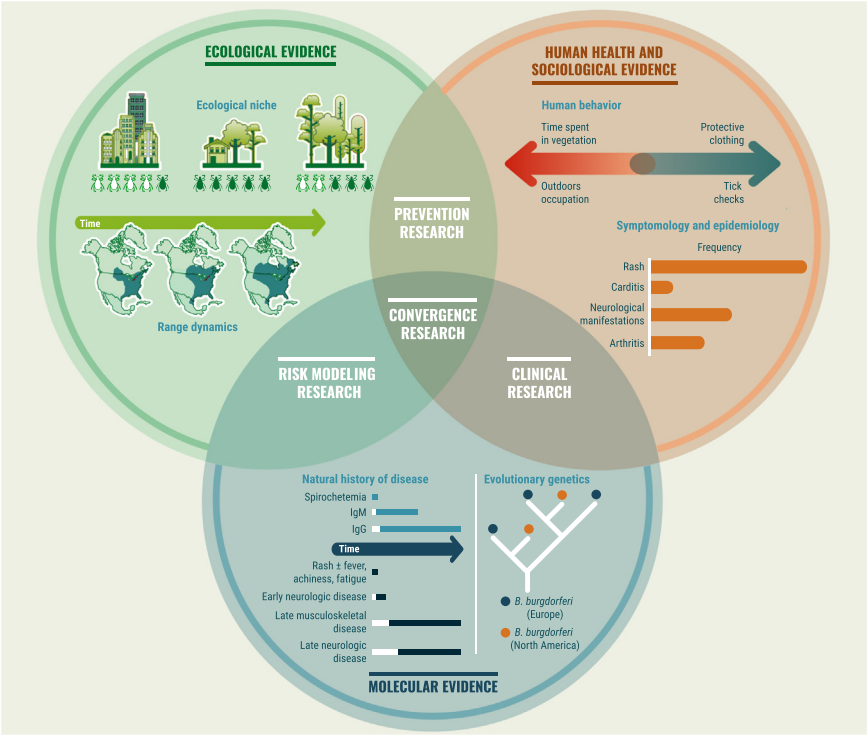

Figure 1. Potential Research Topics around Lyme Disease. Venn diagram of potential solutions to the 'wicked' problem posed by Lyme disease in Canada as a model for convergence research. Individual disciplines (circles) overlap into interdisciplinary projects with a convergence opportunity at the center.

may be especially true in emerging disease hotspots where physicians have more limited experience with symptoms and diagnoses [10]. Human demography and genetics may also affect the manifestation of Lyme disease [11]. Discussions about health impacts and misdiagnosis have inspired many advocacy groups and communities on social media, representing a rich source of data and opportunities for knowledge translation that are largely untapped.

Interdisciplinary and Transdisciplinary Research

In addition to the discipline-specific studies outlined above, Lyme and other vector-borne diseases provide opportunities for interdisciplinary and transdisciplinary research, combining ecology and evolution with genetics, human health, and sociology to better address this 'wicked' problem.

Risk Modeling Research

Research integrating elements of the ecology and evolution of pathogens, vectors, and hosts can deepen our understanding of disease risk and combine with knowledge of human behavior to improve epidemiological models and public health. Modern molecular approaches can offer great assistance, for example to estimate density and movement of vectors and hosts that are difficult to census or track in field surveys, and to provide an accurate assessment of the whole microbial community and potential pathogens therein [12]. Combining modern technologies offers potential for data-rich epidemiological models using advanced machine-learning algorithms incorporating medical data and geospatial/environmental characteristics.

Clinical Research

Conventional diagnosis tends to miss novel and emerging pathogens or genetic variants of known pathogens, especially when pathogens are rare and symptoms are nonspecific. Comprehensive healthcare worker training combined with modern molecular methods can help to identify emerging and re-emerging pathogens [13]. Integrating large molecular datasets within clinical trials, or with larger medical databases, can help to interpret patient symptom profiles. Integrating novel or less studied pathogens into model systems can ultimately refine diagnosis and lead to therapeutic targets.

Prevention Research

Accurate epidemiological risk models are necessary but are not sufficient to reduce disease incidence without effective interventions and knowledge translation activities. Host and vector management strategies can reduce environmental risk, while public health interventions can reduce exposure risk, and combining approaches could be most effective [14]. Ecological interactions are complex, and the efficacy and efficiency of different mitigation strategies can be tested in a scientific framework.

Convergence Research

There is a growing need for changes to academic training and funding infrastructure to incentivize a new generation of researchers to integrate across diverse backgrounds and expertise (Box 1). Whereas interdisciplinary research connects independent research programs, transdisciplinary or convergence research integrates expertise at all stages of the research process, from inception to knowledge translation. Integrating the methods and technologies outlined above, convergence research could guide pathogen and disease discovery based on a consilience of evidence from a coordinated study of (i) patient symptom mapping, (ii) medical records, and (iii) patient/vector/host microbiome surveys, to guide

hypothesis testing in (iv) clinical studies and (v) model systems to assess virulence and potential therapies. Integrating basic science and medicine with sociological research and patient advocacy groups during early planning stages can facilitate larger sample sizes and improve education and outreach efforts. A convergence approach that values divergent research strategies will integrate a wealth of untapped knowledge, methods, and expertise to achieve a common goal for the benefit of society.

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Declaration of Interests

There are no interests to declare.

[1]School of Epidemiology and Public Health, University of Ottawa, Ottawa, ON, Canada
[2]Biology Department, Queen's University, Kingston, ON, Canada

*Correspondence:
benoit.talbot@uottawa.ca (B. Talbot).

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