Backstory

The Wildlife Emerging Pathogens Initiative: Wild EPI and One Health

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One Health is an integrated approach that aims to balance and optimize the interconnectedness of the health of humans, animals, and ecosystems. Using this transdisciplinary approach, experts from across Canada led the formation of the Wildlife Emerging Pathogens Initiative (Wild EPI) to undertake research and surveillance programs evaluating the potential risks of emerging pathogens at the human-animal interface. Wild EPI is dedicated to implementing the One Health approach to enhance our understanding of the epidemiology and burden of zoonotic infections among humans and other animal hosts.

Beginnings

In 2020, the rapid global spread of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) sparked the first recorded coronavirus pandemic, bearing broad health and socioeconomic impacts. Ongoing viral activity was fueled by the initial lack of vaccines and other countermeasures, and the remarkable ability of SARS-CoV-2 to expeditiously adapt to its host, leading to a substantial net burden of virus in the human population. SARS-CoV-2 subsequently spilled over into new host species, including domestic and captive animals and free-ranging wildlife.

A timely expansion of surveillance efforts suddenly became necessary, drawing in new partners to develop collaborative frameworks using a One Health approach. One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of humans,

Above image: White-tailed deer (*Odocoileus virginianus*). Photo taken by Jacob Bowman.

animals, plants, and ecosystems. It recognizes that the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and interdependent.[1] By definition, the implementation of One Health must take a broad perspective that cuts across multiple sectors, including human health, domestic and wild animal health, and the environment. Therefore, One Health requires collaboration across these sectors by people with domain expertise.[2] In the case of SARS-CoV-2 inter-species spillover, this required new scaffolding for joint human and animal health surveillance programs at a time when many jurisdictions were functioning with reduced capacities and resources.

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By mid-2020, a multi-sectoral initiative had evolved in Ontario, Canada, led by the Ontario Ministry of Natural Resources and Forestry and collaborators. Focused primarily on SARS-CoV-2 surveillance in free-ranging peridomestic wildlife, these efforts nucleated a collective of academic and public sector scientists to enact an *ad hoc* surveillance program. The discovery of SARS-CoV-2 in white-tailed deer (*Odocoileus virginianus*) in Ontario and Québec catalyzed working relationships between genomic epidemiologists, virologists, and wildlife ecologists as a picture of human-to-deer-to-human transmission of a deer-adapted virus emerged. This new initiative, known as the Wildlife Emerging Pathogens Initiative (Wild EPI) is dedicated to implementing a One Health approach to gain an understanding of the epidemiology and burden of zoonotic infections among human and other animal hosts. Wild EPI (https://wildepi.ca/our-projects/) has undertaken a research and surveillance program of work to evaluate potential risks of emerging pathogens, with a focus on SARS-CoV-2 and highly pathogenic avian influenza (HPAI) virus. Our group has researchers who direct wildlife field sampling work, bioinformaticians and virologists striving to characterize zoonotic viruses, and human and wildlife health specialists enabling knowledge mobilization. Wild EPI discovered the first cases of SARS-CoV-2 in Canadian wildlife,[3] as well as a unique and highly divergent lineage of SARS-CoV-2 (B.1.641) in white-tailed deer responsible for the first reported deer-to-human transmission.[4] Notably, the viral sequence from the human case was flagged by a bioinformatician working in public health to scientists working on SARS-CoV-2 from deer, making a critical connection across sectors. The follow-on viral risk assessment catalyzed more hypothesis-driven research with the addition of collaborators in computational biology and viral immunology to explore otherwise uncharacterized wildlife host responses to viral infection.

What are the emerging infectious diseases of wildlife and why are they important?

Wildlife diseases include a number of diverse emerging pathogens. In many cases, a plurality of interconnected factors contributes to a limited understanding of these pathogens and the drivers that lead to disease emergence. Social determinants including chronic underfunding of wildlife research, lack of awareness and education, and deprioritization of wildlife health relative to human health contribute to gaps in our understanding of pathogen prevalence and distribution, sylvatic cycles, ecology, impacts on animal health, and mitigation strategies.

> Wildlife health is integral to all animal health, including human health.

Pathogen-related challenges are foregrounded by the same drivers that have led to epidemics and pandemics of human pathogens in the 20th and 21st centuries. Factors such as globalization of travel and trade, urbanization, and other activities impacting land use, including the global effects of climate change, collectively enhance exposure of naive wildlife to various potential pathogens through changing pathogen ecology and epidemiology and/or host susceptibility. Wildlife pathogens can spread rapidly across international boundaries, sustain transmission in new host populations, and lead to potentially destabilizing mortality events. Diseases of note which continue to be found in new species or regions across Canada include white-nose syndrome (caused by the fungus *Pseudogymnoascus destructans*), decimating bats in eastern Canada,[5] chronic wasting disease in cervids which continues to increase in prevalence in western Canada,[6] and West Nile virus which causes substantial mortality in corvids annually.[7]

Some wildlife pathogens are not limited to a sylvatic cycle and may be transmissible to humans and domestic species, including livestock. For example, bovine tuberculosis may spread from wild deer to cattle as well as companion animals[8] and the cestode *Echinococcus multilocularis* can cause alveolar echinococcosis in dogs and humans, leading to severe disease and death.[9] One Health recognizes that

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PhD candidate Simon Jeeves is conducting wildlife sampling in urban parks and green spaces in Toronto, Ontario. His research aims to investigate the diversity and epidemiology of zoonotic pathogens carried by these animals

anthropogenic land use can increase risk of zoonotic spillover, especially when there is an increase in the human-sylvatic interface. Human incursions into wild landscapes increase this interface, thus increasing the risk of spillover.

While there are clear examples of individual animal health effects, die-off events, population declines, extirpations or even extinctions associated with pathogens, the consequences beyond these impacts are often overlooked yet are of critical importance. Wildlife play a cornerstone role in maintaining ecosystem services, as well as protecting and promoting health. These services should be addressed by a comprehensive and well-integrated network of experts and organizations. Such an approach has been proposed in the Pan-Canadian Approach to Wildlife Health, which calls for the creation and implementation of an ongoing program to predict, detect, monitor, and effectively manage the numerous threats to wildlife health in Canada.[10]

As we strive for change at the systems level, we also aim to enable change at local and institutional levels, starting with learner engagement. Trainees form the backbone of Wild EPI, and participating in these highly collaborative projects has provided some unique learning and experiential opportunities. Simon Jeeves is a PhD candidate in Dr. Claire Jardine's group at the University of Guelph and states *"The numerous opportunities to network and collaborate with both local and inter-organizational experts from intersecting fields has provided me with many new connections. Such connections will allow me to design and work on projects with larger, more complete scopes."* He adds: *"The multidisciplinarity of the Wild EPI team has granted me a wider and more nuanced perspective of emerging infectious disease ecology and surveillance. Having a diverse panel of experts and their own teams* *working together in a coordinated manner has made feasible many goals which would otherwise require many years or perhaps decades to complete. In the same way, multidisciplinary groups like ours are able to fully and properly address the numerous logistical obstacles and capacity challenges involved in disease ecology work in ways that monopartite research groups simply cannot. It has become very clear to me that the future of this field lies in organizations like Wild EPI. I hope to be able to incorporate such an idea into my post-doctoral work."*

Trainees form the backbone of Wild EPI; participating in highly collaborative projects provides unique learning and experiential opportunities.

What is the relationship between wildlife pathogens and human health?

Zoonotic pathogens can include prions, viruses, bacteria, fungi, and parasites, and are transmitted between species. Nearly three-quarters of all human pathogens are believed to be of animal origin,[11,12] underscoring the interconnectedness between human and wildlife health. With the true global burden of human diseases of wildlife origin undoubtedly higher than reported, these zoonotic diseases merit attention given the breadth of impact across species and co-benefits of mitigation.

The phenomenon of pathogen transmission between species – known as *spillover* – happens both directly and indirectly, often along the human-animal interface. Certain viruses harbored by wildlife are insidious in their ability to jump between different host species with relative ease, accumulating adaptive mutations. Such viruses will occasionally spillover into humans and cause non-specific disease which will likely be written off as "a cold" or "the flu". When the right virus is contracted by the right human however, repercussions may be unpredictable. The latest and most obvious example of this is SARS-CoV-2.

Advances in diagnostic technology and molecular biology have enabled virus discovery in animals on a global scale. Although spillover of SARS-CoV-2 from a wildlife reservoir or intermediate animal host to humans catalyzed a regional outbreak, global amplification and pandemic spread is attributable to human-to-human transmission. Unsurprisingly, early in the pandemic, SARS-CoV-2 was detected in other species in close contact with humans – zoo animals, farmed mink, and companion animals. However, the frequency of these *reverse* zoonosis events – also sometimes called *spillback* – raised concern for infection in wildlife. This led to another question: what if the virus could establish a new reservoir? Answering this question would not be possible without strong interdisciplinary collaborations between scientists working on local and national levels to establish the ground truth for SARS-CoV-2 in hosts other than humans. SARS-CoV-2 infection in North American wildlife was first discovered in white-tailed deer sampled during early 2021 in Ohio, USA. The virus was then detected in Canada in the same species later that year, marking the first known instance of SARS-CoV-2 infection in Canadian wildlife.[3] Our group leveraged existing capacity for SARS-CoV-2 diagnostics, genomics and virology urgently developed in the course of the human health response by Fin Maguire, Jennifer Guthrie, and Samira Mubareka to stand up surveillance for wildlife co-led by biologists Claire Jardine, Tore Buchanan, Brad Pickering, and Jeff Bowman, whose essential expertise in field studies, animal virology, ecology and wildlife health allowed for the screening of thousands of convenience samples from dozens of species. Shortly after these efforts were launched, sampling of hunter-harvested deer yielded a highly divergent deer lineage of the virus (B.1.641) linked to a human case of COVID-19 in Ontario, Canada.[4] Without the collective effort from this group, this uniquely deer-adapted virus and the first description of deer-to-human transmission would not have been reported. Since then, we have realized that there are substantial gaps in our understanding of inter-host transmission and host-pathogen interactions, particularly where wildlife is concerned. Thus, we expanded the collaboration to include viral immunologist Arinjay Banerjee and host computational biologist and Andrew Doxey to generate the first RNA-seq dataset from SARS-CoV-2 naturally infected deer and determine the immunophenotype(s) from this important host species.[3]

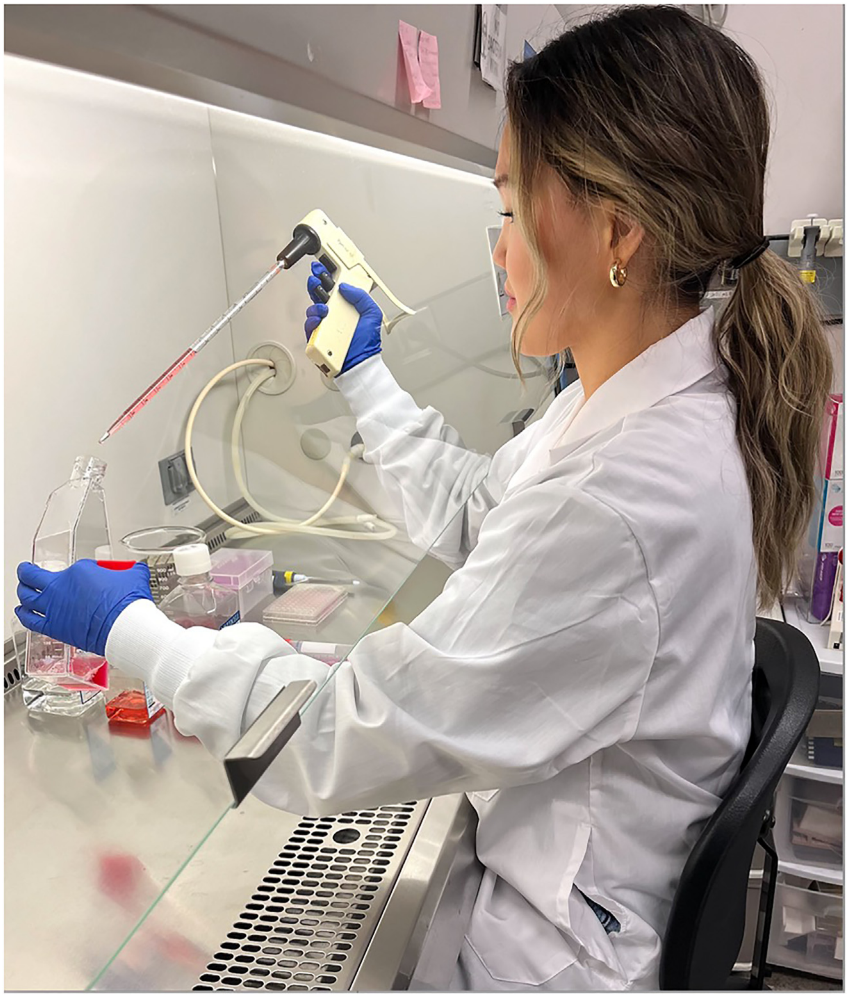
Continued circulation of SARS-CoV-2 in North American white-tailed deer populations has led to purifying selection of certain mutations, presumably making passage between deer more efficient.[13] Evolution of new SARS-CoV-2 strains in deer, or wildlife in general, may be harmless for deer hosts but could hold untold consequences should those strains spillover once again into humans. Significant changes in the SARS-CoV-2 genome during circulation in wildlife could lead to reduced efficacy of vaccines or impact diagnostic testing – as was seen with human SARS-CoV-2 variants such as Omicron – should they spillover and circulate in humans, thus significantly undermining public health efforts.

Challenges

What are the main challenges facing One Health approaches?

The One Health approach relies on multi-sectoral collaboration, necessitating coordinated regional, national, and international efforts across sectors and disciplines. However, the connectivity of wildlife surveillance, reporting systems and response structures remains fragmented due to siloed mandates and communication. The lack of integration across human, animal, and environmental health sectors creates a major gap in establishing multifaceted and sustainable surveillance programs. With ongoing surveillance activities by numerous groups, lack of coordination can make it challenging to gather, access and translate surveillance data in real time, particularly since program development and support are fragmented across jurisdictions, agencies, and institutions.

Data concerning the occurrence of zoonotic diseases are often lacking, particularly for diseases that don't appear to pose an immediate threat. This lack of data creates challenges when it comes to persuading policymakers about the advantages of investing in and supporting



PhD candidate Yaejin's project involves conducting a risk assessment of SARS-CoV-2 (B.1.641), which has been detected in Ontario white-tailed deer. The project involves *in vitro* and *in vivo* work in biosafety containment levels 2 and 3 to characterize the B.1.641 virus isolate

One Health surveillance programs and other key activities. Health dollars are primarily invested in human health with limited commitment to animal and environmental health.

Implementing One Health surveillance systems is resource intensive, complex, and costly, requiring significant funding and partner support. With the right strategic approach however, existing investments can be leveraged across sectors. This is what we strived to do with Wild EPI, whereby resources for SARS-CoV-2 implemented for human health were co-leveraged with existing wildlife disease detection and control programs. However, as resources for SARS-CoV-2 response and research atrophy, the absence of adequate support presents challenges in establishing a sustainable and integrated surveillance effort across diverse domains. This includes building essential surveillance capacity, integrating data and information, and standardizing data quality. For instance, wildlife rehabilitators, who are key stakeholders for disease surveillance due to their unique access to a wide range of species, face challenges providing consistent, long-term samples crucial for the surveillance work. This was particularly challenging for more recent SARS-CoV-2 and HPAI surveillance due to funding and staff limitations. Despite rehabilitators' willingness to contribute, most rely on donations and cannot afford costly tests, creating a substantial gap in early disease detection. Similarly, funding streams for hypothesis-driven, fundamental research at the human-animal-virus interface remains siloed between human health and natural sciences, with very few opportunities in Canada to develop projects that intersect, despite substantial interest and drive from the scientific community.

Furthermore, the absence of adequate support presents an additional challenge in the education and training of competent One Health scientists, scholars, and practitioners to facilitate integrated One Health programs. Specifically, there is a deficiency in One Health training programs that emphasize collaborative approaches, including hands-on field training and multidisciplinary experiences. Academic and institutional support for the One Health approach remains minimal, resulting in a shortage of well-trained personnel capable of conducting collaborative research. There is also a need for well-trained individuals to establish ground truths. Unfortunately, there is a shortage of highly qualified personnel with in-depth knowledge of wildlife sampling procedures, a factor that significantly impacts the success of surveillance programs. Indigenous-led surveillance, research and teaching is also under-supported despite the immense value of Indigenous knowledge and experience.

Wild EPI is striving to fill some training gaps, creating opportunities for a range of learners from different disciplines. Yaejin Lee is a PhD candidate who describes her experience learning through a One Health lens: "*Being part of a multidisciplinary group has broadened my perspective, exposing me to diverse research areas. In the lab, handling deer cells constantly reinforces the collaborative efforts and shared passion enabling meaningful work with our collaborators. It serves as a continual reminder of the interconnectedness of fields and the potential for impactful work when diverse minds unite. One of the most meaningful lessons I've gained from this project is the importance of embracing collective efforts across diverse fields toward a common goal. This experience not only connects me with new researchers and trainees but also involves coordinating various aspects of the work. It helps me evolve into a more mature trainee, laying the groundwork for my future career, where I aim to excel in multidisciplinary initiatives.*"

Wild EPI is striving to fill training gaps, creating opportunities for a range of learners from different disciplines.

Future

How can all stakeholders work together to address these challenges?

Effective coordination plays a pivotal role in the One Health approach.[1] From initiation, stakeholders must maintain open communication channels to comprehend gaps, identify available resources, recognize potential collaborations, and establish robust systems for reporting and data sharing. Coordination should involve clear responsibilities for varying sectors, fostering collaboration among existing surveillance programs while practicing timely sharing of surveillance updates and data.[14] Additionally, limitations of data and information sharing among stakeholders need to be urgently addressed through establishment of centralized, consistent, and timely reporting mechanisms for surveillance activities. To turn valuable data into actionable knowledge, we connected a diverse team of experts to characterize pathogens and conduct risk assessments of emerging zoonotic diseases. Through this work, we have also established a close, collegial community of practice for science and stakeholder engagement. Not only do we exchange knowledge and skills as we strive to identify and address key gaps, but we have also developed close working relationships that form the connective tissue for both rapid research response capacity and means by which to pursue more in-depth scientific inquiry. Therefore, active engagement in connecting stakeholders from multiple disciplines is crucial for establishing common goals and a shared purpose in addressing challenges from a One Health perspective.

Effective collaboration is essential at all levels of society to combat health inequalities, disseminate vital information on zoonotic diseases to high-risk populations and build trust with stakeholders. This includes following the lead of Indigenous knowledge holders, as well as engaging local communities and collaborators in decision-making, ensuring a more resilient and equitable health ecosystem.

Wild EPI aims to help address One Health challenges by establishing a coordinated, cross-sectoral research and surveillance program focused on emerging infectious diseases, and also serves as an early career training ground to acquire technical expertise that can be applied to One Health challenges. Wild EPI, and initiatives like it, can help to implement One Health through academic initiatives in partnership with the public sector to knit together cohesive efforts to generate and transform data into knowledge. It is insufficient to collect and report data without impacting evidence-based decision-making. Wild EPI not only strives to enable knowledge mobilization in the immediate term to inform preparedness and response to emerging zoonoses, but also to foster longer-term, hypothesis-driven research on pathogen and host ecological and biological interactions, evolutionary biology, and pathogenesis for pre-emergent, emergent and endemic pathogens to further our understanding of health and the conditions essential to maintaining it for all species.

The Wildlife Emerging Pathogens Initiative (Wild EPI) is dedicated to implementing a One Health approach to research on viral zoonoses through multidisciplinary collaboration and intersectoral partnerships to transform data into knowledge.

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