Navigating the complexities of "One Health"

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Introduction

Widespread circulation of avian influenza in cattle, with some currently limited spillover infections into humans,[1] and the recent declaration of an mpox global emergency,[2] once again highlight the dramatic risk that zoonoses pose for human health. Additionally, the potential for human-to-animal transmission has been underscored by recent findings of abundant circulation of SARS-CoV-2 in wildlife.[3] Taken together, these case studies reveal the importance of a broad view of pathogen dynamics that includes sylvatic, urban, and human transmission cycles. While the concept of a "One Health" approach[4] can be difficult to conceptualize and daunting to contemplate, we argue here that certain unifying pillars can simplify this task, as in the integrative framework we present in Fig. 1 to detect epizootic or endemic pathogen spillovers (see Figure 1) with Covid-19-like pandemic potential.

Framework basics and concept of 'indicator' wildlife species

At the crux of One Health programs is the monitoring of three classes of populations: humans, domesticated animals, and wildlife. The difficulty of monitoring each of these is highly variable and high quality data is paramount. Certain forms of pathogen surveillance among humans have dramatically improved since their initial deployment, especially wastewater,[5] and infection surveys[6] during and after the COVID-19 pandemic. Further, important recent calls have been made for a Global Immunological Observatory[7,8] that would identify changes in immunological signatures at the population level and more rapidly reveal cryptic pathogens spreading among humans.

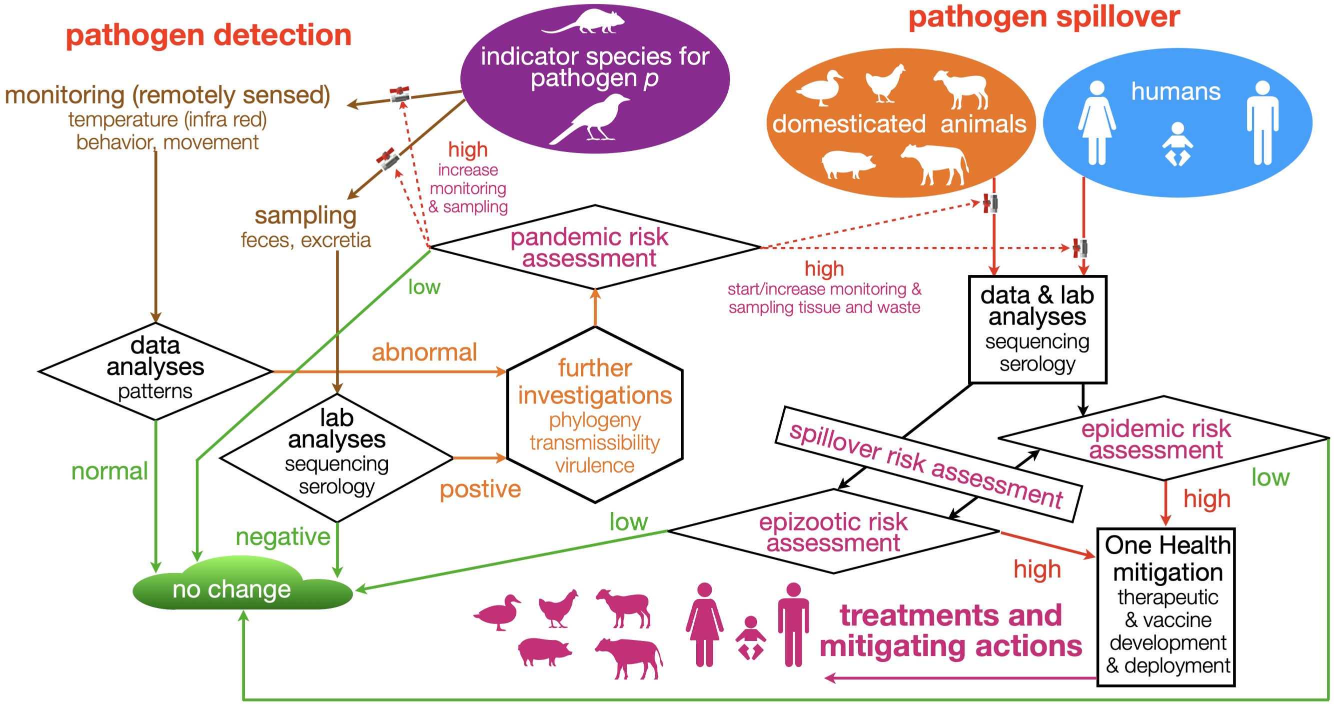

Figure 1: An integrative "One Health" monitoring framework that consists of the adaptive monitoring of humans, domestic animals, and wildlife, the latter via one or more indicator species, to assess the risk of zoonotic spillover and the possible emergence of a new global pandemic.

Comparably less surveillance among farm animals or wildlife is ongoing, however, and this may be necessary to anticipate and prevent future pandemics. To address this gap, a pillar of our conceptual framework is the identification and detailed monitoring of one or more wildlife 'indicator' species for each pathogen of concern.

Tracking and monitoring of temperature, behavior, and movement patterns,[9] in addition to sampling feces and excretia, should be ongoing in a manner designed to reveal disease-induced changes. While detecting disease via the behavior and movement of individuals is a relatively new concept, we see this (see Dougherty et al.[9] for further discussion) as central to a One Health approach (Fig. 1). In particular, areas of spatio-temporal overlap among wildlife, domesticated animals, or humans are ideal regions of focus for monitoring indicator species. In the case of pathogens with durable environmental persistence, these regions can form 'Local Infectious Zones'[10] or infectious 'hot spots'. An additional general benefit of monitoring regions of spatio-temporal overlap is that their size can also be observed for changes (*e.g.*, due to urbanization or climate change) that may increase the likelihood of pathogen spillover. In tandem, monitoring may facilitate the implementation of mitigating actions such as measures to reduce human-animal or animal-animal contacts on temporary or permanent basis to reduce the probability of zoonotic spillovers in hot spots.

A key benefit of movement monitoring is that sampling can be automated, continuous, and fed immediately into AI systems using state-of-the-art machine learning algorithms for real-time analysis. Then One Health program managers and scientists need only be alerted when changes in movement and behavior are detected. In turn, active monitoring can be deployed (*e.g.*, with serology and sequencing), and further investigations used to reveal the causative agent, and the degree to which such a pathogen has the potential to ignite either a localized epidemic or a new global pandemic. Finally, risk assessment of the potential for local versus a global outbreak could be used to inform the policies needed for the rapid deployment of mitigation strategies in at-risk domesticated animal populations and human communities.

While deploying monitoring systems in humans and domesticated animals is relatively straightforward, identifying an indicator species in wildlife is more difficult. A pathogen with pandemic potential, however, may already be established (or emergent) in either the sylvatic, urban, or human transmission cycles. In these cases, some of its details would already be known, and difficulties associated with deploying surveillance should be partially alleviated. For example, current global circulation of H5N1 avian influenza was first in birds and is now circulating abundantly in domesticated cattle, with a few spillover infections in humans to date.[1] Further, SARS-CoV-2 is now circulating widely in humans and animals;[3] and in the latter, pathogens variants with the potential to give rise to future pandemics may well emerge.

In systems where novel pathogens have the potential to emerge, it is possible that close relatives of these pathogens have been identified and are currently circulating in humans, domestic animals, or wildlife. These pathogens may then be monitored in a One Health program to see rates of new variant emergence and evaluate these new (now circulating) variants in highly regulated (biosafety level 3) labs that study their transmission and pathogenicity in appropriate animal model systems. For example, multiple coronaviruses and influenza viruses are known to circulate in humans[11] and animals.[12] Finally, it is possible that a pathogen with pandemic potential has no known relatives in current circulation. To anticipate these, large-scale indicator species monitoring is required, particularly across the sylvatic transmission cycle, to detect their emergence before they spill over. If changes in organism temperature, behavior, or movement are detected, further investigation and genome identification should occur.

Risk assessments

For general One Health approaches to succeed, there must be continual pandemic, epizootic, and epidemic risk assessment using the latest quantitative methods, with an additional assessment of spillover to evaluate the risk of zoonoses (Fig. 1). In our framework, we propose that each of these specific assessments follows from data collected from either the indicator species (pandemic potential), domesticated animals (epizootic potential) and human populations (epidemic potential). For epizootic and epidemic potential, data should be routinely monitored, and appropriate mitigation measures consequently taken. Most importantly, if the risk of a potential zoonotic pandemic is evaluated to be high, monitoring and sampling of the indicator species should be increased. If these measurements remain abnormal, domesticated animals and humans need to be monitored closely, including via sequencing and serology. With those data, risk assessments for epizootic and epidemic potentials should be performed using the best available quantitative methods, and appropriate therapeutics and vaccines developed and deployed according to cost-benefit analyses.

In our framework, we view animal vaccination primarily as a treatment strategy when epizootic risks are high. However, such strategies could themselves affect risk assessments, creating an important feedback loop between intervention and epidemiology. The magnitude of these effects could be quantitatively captured with our proposed conceptual monitoring framework. While animal vaccination is currently underutilized, there have been recent calls to develop and deploy mass animal vaccination globally.[13] With mass vaccination, our proposed monitoring approach would also enable detailed cohort studies for the effects of such vaccines in wild and domesticated animal populations. For example, epidemiological characteristics, such as vaccine efficiency for both transmission-blocking and severity-reduction capacities, could be determined. Further, the effects of animal vaccination on pathogen evolution could be monitored, and the vaccinal reductions in cross-species transmission (and risk of spillover) determined. Finally, these cohort studies would also clarify basic immunology (*e.g.*, strength and duration of immune response) and host-pathogen interactions in these organisms (in humans, see Saad-Roy[14] for a perspective on potential cohort studies for immuno-epidemiology and evolution).

Future outlooks

For a One Health program to be successful, many regional, national, and global challenges must be overcome. Locally, laboratory capacity must be sufficient to process a constant flow of samples. In tandem, local computational availability is required to perform the necessary data analyses for monitoring. While both already exist in some regions, the COVID-19 pandemic revealed that there remains high inequity across the world. Further, since a One Health monitoring framework would ideally span large physical areas, regional coordination of efforts is required. Finally, regional policies should be synergized, and data shared immediately. These challenges are only magnified at the global level, but resolving them is key for rapid identification and proper mitigation.

Importantly, climate change is poised to dramatically alter the landscape of infectious disease transmission and spillover within the next decades. For example, recent phylogeographic modelling suggests that such changes in climate will significantly accelerate animal-to-human zoonoses.[15] Since the details of where and when these events will occur remains unknown, it is imperative to deploy One Health monitoring mechanisms widely and rapidly. As the regions of contact between wildlife and domestic animals, or between wildlife and humans, grow, surveillance mechanisms should be enhanced to increase data collection at these critical junctions. In turn, these data could also provide valuable insights on the effects of climate change on pathogen spillover and evolution.

While the specifics of our framework hinge on a variety of factors, ranging from pathogen-specific details to regional and national policies, the key elements of our framework make complexities that are often associated with One Health more coherent and comprehensible. While many One Health programs currently exist, none seamlessly integrate across domestic animals, wildlife, and humans. Our proposed framework accomplishes this, as well as identifies the kinds of data that require collection at each scale. If our framework was deployed in conjunction with a potential Global Immunological Observatory and ongoing wastewater surveillance, our societies would have a very robust multi-pronged approach to pathogen detection. This could both anticipate and prevent the next pandemic.

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