Navigating the complexities of “One Health”

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Abstract

For two decades, a One Health approach to managing the emergence of novel zoonotic pathogens has been increasingly called for by the animal and public health sectors. One health systems are complex. They require the integration of data from wildlife indicator and reservoir species, domesticated animals, and humans into a framework of adaptive monitoring and analysis that provides for early warning of impending pathogen spillover and novel strain emergence accompanied by mitigating action to constrain zoonotic and enzootic outbreaks. Here we provide a graphic description laying bare the key elements of a One Health preparedness system and discuss a monitoring and quantitative analysis framework designed to meet the needs of a well planned One Health approach to pandemic preparedness. This especially includes automated remote sensing of pathogen-specific indicator wildlife species and the development of a quantative tool box suitable for pandemic risk assessment.

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

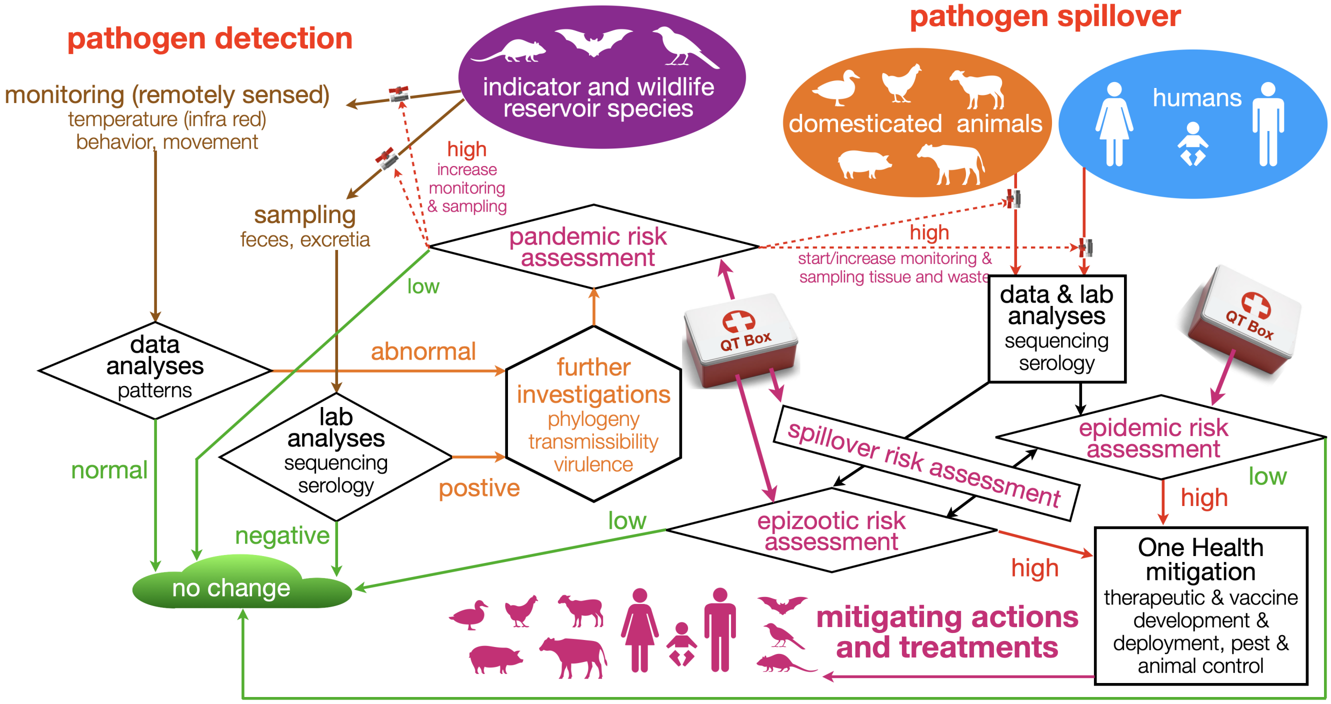

Figure 1: An integrative "One Health" monitoring framework that consists of the adaptive monitoring of humans, domestic animals, and wildlife, the latter via one or more indicator species, and a quantitative tool box (QT Box, see Figure 2) to assess the risk of zoonotic spillover and the possible emergence of a new global pandemic.

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 and analyse epizootic or endemic pathogen spillovers (see Figure 1) with Covid-19-like pandemic potential.

Framework and 'indicator' species concept

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. 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, the first pillar of our conceptual framework is the identification and detailed monitoring of one or more wildlife 'indicator' species for each pathogen of concern. A second pillar is the application of a comprehensive quantitative tool box (QT Box) for curating data and assessing, visualizing, and managing the risks of zoonotic spillover and pandemic outbreaks.

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 extent 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.[11] 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 implied using an appropriate QT Box with the results 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[12] and animals.[13] 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 (Fig. 2), 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 using an appropriate QT Box, 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, QT Box risk assessments for epizootic and epidemic potentials should be performed 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.[14] With mass vaccination, our proposed monitoring and QT Box analysis 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 through QT Box analysis. 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 et al.[15] for a perspective on potential cohort studies for immuno-epidemiology and evolution).

A quantitative tool box for data integration, visualization, and risk assessment

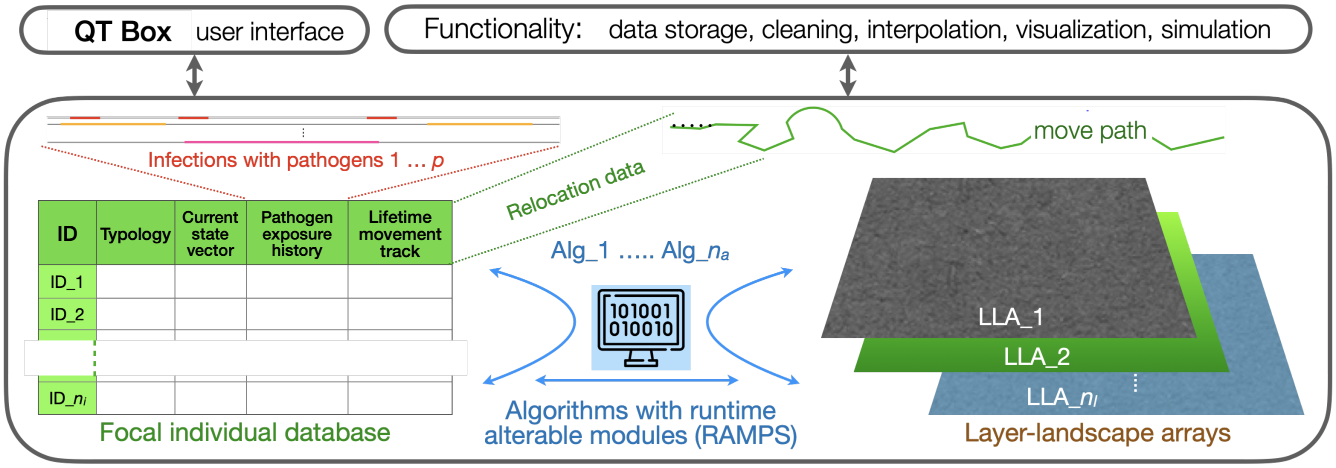

Figure 2: A quantitative toolbox (QT Box) designed to aid in pandemic, epizootic, spillover, and epidemic risk assessment in One Health settings (see Figure 1). This tool box has three major components: 1.) a data base for individuals belonging to a focal group (green data array on left) that includes the typology of each individual (age, sex, current location and state of health, group membership, etc.), a pathogen exposure history and forecast (top left orange and red trace) and a movement pathway (history and forecast; top right green trace); 2.) a set of layered landscape arrays (LLA——some array elements may be multivalued) for vegetation, resources, typography, resistance to movement, pathogen contagion risk maps including the distribution and disease state of various reservoir populations; and, 3.) a set of interpolating, updating and projection algorithms (Alg) that have the flexibility for selected runtime modifications.

A modern quantitative tool box (QT Box) should constitute a fully integrated data empirical data visualizer augmented with an individual movement and disease progression simulator able to evaluate the impacts of different disease mitigating and pathogen control strategies. The platform should be centered around one or more focal populations for which both pathogen exposure history and host movement data are stored for one to several thousand individuals moving within a multilayered set of dynamic landscape maps. These maps should include geographic information for QT-Box-user orientation, resource and topography data needed to understand movement drivers and project future movement behavior,[16] and the distribution of pathogen hotspots arising from infected individuals in reservoirs populations[17] or environmental sources (so-called locally infectious zones[18]).

A modern QT Box should also include a number of algorithms for performing various data management, map generation, and individual movement and disease progression algorithms. Beyond filtering and interpolating empirical data for visualization and analyses, projected movement data should be used to compute the exposure of individuals to regions where pathogens are prevalent.[9, 19] Additionally, the exposure history of individuals can be used to compute the likelihood of new pathogen strains emerging as a pandemic unfolds.[20, 21]

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, availability of intensive computing power may be needed to perform the necessary data analyses implementing a full-feature QT Box. While appropriate laboratory and computational facilities already exist in some regions, the COVID-19 pandemic revealed that there remains high inequity across the world with regard to such resources. 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.[22] 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 (see Metcalf et al.[7] and Mina et al.[8]) 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.

Acknowledgments

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