excerpted from

*Reducing Pandemic Risk, Promoting Global Health*

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FUTURE DIRECTIONS
Historically, attempts to control deadly viruses, such as SARS and Middle Eastern Respiratory Syndrome (MERS) coronaviruses, influenza, and Ebola, have been almost entirely reactionary. The World Bank estimates that from 1997 to 2009, at least $80 billion was spent responding to just six outbreaks of deadly zoonotic diseases caused by viruses shared between people and animals (World Bank 2012).

In recognition of the costs of emerging infectious diseases (EID) in both lives lost and dollars spent on treatment and control and the need for a more proactive paradigm, the PREDICT project conducted the most comprehensive zoonotic pathogen and EID surveillance capacity building program in the world to date. As detailed in this report, a risk-based surveillance strategy was used in regional “hotspots” for emerging diseases with the aim of targeting efforts toward early detection and response to potentially high-consequence animal viruses before they become significant public health threats.

In order to further focus surveillance and interventions at the source of pathogen emergence, amplification, and spread in human populations and especially to predict risk from viruses before they emerge, future work should:

• Expand characterization of pathogens of known epidemic and unknown pandemic potential and their dynamics among hosts;

• Document pathogen sharing between wildlife, domestic animals, and people;

• Target surveillance at high-risk pathways for disease emergence, spillover, and spread in order to identify social and ecological drivers of (i.e. factors influencing) pathogen emergence and transmission and determine appropriate targets for intervention; and

• Build on global One Health initiatives for effective collaboration across disciplines and geographic borders.

EXPANDING CHARACTERIZATION OF PATHOGENS OF KNOWN EPIDEMIC AND UNKNOWN PANDEMIC POTENTIAL AND THEIR DYNAMICS AMONG HOSTS

For the PREDICT project, the selection of viral families/genera targeted for testing was necessarily broad. It included families of known zoonotic, epidemic, and pandemic risk, as well as those that, despite their perceived lower pandemic risk, had sufficient abundance and diversity in wildlife to act as useful targets for laboratory capacity building. To increase efficiency for targeting pathogens of highest consequence, future efforts should focus on ranking risk of spillover, amplification, and spread of these newly detected viruses using all available virological, epidemiological, ecological, and host-specific data. The development of modeling and analytical
tools needed to derive both spillover and pandemic risk from viral genetic material and ecological data remains a significant challenge. Developing this analytical toolkit to identify the highest risk viruses is a critical next step and will allow for the prioritization of resources for advanced laboratory characterization of select viruses, as well as better targeted surveillance and viral detection and discovery efforts. A focus on those viruses with previous association with Influenza-like Illness (ILI), Severe Acute Respiratory Illness (SARI), Fever of Unknown Origin (FUO), and hemorrhagic disease in people will also be beneficial.

The study of diseases of unknown origin (DUO) provides an important tool for the identification of new and previously undetected pathogens that have the certain capacity to infect and potentially the ability to spread in human populations. Because current laboratory and health systems are targeted at identification of known pathogens that have caused disease in the past, many diseases go undiagnosed, at best making treatment and control very difficult and, at worst leaving treatment of affected individuals limited to supportive care. Further examination of syndromic surveillance samples is needed to identify novel agents associated with ILI, SARI, FUO, as well as other syndromes, such as hemorrhagic fever and encephalitis. In addition to viruses, the full range of bacterial pathogens should be identified in specimens from DUO patients.

Using this approach will allow advanced characterization to be targeted to new viruses detected from viral families/genera of potential pandemic significance that have a relatively wide range of hosts, are related to known pathogens, are detected in new or unusual host species, or cluster with known pathogens found in other host taxa. Full genome sequencing and virus isolation will allow for accurate taxonomic placement, characterization of virus-host cell receptor interactions, and improved understanding of host diversity and the evolutionary processes that shape viral diversity (e.g. reassortment/recombination). This approach will lead towards more effective intervention, enabling the design of treatments, preventives, and serological assays to investigate human exposure to these agents and facilitate the tracing of novel pathogens back to potential animal reservoirs and amplification hosts in order to identify and mitigate risky behaviors at the source of viral spillover and amplification interfaces.

**DOCUMENTING PATHOGEN SHARING AMONG WILDLIFE, DOMESTIC ANIMALS, AND PEOPLE**

Human behaviors and practices are key risk components for pathogen spillover, amplification, and spread. Understanding these behaviors and more comprehensively characterizing the type and frequency of contact among people, livestock, and potential wildlife reservoirs are key next steps to reduce these risks. To investigate interspecies transmission along high-risk pathways for emergence and identify critical control points to prevent pathogen spillover – human, livestock, and wildlife sampling must align in time and space at key high-risk interfaces. Intensive livestock production systems, points
of potential contact along animal value chains, and land conversion for commercialization have been identified as high-risk settings for the emergence of pandemic threats (Figure 1). To improve our understanding of the behavioral mechanisms involved in high-risk pathways, these data should be used to develop analytical models that link specific human behaviors and zoonotic disease risk across sites. It is essential to identify critical control points and risk-mitigation options, field piloting strategies to gauge individual and community willingness and uptake potential in order to determine which interventions might be taken to scale. Critical examination of scenarios that integrate epidemiological models with cost-benefit analyses for different pandemic control strategies can then be used to inform policy makers on the most likely effective interventions.

In addition, it is important to compare novel agents detected in people with diseases of unknown origin to newly discovered animal viruses and bacteria to identify animal hosts and practices heightening risk for spread. Genomic sequencing combined with new approaches that integrate molecular evolution, phylogenetics, and coevolution will be used to help unravel the mysteries that influence pathogen sharing across the animal-human interface. Further, disease outbreaks in people and animals also present unique opportunities for parallel sampling of wildlife, livestock, and people; pathogen discovery; and investigations of spillover events resulting in disease.

Figure 1. Land conversion for commercialization, animal production systems, and animal value chains are three high-risk pathways for pathogen emergence, spillover, and spread.
IDENTIFYING DRIVERS OF PATHOGEN EMERGENCE AND TRANSMISSION AND DETERMINING POTENTIAL TARGETS FOR INTERVENTION

To increase efficiency for identifying viruses that pose the greatest risk for emergence in people, future efforts should be most focused in areas where environments and systems are changing in ways that are conducive to the spillover of viruses from animals into humans. Rapidly improving, advanced analytical approaches based on quality science, will provide key information on the potential for spillover, amplification, and spread within identified emergence pathways. To better forecast risk of emergence along key pathways, high resolution spatial datasets that include changes in land cover, specific land-use, livestock density, patterns of wildlife trade, and changes in wildlife distribution will need to be analyzed under realistic future scenarios of demographic, environmental, economic, and climate change. Further, an epizonal approach (Figure 2), in which the whole geographic, ecological, and sociological space of these disease emergence and transmission pathways is characterized, offers opportunities to improve understanding of pre-spillover conditions that drive viral evolution, transmission of zoonotic pathogens, and circumstances of pathogen amplification and spread.

Figure 2. An epizone for SARS Coronavirus includes the wildlife markets of Guangdong where it amplified and spread, but also the whole wildlife trade along Southern China back to Yunnan Province, where PREDICT identified a diverse cluster of bat SARS-like coronaviruses capable of infecting human cells. From Ge et al. 2013.
Identifying key processes influencing the evolution, spillover, amplification, and spread of pathogen threats could likely best be achieved through augmenting and integrating data generated through PREDICT and partner networks with 1) selective longitudinal sampling of wildlife, livestock, and at-risk human populations with a special focus on ILI, SARI, and DUO patients; 2) detection and characterization of pathogens with evidence of infectivity and transmissibility among hosts, including people; 3) simultaneous collection of data on human behaviors, movements, practices, and the ecological conditions governing these aspects of human ecology; and 4) analyses of key viral characteristics in combination with data collected on hosts, ecological drivers, human behaviors and practices, exposure rates, and ecological conditions.

Advanced informational technologies and dynamic analytical frameworks could then be applied to the integrated biological surveillance, behavioral risk characterization, and economic and anthropologic data to identify potential targets for intervention and informed policy development.

BUILDING ON GLOBAL ONE HEALTH INITIATIVES FOR EFFECTIVE COLLABORATION ACROSS DISCIPLINES AND GEOGRAPHIC BORDERS

Through its local and global One Health initiatives, PREDICT and its partners enabled a structure for effective collaboration across disciplines and geographic borders to promote global health through prevention of emerging zoonotic disease threats. This infrastructure can be built upon to include additional regions and stakeholders. In fact, the Emerging Pandemic Threats program has developed two additional new initiatives, PREPAREDNESS and RESPONSE and ONE HEALTH WORKFORCE to build capacity and streamline prevention and control measures. The projects, in collaboration with PREDICT, will build on One Health advancements through:

• Development of national and regional strategies for the sustainability and broadening of One Health initiatives, including systems for disease prevention and early detection;

• Engagement and training of more stakeholders, including representatives from additional ministries, health and industry sectors, and local at-risk communities;

• Facilitation of regional and global collaboration on pandemic prevention and preparedness; and

• Illustrations of proofs of concept, including cost/benefit analyses to demonstrate improved outcomes resulting from a One Health approach.

REFERENCES
