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Reducing Pandemic Risk, Promoting Global Health

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INTRODUCTION
Emerging infectious diseases (EIDs) pose substantial threats to the health of animals and people and economies globally. Over the past several decades, the emergence and spread of viruses such as severe acute respiratory syndrome (SARS) coronavirus, Ebola virus, and H5N1 and H1N1 pandemic influenza A viruses, have had profound global health and economic impacts, illustrating our vulnerability to the emergence and re-emergence of zoonotic diseases.

Zoonotic diseases result in millions of deaths annually, and the economic losses from a single outbreak can amount to tens of billions of dollars (e.g. SARS; Lee and McKibbin 2004; Keusch et al. 2009; World Bank 2012). Prevention and early control of outbreaks is key to reducing their impact, but there remains a critical need to improve the capacity of developing countries to effectively implement prevention and control activities as demonstrated by the 2014 Ebola virus disease outbreak in West Africa.

Zoonotic pathogens shared with wildlife or livestock account for the majority of emerging infectious diseases of people, and viruses comprise 25-44% of these emerging and re-emerging pathogens (Jones et al. 2008; Taylor et al. 2001). Because of their diversity and rapid evolution, viruses, in particular RNA viruses, are perceived to pose the greatest global pandemic threat (Morse 1995; Cleaveland et al. 2001; Pulliam 2008). For instance, two of the most devastating pandemics in human history, the 1918 influenza pandemic (50 million deaths) and the HIV/AIDS pandemic (35 million deaths as of 2012; Morens et al. 2008; Fauci and Folks 2012), were caused by zoonotic RNA viruses.

Despite greater recognition of EIDs on a global scale, there is limited understanding of the underlying causes for emergence and spread of zoonotic pathogens in people (Murray and Daszak 2013). Factors associated with emergence, re-emergence, and spread of pathogens have been categorized into four broad domains worthy of investigation: 1) genetic and biological factors of pathogens and hosts, such as microbial adaptation and human susceptibility to infection; 2) physical environmental factors (e.g. climate variability and weather); 3) ecological factors (e.g. land-use change); and 4) social, political, and economic factors, including poverty and animal and public health infrastructure (Bogich et al. 2012; Daszak et al. 2001; Smolinski et al. 2003). For example, factors such as rapid human population growth, land use change, intensification of livestock production, natural resource extraction, and...
Figure 1: Emergence of pandemic zoonotic disease. From Morse et al. 2012.

Stage 1 is a pre-emergence state, in which microbes are transmitted between animal reservoirs. Ecological disturbances (e.g. due to land use change) modify the dynamics of microbial transmission, which can lead to a heightened risk of pathogen spillover to wildlife or livestock hosts.

Stage 2 is localized emergence, either through self-limiting spillover events (green peaks and troughs, representing increases and decreases in the numbers of infected people with time) or large-scale spillover (red peaks, representing spikes in the number of infected people with time), that leads to person-to-person transmission for a few pathogen generations.

In stage 3, some spillover events might lead to sustained person-to-person outbreaks, international or global spread, and the emergence of a pandemic. The size, spread, and potential effect of events increase from stage 1 to stage 3, but the frequency falls so that full stage 3 pandemics are quite rare. By dissecting this process and analyzing the interactions of the underlying drivers with the risk of spillover and spread, development of a more structured approach to pandemic prevention is possible. The ultimate goal of successful pandemic prevention is to target control at stage 1.
the demands for global trade result in greater interactions between animals and people and therefore more opportunities for cross species transmission and disease emergence (Daszak et al. 2001; Smolinski et al. 2003). International travel has also contributed to the spread of many infectious diseases regionally or globally with one of the most notable being the spread of SARS coronavirus from Hong Kong to North America, Latin America, Europe, Asia, and Australia resulting in 8,422 documented cases and 916 deaths worldwide (Heymann and Rodier 2004).

Wildlife play a major role in the emergence of infectious diseases in human populations. Analysis of over 300 EID events occurring between 1940 and 2004 revealed that more than 70% of emerging zoonotic pathogens originated in wildlife, and that the incidence of EID events caused by wildlife pathogens has significantly increased over time (Jones et al. 2008). Certain wildlife taxa are known to harbor a high proportion of zoonotic pathogens. Among assessed wildlife taxa, zoonotic viruses have been most commonly detected in rodents, bats, primates, ungulates, and birds (Woolhouse and Gowtage-Sequeria 2005; Calisher et al. 2006; Luis et al. 2013; Smith and Wang 2013). Therefore, focusing surveillance efforts on these wildlife hosts is likely to enhance the identification of viruses with pathogenic and disease emergence potential prior to spillover to people (Parrish et al. 2008; Morse et al. 2012). Efforts in this realm must also be cognizant of the need for clear messaging to not vilify wildlife, as the mechanisms for disease spillover tend to be primarily human-induced, not animal-driven, and biodiversity and conservation goals must also be maintained for a healthy world.

The seriousness of these threats has led to the recognition that a shift from a conventional, reactive approach toward a proactive, predictive approach is necessary for EID prevention and timely control (Figure 1; Karesh et al. 2012; Morse et al. 2012). Infrastructure improvements and technological advances have dramatically and rapidly improved our ability to identify high-risk interfaces for disease transmission and to detect novel pathogens before widespread spillover occurs. These advances include improvements in information technology, molecular diagnostics, and risk modeling. The challenge lies in developing a strategic framework to identify zoonotic pathogens of pandemic potential that have not yet emerged in human populations.

To this end, USAID initiated the Emerging Pandemic Threats (EPT) program in 2009. The initial goal of the EPT program was to strengthen capacities in developing countries to prevent, detect, and control infectious diseases. Efforts were focused on early detection and response to potentially high-consequence animal viruses before they became significant public health threats in regional “hotspots” for emerging diseases, such as central Africa, South and Southeast Asia, and Latin America (USAID 2013).
PREDICT, a surveillance and virus discovery component of the EPT program, focused on building capacity to identify potential zoonotic disease threats at high-risk wildlife-human disease transmission interfaces where diseases are most likely to emerge. PREDICT was implemented in more than 20 countries, including Bangladesh, Bolivia, Brazil, Cambodia, Cameroon, China, Democratic Republic of Congo, Gabon, Indonesia, Laos, Malaysia, Mexico, Nepal, Peru, Republic of Congo, Rwanda, Tanzania, Thailand, Uganda, and Vietnam. The program aimed to improve early detection and response to disease threats through five main objectives: 1) strengthening disease surveillance systems; 2) improving viral discovery by developing laboratory and disease outbreak response capacity; 3) characterizing drivers of pathogen spillover and spread from animals to people; 4) optimizing predictive models for disease emergence and spread, and 5) deploying cutting-edge information management and communication tools to advance a more integrated, global approach to emerging zoonotic diseases.

Through EPT, PREDICT worked to enhance in-country capacity for response and prevention of pathogen spillovers by strengthening laboratory and diagnostic systems and increasing connectivity among government sectors (wildlife, livestock, and human health) to operationalize a One Health platform and promote early detection. In addition, PREDICT conducted surveillance and monitoring for viruses in wildlife at high-risk animal-human interfaces to detect potential zoonotic threats and prevent their emergence in human or livestock populations.