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19

The United States Agency for International Development Emerging Pandemic Threats PREDICT Project—Global Detection of Emerging Wildlife Viral Zoonoses

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This chapter is based heavily on the more detailed PREDICT-1 Final Report.³¹ The authors wish to acknowledge the contributions to the success described herein of the PREDICT Consortium (<http://www.vetmed.ucdavis.edu/ohi/predict/publications/Authorship.cfm>).

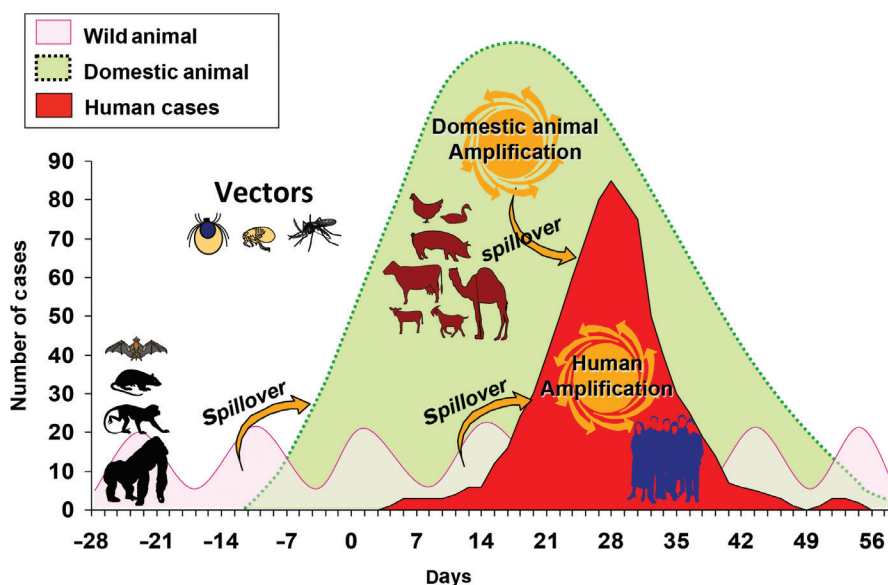
Introduction

The global burden of infectious disease disproportionately impacts developing nations, where human communities have less access to clinical care, clean water, and sanitation. Of particular concern and urgency for global health is the fact that the majority of emerging infectious diseases (EIDs)—diseases caused by previously undescribed pathogens, or by known pathogens that have recently expanded their host and/or geographic range—are of wildlife origin.^{1,2} As human population growth and environmental change bring people into contact with wildlife in unprecedented ways and increasing frequency, pathogens carried by wildlife are “spilling over” into domestic animal and human populations.³ Commonly, these events are occurring in places where a lack of diagnostic testing facilities and planning and infrastructure for outbreak control means that by the time a wildlife zoonotic EID event is recognized, opportunities for effective control measures have passed, resulting in devastating loss of life (Fig. 19.1).

Drivers for wildlife zoonotic disease emergence are biological, ecologic, and behavioral. Viruses, especially RNA viruses, are of greatest concern, because of their ability to rapidly evolve to gain virulence and adapt to new hosts.⁴ Ecologically, certain wildlife taxa are of more concern than others. For example, because bats are an ancient vertebrate

taxon that has co-evolved with a diversity of endemic viruses, are highly communal in their biology and behavior, and may migrate long distances, they have proven to be a frequent source of new zoonotic pathogens for people.⁵ Nonhuman primates, due to their genetic relatedness to people, have been the source for global pandemic infections like HIV/AIDS and persistent outbreaks of sylvatic yellow fever.^{6,7} Direct and indirect contact with rodents, which commonly commingle with people in dwellings worldwide, have also resulted in the emergence of hantavirus and the geographical spread of Chagas Disease (see Chapter 35).^{8,9}

Furthermore traditional practices such as hunting lead to human use of wildlife habitat, and human enterprises such as agricultural development and natural resource extraction convert wildlife habitat for human use. These behaviors and activities bring people into close contact with wildlife. As a result, pandemic EIDs such as Ebola virus disease have emerged, particularly in areas of high biodiversity (see Chapter 34).^{10,11} Nipah virus, for example, was first reported in Malaysia in 1999, causing pneumonia in domestic swine and encephalitis in swine farmers (see Chapter 40).¹² Once the previously unknown paramyxovirus was isolated from patients, the source of the virus was traced back to Pteropid fruit bats that were roosting in trees in swine facilities that had been constructed in newly deforested habitats. Similarly, severe acute respiratory syndrome (SARS) emerged in November 2002 in southern China, causing flu-like illness in people and causing mortality in 10% of cases.¹³ By July 2003, SARS had been detected in 37 countries. A novel coronavirus was isolated from patients and also detected in wild palm civets (*Paradoxurus hermaphroditus*) being sold



• **Figure 19.1** Wildlife Viral Pathogen Spillover Transmission of emerging zoonotic pathogens from wildlife populations (pink) into livestock (green) and/or people (red) may lead to devastating outbreaks. (Modified from Karesh WB, Dobson A, Lloyd-Smith JO, et al: The ecology of zoonoses: natural and unnatural histories. *Lancet* 380:1936–1943, 2012.)

live in markets for human consumption. This unfortunately triggered large-scale extermination of civets in a misguided attempt to curb the outbreak, as it was later determined that SARS-like coronaviruses (Co-V) were endemic in wild bats, with civets and humans as spillover hosts.¹⁴

United States Agency for International Development Emerging Pandemic Threats PREDICT Project (2009–2014)

The US Agency for International Development (USAID) has been working globally to improve both our collective understanding of the risk for transmission of pathogens from wildlife to humans, and to increase the capacity in developing countries for effective response and containment. Expanding upon its substantial investments in building worldwide capacity for avian influenza surveillance and control, USAID launched the Emerging Pandemic Threats (EPT) program in 2009 with the goal of strengthening capacities in developing countries to prevent, detect, and control all emergent wildlife zoonotic diseases (not just avian influenza). The EPT program was designed to be proactive and preemptive in its approach to wildlife zoonoses: to increase our understanding of the ecologic, viral, and behavioral drivers of wildlife virus spillover; train people in biodiversity hotspots around the world to detect and control zoonoses and disease emergence; and build capacity among government ministries for outbreak response and mitigation.¹⁵

Of several core projects that comprised the first 5-year phase of the EPT (2009–2014), PREDICT’s mandate was to build the evidence base for zoonotic disease emergence

from wildlife sources that would inform capacity-building for EID mitigation, control, and prevention. Led by the University of California, Davis, One Health Institute (in the School of Veterinary Medicine), PREDICT was initially implemented in 20 countries in Africa, South and Southeast Asia, and Latin America by a consortium of organizations including EcoHealth Alliance, Metabiota, the Smithsonian Institution, and the Wildlife Conservation Society (Fig. 19.2). PREDICT’s objectives were to: (1) conduct wildlife surveillance and virus discovery in EID “hotspots” characterized by high wildlife diversity and increasing human pressure on natural resources; (2) characterize high-risk human-animal interfaces, behaviors, and drivers of pathogen spillover from wildlife to people; (3) improve virus detection and discovery by developing laboratory and disease outbreak response capacities; (4) optimize predictive models for zoonotic disease emergence and spread; and (5) deploy cutting-edge information management and communication tools to advance a more integrated, global approach to sharing data from zoonotic virus surveillance. As well, the PREDICT Consortium was wholly committed to limiting potential harm to wildlife populations by implementing live-capture protocols only and by expressing a conservation ethic in all activities, especially communications with stakeholders. For example, when discussing bats as hosts of potential zoonoses, PREDICT teams always coupled these messages with an explanation of the importance of bats to ecosystems, agriculture, and biodiversity. Also, in order to discourage bat depopulation, messages emphasized that killing bats would likely result in increased risk for viral transmission due to dispersal of disturbed populations and increases in reproductive rates to compensate for mortality.

PREDICT Countries

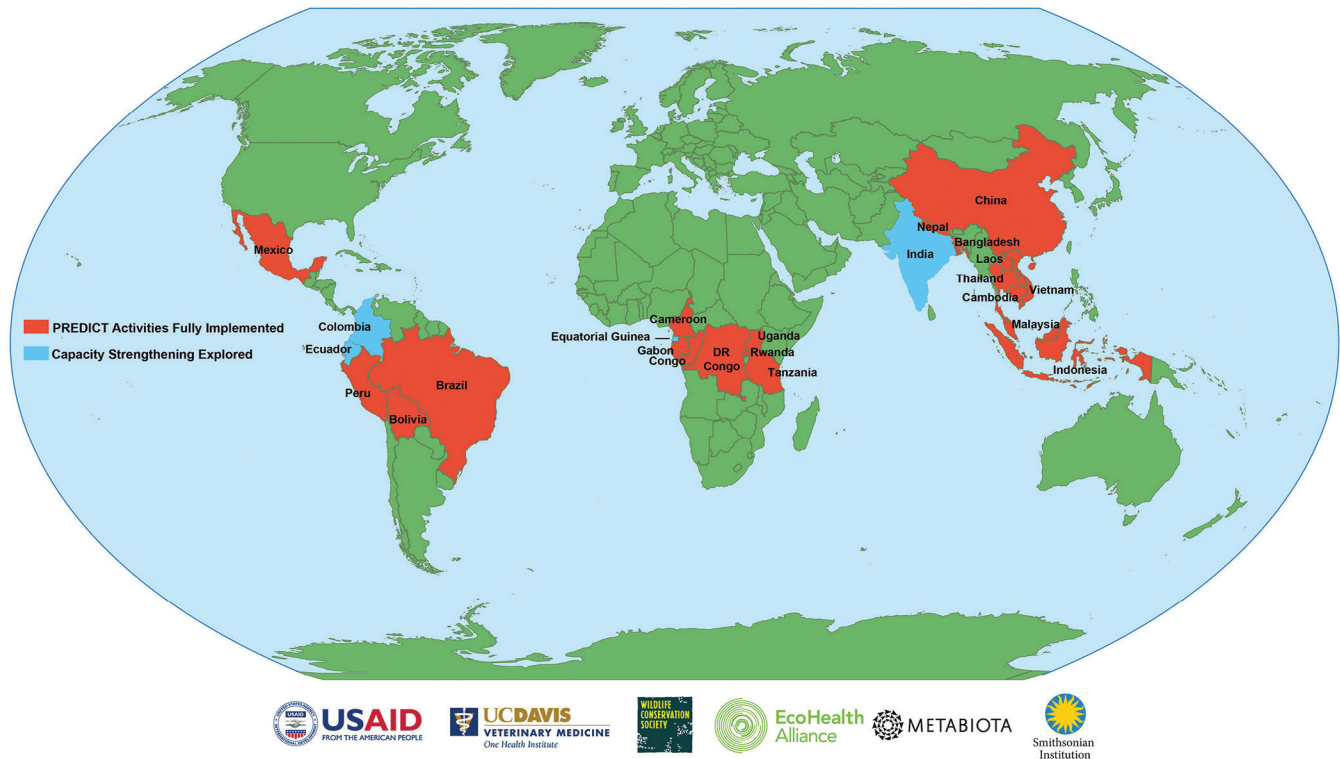


Figure 19.2 PREDICT Consortium and Countries from 2009 to 2014, a consortium comprised of the University of California, Davis, EcoHealth Alliance, Metabiota, Wildlife Conservation Society, and Smithsonian Institution implemented the USAID Emerging Pandemic Threats PREDICT project in 20 countries in Africa, South and Southeast Asia, and Latin America. (From PREDICT Consortium: *Reducing pandemic risk, promoting global health*. One Health Institute, University of California, Davis, December 2014. http://www.vetmed.ucdavis.edu/ohi/local_resources/pdfs/chapters/6_predict_virus_detection_discovery.pdf)

PREDICT Approach

Wildlife Surveillance at Human-Wildlife Interfaces

While most large-scale animal disease surveillance programs have targeted known or expected pathogens and have been conducted in areas of known disease occurrence, PREDICT's approach had to achieve the early detection of unknown yet potentially emergent viruses. Therefore, a risk-based approach to viral surveillance was utilized. PREDICT country-based teams worked with governmental and nongovernmental partners to identify sites where human activities were resulting in a high level of contact between wildlife and people. Sampling also took place at sites where there were extensive anthropogenic impacts on habitats and landscapes (e.g., not in pristine habitats) adjacent to human communities deemed vulnerable to zoonoses due to a lack of infrastructure for quality food storage, safe hygiene, or accessible health care. Field personnel then conducted sampling specifically at these high-risk human-wildlife interfaces and focused their sampling on the specific taxa—primates, rodents, and bats—for which there was a preponderance of scientific evidence for their

role in zoonotic disease emergence.¹⁶ Wild animals were live-caught with traps, nets, or remote immobilization techniques, according to established protocols approved by the Institutional Animal Care and Use Committee (IACUC) for safe and humane capture, and were released post sampling. Standard morphometric measurements and photographs were obtained to aid species identification. Whole blood, mucosal (oral, nasal, rectal, genital) swabs, feces, and urine (when feasible) were collected from each animal, placed in a variety of media (lysis buffer, viral transport media), and then transferred within hours to -80°C freezers or liquid nitrogen dewars for safe storage until testing. PREDICT also developed and utilized techniques for noninvasive sampling of wildlife for application in circumstances that made safe capture of wildlife difficult or impossible.¹⁷ At these sites, qualitative data were collected on the nature and extent of these human-wildlife interactions, and on the presence of domestic animals, water sources, etc.

Virus Detection and Discovery

PREDICT applied consensus polymerase chain reaction (cPCR) and high-throughput sequencing (HTS) tools to detect and describe DNA and RNA viruses present in

wildlife samples. This approach allowed for the detection of viruses presumably present at low levels in the populations surveyed, while also enabling a broad search for known and new viruses in the range of zoonotic viral families, including alphaviruses, arenaviruses, astroviruses, bunyaviruses (including hantaviruses), coronaviruses, filoviruses, flaviviruses, herpesviruses, orthomyxoviruses, paramyxoviruses, poxviruses, reoviruses, retroviruses, and rhabdoviruses. The use of cPCR was appropriate technology for use by PREDICT laboratories around the world, as it was relatively inexpensive and easy to implement in resource-limited countries. Samples identified by PCR were further cloned and sequenced, enabling discernment between previously described and new viruses.

Information Management and Reporting

In order to handle the enormous quantity of wildlife surveillance, site characterization, and laboratory testing data generated by all 20 countries, PREDICT developed an in-house on-line platform for secure, internal, standardized and centralized data collection, collation, and management. Policies on data ownership, governance, and release were developed in collaboration with host governments and tailored to each country. Once laboratory test results were verified and interpreted by the global viral discovery team, test results reports were shared exclusively with host country governments, and any findings of potential concern were discussed with governments first. Once host governments had an adequate period of time to receive and consider the potential implications of PREDICT findings, data were made publically accessible through the public data-sharing and visualization platform, HealthMap.¹⁸

PREDICT Results

PREDICT is likely the most comprehensive wildlife viral detection and zoonotic disease capacity development program in the world to date. It achieved major advances in understanding wildlife viruses and the factors that contribute to their spillover into human populations on a global scale and in building capacity in less developed countries for the rapid detection and control of EIDs (Fig. 19.3). Through PREDICT, more than 2500 people, including government personnel, veterinarians, students, physicians, laboratory technicians, field biologists, and hunters, were trained in biosafety and PPE, surveillance methods, laboratory techniques, and disease outbreak investigation. PREDICT worked with more than 32 diagnostic laboratories around the world to institute low-cost methodologies for conducting PCR assays for rapid detection of viruses in wildlife samples. By humanely sampling more than 56,000 nonhuman primates, bats, rodents, and other wildlife at high-risk human-wildlife interfaces, PREDICT detected 984 unique viruses in wild animals and people, 815 of which were novel. This effort more than doubled the number of known mammalian viruses in the world.

Novel Viruses (Table 19.1)

Among hundreds of viral discoveries, many have implications as potential sources of pandemics of wildlife origin. For example, PREDICT effectively doubled the known number of viruses in the family Coronaviridae that includes SARS and Middle Eastern Respiratory Syndrome (MERS) (see Chapter 42). Novel retroviruses and paramyxoviruses were also detected, including the detection of novel henipaviruses (the same viral family that contains Nipah and Hendra viruses) and filovirus exposure in bats.^{19–24} As well, PREDICT researchers found strong evidence for western lowland gorillas (*Gorilla gorilla gorilla*) as the nonhuman primate reservoir for Human T-lymphotropic virus in western Africa, and discovered a new simian immunodeficiency virus strain in a naturally infected chimpanzee (*Pan troglodytes troglodytes*) with AIDS-like symptoms.^{25,26} Hepatitis B virus (HBV) was found to be circulating among gorillas and chimpanzees and among subspecies of chimpanzees, refuting the previously held assumption that HBV genotypes are host-specific, with implications for the potential for spillover in this group of viruses.²⁷ Furthermore, PREDICT documented anthroozoonoses—human to primate transmission of viruses—including a human metapneumovirus that caused fatal respiratory disease in wild mountain gorillas (*Gorilla beringei beringei*) and human herpes simplex-1 virus that caused classic stomatitis in confiscated eastern lowland gorillas (*Gorilla beringei graueri*).^{28,29}

New Models for Emergence

PREDICT built upon the original “hotspots” model to further assess patterns of wildlife disease emergence in time and space, confirming that the risk of EIDs is highest in areas of high mammalian biodiversity, and finding that mammal diversity, land use type, and land use change are the most important factors for predicting wildlife EIDs.^{3,30} As well, PREDICT searched all published data available through 2010 to identify animal hosts, human activities, and high-risk disease transmission interfaces implicated in zoonotic virus spillover. Network analyses were used to examine these data for transmission pathways, viral traits, host species characteristics, taxonomic ranges, and geographic distributions of zoonotic viruses, to provide fresh insight on the virus characteristics and conditions that pose a risk for future wildlife EIDs.¹⁶

Outbreak Response

In addition to conducting wildlife viral discovery, PREDICT provided support to governments and institutions during 23 zoonotic disease outbreaks in 10 countries between 2010 and 2014, most of which were impacting human populations. For example, PREDICT collected bat samples and integrated wildlife and human response teams to help respond to a Nipah virus outbreak in Bangladesh and participated in several Ebolavirus outbreak response

PREDICT

THE WORLD'S MOST COMPREHENSIVE ZOO NOTIC DISEASE SURVEILLANCE & CAPACITY DEVELOPMENT PROGRAM

TRAINED 2,500 government personnel, physicians, veterinarians, resource managers, laboratory technicians, hunters, and students on biosafety, surveillance, lab techniques, and disease outbreak investigation.



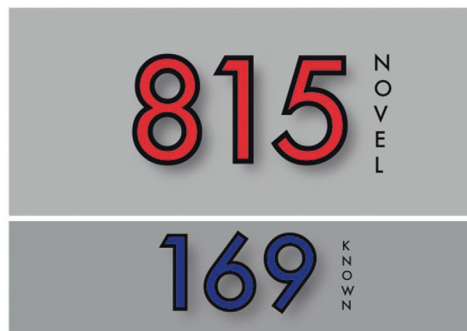
SAMPLED 56,000+ nonhuman primates, bats, rodents, and other wild animals (including bushmeat samples) at human-wildlife interfaces with high-risk and opportunity for viral spillover from wildlife hosts to humans.



DEVELOPED & OPTIMIZED low-cost viral family level consensus PCR methods and synthetic controls for the detection and discovery of new viruses from the target viral families in 32 labs in 20 developing countries around the world.



DETECTED a total of 984 unique viruses in wild animals and humans: 815 novel viruses and 169 known viruses – the most comprehensive viral detection and discovery effort to date.



• **Figure 19.3** PREDICT Results The first 5-year phase of the USAID Emerging Pandemic Threats PREDICT was the most comprehensive zoonotic disease surveillance and capacity-building effort ever undertaken; it trained 2500 people, built capacity in 32 laboratories, humanely sampled more than 56,000 wild animals, and detected 984 viruses, the majority of which were new discoveries. (From PREDICT Consortium: *Reducing pandemic risk, promoting global health*. One Health Institute, University of California, Davis, December 2014. http://www.vetmed.ucdavis.edu/ohi/local_resources/pdfs/chapters/6_predict_virus_detection_discovery.pdf)

efforts in Uganda by collecting samples from wildlife and domestic livestock and conducting surveys in Ebola-affected communities to better understand how people were coming into contact with wildlife. In 2012, PREDICT provided post-mortem and field investigation support to diagnose a yellow fever outbreak causing mortality in red howler monkeys in Peru, in time for the government to mount a vaccination program to prevent spread to local human

communities. During the devastating 2014–2015 West Africa Ebolavirus outbreak, PREDICT achieved the early detection of an Ebola virus causing an outbreak in the Equateur Province, Democratic Republic of Congo, which arose independently of the West Africa outbreak. Rapid and accurate detection of the virus facilitated early control procedures by the government, which effectively contained the outbreak before it could spread.

TABLE 19.1 PREDICT Viral Discovery

Viral Family	Novel Bat	Known Bat	Novel Primate	Known Primate	Novel Rodent/Shrew	Known Rodent/Shrew	Novel Human	Known Human
Adenovirus	53	3	6	4	32	1	1	3
Astrovirus	153	33	19	3	31	1	0	1
Coronavirus	61	30	3	0	6	0	0	2
Dependovirus	0	0	11	0	0	0	0	0
Flavivirus	3	0	0	1	0	0	0	2
Hantavirus	3	1	0	0	0	2	0	1
Herpesvirus	46	0	48	25	43	6	0	5
Orbivirus	1	0	1	0	0	0	0	0
Paramyxovirus	63	7	0	2	11	2	0	3
Polyomavirus	27	1	4	3	8	0	0	1
Arenavirus	0	0	0	0	2	2	0	0
Rhabdovirus	19	0	2	0	7	0	1	0
Bocavirus	1	0	0	0	0	0	0	0
Enterovirus	0	2	1	3	0	0	0	0
Retrovirus	0	0	5	4	2	0	0	5
Alphavirus	0	0	4	7	0	0	0	1
Poxvirus	0	0	0	1	0	0	0	0
Influenza	0	0	0	1	1	0	0	0
Mononegavirales	0	2	0	0	0	1	0	5
Papillomavirus	0	0	1	0	0	0	0	0
Picobirnavirus	0	0	120	0	0	0	0	0
Picornavirus	0	0	4	0	0	0	0	0
Picornavirales	0	0	4	0	0	0	0	0
Phlebovirus	1	0	0	0	0	0	0	0
Rotavirus	0	0	1	0	0	0	0	0
Anellovirus	0	0	0	0	0	0	1	1
Hepadnavirus	0	0	0	0	0	0	0	1

Note numbers of viruses do not total to 984 as viruses have been found in more than one wildlife host taxa.

From PREDICT Consortium: *Reducing pandemic risk, promoting global health*. One Health Institute, University of California, Davis, December 2014. http://www.vetmed.ucdavis.edu/ohi/local_resources/pdfs/chapters/6_predict_virus_detection_discovery.pdf.

Next Steps: PREDICT 2014–2019

The first phase of PREDICT realized significant advances in our knowledge of the global wildlife virome and the human activities and land use changes that put people at greater risk for spillover infections from wildlife viruses.³¹ PREDICT served as a real-world proof of concept of the relevance and appropriateness of addressing disease risk at the human-animal-environment or One Health interface and achieved it with a conservation ethos.³² Presentations

to government partners and interactions with communities about PREDICT created unique opportunities to allay fears about or animosity toward wildlife and to talk about the intrinsic value of wildlife populations, intact habitats, and biodiversity.

In its current phase (2014–2019), PREDICT has embarked upon an even larger scope with a more intense focus on the dynamics of zoonotic viruses in wildlife, people, and livestock (primarily influenza, filovirus, paramyxovirus, and coronavirus) and the human behaviors that drive their

spillover, amplification, and spread. Working with new governmental and nongovernmental organization partners in 30 countries, the team is documenting viral sharing among diverse hosts and targeting even more intense surveillance at high-risk pathways for viral transmission to identify the social and ecological drivers of pathogen emergence. In particular, PREDICT is addressing the risk of wildlife sold as food and medicine in markets in Asia and Africa, exploring both the magnitude of the conservation and disease risks, as well as the palatability of specific interventions to motivate behavior change. Ultimately, the goal is to provide essential information for helping less developed nations strengthen their capacities for epidemic prevention, thereby contributing to pandemic prevention and improving global health security.

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