

# PREVENTING THE NEXT PANDEMIC

An international network for monitoring the flow of viruses from animals to humans might help scientists head off global epidemics **By Nathan Wolfe**

## KEY CONCEPTS

- Most human infectious diseases originated in animals.
- Historically, epidemiologists have focused on domestic animals as the source of these scourges. But wild animals, too, have transmitted many diseases to us, including HIV.
- To address the threat posed by wild animals, researchers are studying the microbes of these creatures and the people who come into frequent contact with them.
- Such monitoring may enable scientists to spot emerging infectious diseases early enough to prevent them from becoming pandemics.

—The Editors

Sweat streamed down my back, thorny shrubs cut my arms, and we were losing them again. The wild chimpanzees my colleagues and I had been following for nearly five hours had stopped their grunting, hooting and screeching. Usually these calls helped us follow the animals through Uganda's Kibale Forest. For three large males to quiet abruptly surely meant trouble. Suddenly, as we approached a small clearing, we spotted them standing below a massive fig tree and looking up at a troop of red colobus monkeys eating and playing in the treetop.

The monkeys carried on with their morning meal, oblivious to the three apes below. After appearing for a moment to confer with one another, the chimps split up. While the leader crept toward the fig tree, his compatriots made their way up two neighboring trees in silence. Then, in an instant, the leader rushed up his tree screaming. Leaves showered down as the monkeys frantically tried to evade their attacker. But the chimp had calculated his bluster well: although he failed to capture a monkey himself, one of his partners grabbed a juvenile and made his way down to the forest floor with the young monkey in tow, ready to share his catch.

As the chimps feasted on the monkey's raw flesh and entrails, I thought about how this scene contained all the elements of a perfect storm for allowing microorganisms to jump from one species to the next, akin to space travelers leaping at warp speed from one galaxy to another. Any disease-causing agent present in that monkey now had the ideal conditions under which to enter a new type of host: the chimps were handling and consuming fresh organs; their hands were covered with blood, saliva and feces, all of which can carry pathogens; blood and other fluids splattered into their eyes and noses. Any sores or cuts on the hunters' bodies could provide a bug with direct entry into the bloodstream. Indeed, work conducted by my group and others has shown that hunting, by animals such as chimpanzees as well as by humans, does provide a bridge allowing viruses to jump from prey to predator. The pandemic form of HIV began in this way, by moving from monkeys into chimpanzees and, later, from chimpanzees into humans.

Today HIV is so pervasive that it is hard to imagine the world without it. But a global pandemic was not inevitable. If scientists had been looking for signs of new kinds of infections in



**DANGER:** Wild animals can carry pathogens capable of jumping into humans—the first step toward becoming a major infectious killer—so a new plan for avoiding pandemics begins with them.

Africans back in the 1960s and 1970s, they could have known about it long before it had afflicted millions of people. With a head start like that, epidemiologists might well have been able to intervene and mitigate the virus's spread. HIV is not alone in having emerged from an animal reservoir. More than half of human infectious diseases, past and present, originated in animals, including influenza, SARS, dengue and Ebola, to name a few. And today the vast interconnectedness of human populations, linked so extensively by road and air travel, allows new diseases to become pandemic more quickly, whether they come directly from wild animals, as did HIV, or indirectly, by passing from wild animals to domestic ones and then to us, as in the case of Japanese encephalitis virus and some strains of influenza. In response to these threats, my colleagues and I recently developed a bold new plan to monitor wild animals and the people who come into frequent contact with them for signs of new microorganisms or changes in the bugs' activity. We believe such eavesdropping may provide the early warning needed to stop pandemics before they start.

## Stalking Viruses

Our surveillance vision grew out of research we began 10 years ago, when we initiated a study of viruses in rural villagers in the Central African country of Cameroon who hunt and butcher wild animals, as well as keep them as pets. We were trying to determine whether new strains of HIV were entering into human populations, and we suspected that these people would be at particularly high risk of infection.

To understand why we thought these Central African populations are vulnerable, consider a typical bushmeat hunter going about his day. The hunter wears only simple cotton shorts as he walks barefoot along a forest path, carrying on his back a 50-pound baboon. He has transported the animal for some miles and still has more to go before he reaches his village. As the hunter travels, the blood from his prey mingles with his own sweat and drips down his leg, flowing into open cuts along the way. Any infectious agents in the baboon's blood now have access to the hunter's circulatory system and tissues.

If the hunter had his choice, he and his fellow villagers might very well prefer pork or beef to monkey. But those forms of animal protein are rare here. And so he does what humans throughout the world have done for millennia: he hunts the local fauna, just as my friends in New Jersey

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do on their farm during deer season, in preparation for their annual venison dinner party. The only differences, perhaps, are that the Central African hunter relies on this food for his own survival and that of his family and that his primate quarry is more likely to transfer its viruses and other microorganisms to the hunter than is a deer, which is related to humans much more distantly.

Persuading the villagers to cooperate with us on this project was not easy. Many feared that we were going to seize their game. Only after gaining their trust could we begin collecting data. Their cooperation was essential: in addition to drawing samples of their blood for study and peppering them with questions about their health and hunting activities, we needed blood samples from their prey. We relied on them to obtain these samples by using pieces of filter paper we gave them.

Our analyses of the blood from the hunters and the hunted revealed several animal viruses not previously seen in humans. One agent, which we first reported in a paper published in 2004 in *Lancet*, is known as simian foamy virus (SFV), and it is a member of the same family of viruses—the so-called retroviruses—to which HIV belongs. SFV is native to most primates, including guenon monkeys, mandrills and gorillas, and each of these primate species harbors its own genetically distinctive variant of the bug. We found that all three variants had entered the hunter populations. In one particularly telling example, a 45-year-old man who reported having hunted and butchered gorillas—animals rarely pursued by subsistence hunters—had contracted gorilla SFV.

COURTESY OF TOM CLYNES (Wolfe)

### [CONTEXT]

## Infectious Diseases from Wild Animals

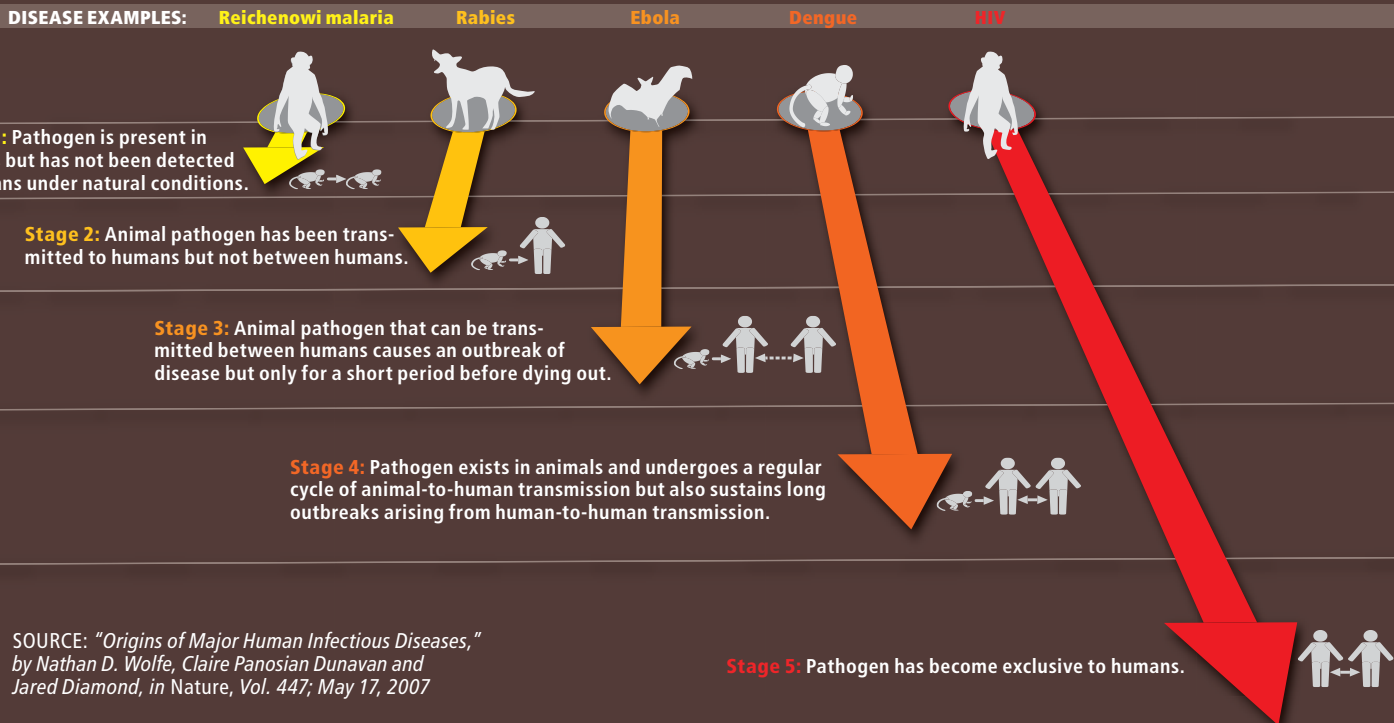
Many of the major infectious diseases of humans are believed to have come from wild animals. This fact underscores the need to monitor the microbes of wild creatures, in addition to those of livestock. The table at the right lists 10 such diseases and the animals from which they likely emerged.

DISEASE	SOURCE
AIDS	Chimpanzees
Hepatitis B	Apes
Influenza A	Wild birds
Plague	Rodents
Dengue fever	Old World primates
East African sleeping sickness	Wild and domestic ruminants
Vivax malaria	Asian macaques
West African sleeping sickness	Wild and domestic ruminants
Yellow fever	African primates
Chagas' disease	Many wild and domestic mammals

[STAGES TO WATCH]

# From Animal Microbe to Human Pathogen

The process by which a pathogen of animals evolves into one exclusive to humans occurs in five stages. Agents can become stuck in any of these stages. Those in early stages may be very deadly (Ebola, for example), but they claim few lives overall because they cannot spread freely among humans. The better able a virus is to propagate in humans, the more likely it is to become a pandemic.



SOURCE: "Origins of Major Human Infectious Diseases," by Nathan D. Wolfe, Claire Panosian Dunavan and Jared Diamond, in *Nature*, Vol. 447, May 17, 2007

In those same Central African populations we also found a variety of retroviruses known as human T lymphotropic viruses (HTLVs), so named because of their propensity for infecting immune cells called T lymphocytes. Two of the HTLVs, HTLV-1 and HTLV-2, were already well known to affect millions of people around the world and contribute to cancer and neurological disease in some infected individuals. But HTLV-3 and HTLV-4, which we described in 2005 in the *Proceedings of the National Academy of Sciences USA*, were new to science. Given the high degree of genetic similarity between HTLV-3 and its simian counterpart, STLV-3, it appears as if this virus was picked up through hunting STLV-3-infected monkeys. The origin of HTLV-4 remains unclear, but perhaps we will find its primate ancestor as we continue to explore these viruses in monkeys. We do not yet know whether SFV or the new HTLVs cause illness in people. Viruses do not necessarily make their hosts sick, and viruses that do sicken people and even spread from person to person do not always cause pandemics; often they retreat

## TWO-WAY STREET



**Pathogens do not jump only from animals into humans—they can also travel in the other direction. Some infectious diseases that people have transmitted, and continue to transmit, to animals include:**

- Tuberculosis (cattle)
- Yellow fever (South American monkeys)
- Measles (mountain gorillas)
- Poliomyelitis (chimpanzees)

spontaneously. But the fact that SFV and HTLV are in the same family as HIV, which did spawn a global epidemic, means that epidemiologists must keep a close eye on them.

My colleagues and I have outlined five stages in the transformation of a pathogen of animals into one that specializes on humans. In stage 1, the agent lives only in animals. In stage 2, it can be transmitted to a human only from an animal. A stage 3 germ is transmitted primarily from animals to humans, but it can also spread among humans for a short time before dying out. Once the agent reaches stage 4, it can sustain longer outbreaks among humans. By the time it attains stage 5, it has become an exclusive pathogen of humans and no longer utilizes an animal host. Pathogens in stage 4 or stage 5 have the potential to cause massive human die-offs.

## Forecasting the Next Pandemic

Had we been watching hunters 30 years ago, we might have been able to catch HIV early, before it reached the pandemic state. But that moment has passed. The question now is, How can we

WILFRIED KREICHHWOST/Getty Images (header in ital); MELISSA THOMAS (illustration)



COUNTRY: Cameroon  
 VIRUSES PREVIOUSLY SPAWNED: HIV  
 SENTINEL POPULATION UNDER STUDY FOR NEW PATHOGENS:  
 People who hunt and butcher wild animals

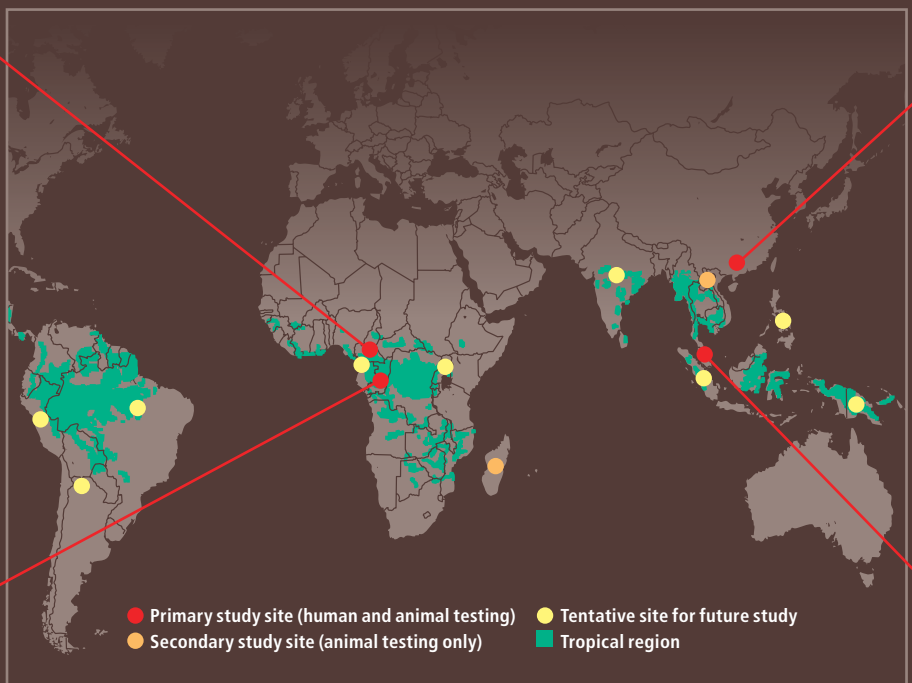


COUNTRY: Democratic Republic of the Congo  
 VIRUSES PREVIOUSLY SPAWNED: Marburg, monkeypox, Ebola  
 SENTINEL POPULATION:  
 People who hunt and butcher wild animals

[PREVENTION PROPOSAL]

# Building a Surveillance Network

By monitoring microorganisms in wild animals and the people who are frequently exposed to them, scientists may be able to spot an emerging infectious disease before it becomes widespread. To that end, the author recently organized the Global Viral Forecasting Initiative (GVFI), a network of 100 scientists and public health officials in six countries (red and orange dots) who are working to track potentially dangerous agents as they move from animals into human populations. The GVFI focuses on tropical regions (green) in particular, because they are home to a wide variety of animal species and because humans there commonly come into contact with them through hunting and other activities. Eventually the GVFI hopes to expand the network to include more countries with high levels of biodiversity, some of which are shown here (yellow dots).



## TAKING ACTION

If investigators find signs that an emerging pathogen has spread beyond humans who have direct contact with animals into the mainstream population, they will sound an alarm. Protecting the blood supply will be one important step toward preventing a pandemic. This measure will require rapid development and deployment of a diagnostic test for the germ.

prevent the next big killers? Once my colleagues and I had determined that we could study remote populations effectively, we knew we could extend our work more broadly to listen in on viral “chatter”—the pattern of transfer of animal viruses to humans. With global surveillance, we realized, we might be able to sound the alarm about an emerging infectious disease before it boils over.

Fortunately, through partnership with Google.org and the Skoll Foundation we were able to launch the Global Viral Forecasting Initiative (GVFI), a program in which epidemiologists, public health workers and conservation biologists the world over collaborate to identify infectious agents at their point of origin and to monitor those organisms as they bubble up from animals into humans and flow outward from there. Instead of focusing narrowly on just viruses or a particular disease du jour, the GVFI

works to document the full range of viruses, bacteria and parasites that are crossing over from animals into humans.

Though still a fledgling effort, the GVFI now has around 100 scientists following sentinel populations or animals in Cameroon, China, the Democratic Republic of the Congo, Laos, Madagascar and Malaysia—all hotspots for emerging infectious diseases. Many of the sentinels are hunters, but we are also screening other populations at high risk of contracting diseases from wildlife, such as individuals who work in Asia’s “wet markets,” where live animals are sold for food.

Finding a new microorganism in a hunter is only the first step in tracking an emerging pathogen, however. We must then determine whether it causes disease, whether it is transmissible from person to person, and whether it has penetrated urban centers, where the high density of occu-

KARL AMMANIN (hunter in Cameroon); SCHALF VAN ZUIDAM/AP Photo (workers in DRC market); MELISSA THOMAS (illustration)



COUNTRY: China  
VIRUSES PREVIOUSLY SPAWNED: SARS, H5N1  
SENTINEL POPULATION: "Wet market" workers



COUNTRY: Malaysia  
VIRUSES PREVIOUSLY SPAWNED: Nipah  
SENTINEL POPULATION: Wildlife hunters

KIN CHEUNG Reuters (wet market); KAZUYOSHI NOMACHI Corbis (hunter in Malaysia); THOMAS BARWICK Getty Images (dog)

pants could fuel its spread. The appearance in an urban center, away from the original source, would be a particularly worrisome sign of pandemic potential.

In the cases of HTLV-3 and HTLV-4, we are beginning to study high-risk populations in cities near hotspots for emerging infectious disease, regularly testing them for these viruses. Individuals with sickle cell disease who receive routine blood transfusions for their condition are one such population that could become infected early on. If we find people in these populations who are infected, we would work to initiate worldwide monitoring of blood supplies, to protect blood recipients. To that end, we are working with our long-term collaborator Bill Switzer and our colleagues at the U.S. Centers for Disease Control and Prevention to develop new diagnostic tests to check for the presence of viruses in the blood supply. Another urgent pri-

ority would be to determine the agent's mode of transmission, which would inform tactics for blocking its spread. If an agent were sexually transmitted, for example, public health officials could launch awareness campaigns urging condom use, among other precautions.

Governments can also take measures to keep new viruses from entering the blood banks in the first place. In fact, following our discoveries concerning the relation between exposure to primates and these new viruses, the Canadian government modified its blood donation policies to exclude donors who have had contact with nonhuman primates.

In addition to our forecasting efforts, the new science of pandemic prevention includes programs such as HealthMap and ProMED, which compile daily reports on outbreaks around the world, and cutting-edge cyberwarning systems such as those piloted by Google.org to use patterns in search engine data to successfully forecast influenza. Likewise, national and international surveillance and response systems of local governments and the World Health Organization will play an important role in stopping the next plague.

For our part, we would ultimately like to expand our surveillance network to more countries around the world, including such nations as Brazil and Indonesia, which have a tremendous diversity of animal species that could transmit pathogens to humans. Fuller development of the GVFI will be expensive: building out our network so that we have adequate staff and lab facilities for testing the sentinel populations every six months and testing the animals with which these people are in contact will cost around \$30 million, and keeping it running will cost another \$10 million a year. But if it succeeds in averting even a single pandemic within the next 50 years, it will more than pay for itself. Even just mitigating such an event would justify the cost.

Humans work to forecast a variety of very complex natural threats. We rarely question the logic behind trying to predict hurricanes, tsunamis, earthquakes and volcanoes. Yet we really have no reason to believe that predicting pandemics is inherently harder than predicting tsunamis. Given the enormous sums of money required to stop pandemics once they have already been established, it only makes sense to spend a portion of those public health dollars on stopping them in the first place. The ounce of prevention principle has never been more apt.

## THE THREAT FROM PETS



Wild animals and farm animals are not the only potential sources for the next major pandemic. Fido and Fluffy—and other pets, too—could harbor pathogens devastating to humans. This possibility arises when pets come into contact with germ-carrying wild animals. The germs can jump into pets, which can then transmit these agents to their owners.

## MORE TO EXPLORE

**Naturally Acquired Simian Retrovirus Infections in Central African Hunters.** Nathan D. Wolfe et al. in *Lancet*, Vol. 363, No. 9413, pages 932–937; March 20, 2004.

**Emergence of Unique Primate T-Lymphotropic Viruses among Central African Bushmeat Hunters.** Nathan D. Wolfe et al. in *Proceedings of the National Academy of Sciences USA*, Vol. 102, No. 22, pages 7994–7999; May 31, 2005.

**Bushmeat Hunting, Deforestation, and Prediction of Zoonotic Disease Emergence.** Nathan D. Wolfe et al. in *Emerging Infectious Diseases*, Vol. 11, pages 1822–1827; December 2005.

**Origins of Major Human Infectious Diseases.** Nathan D. Wolfe, Claire Panosian Dunavan and Jared Diamond in *Nature*, Vol. 447, pages 279–283; May 17, 2007.

The Global Viral Forecasting Initiative  
Web site: [www.gvfi.org](http://www.gvfi.org)