

Researchers Endorse Global Early Warning System to Prevent Pandemics

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Could the HIV pandemic have been prevented? Nathan Wolfe, professor of epidemiology at the UCLA School of Public Health, says yes, and he's working to prevent the next one.

Writing in the May 17 edition of the journal *Nature*, Wolfe and UCLA colleagues Jared Diamond and Dr. Claire Panosian Dunavan identify five evolutionary stages in a pathogen's journey from exclusive transmission among animals to exclusive transmission among humans. They also re-examine the origins and characteristics of 25 of the most important diseases in human history.

The extensive review provides evidence supporting the development of the first global monitoring system for tracking the transmission of disease from animals to humans. Such a system would help scientists catalog the diversity of microbial agents, characterize animal pathogens that might threaten humans in the future, and perhaps detect and control emergence of a disease in humans before it can spread.

"We can not just sit around and wait for the next HIV pandemic," Wolfe said. "We need to move away from the old-fashioned fire brigade approach to disease control and move toward disease forecasting."

Infectious diseases springing from wild primate populations regularly infect human populations of hunters and gatherers, a cycle that presumably has endured for millions of years. A handful of pathogens evolve into specialized diseases transmitted only through human to human contact — sometimes, as in the case of HIV, with devastating results.

In 1999, Wolfe began field work in the jungles of Cameroon to track "viral chatter," or the regular transmission of diseases from animals to people, usually without further spread among humans. By monitoring the habits and the blood pathologies of

bushmeat hunters and their kills, Wolfe and his team have identified at least three previously unknown retroviruses from the same family as HIV, as well as promoted safe practices for handling animals and animal carcasses.

"The Cameroon project demonstrated that it's possible to collect information on viral transmission under very difficult circumstances from these highly exposed people," Wolfe said.

With Cameroon as a prototype and a \$2.5 million National Institutes of Health Pioneer Award as seed money, Wolfe has gone on to create a network of virus-discovery projects that monitor hunters, butchers, and wildlife trade and zoo workers in some of the world's most remote viral hotspots. The network of a dozen sites in China, the Democratic Republic of Congo, Malaysia, Laos, Madagascar and Paraguay include source locations for such emerging diseases as SARS, avian flu, Nipah, Ebola and monkeypox.

In addition to the NIH award, funding included a Fogarty International Research Scientist Development Award, a W.W. Smith Foundation award and a grant from the National Geographic Society.

Wolfe and his colleagues begin by identifying five intermediate stages through which a pathogen exclusively infecting animals must travel before exclusively infecting humans. The research team identifies no inevitable progression of microbes from Stage 1 to Stage 5 and notes that many microbes remain stuck at a specific stage. The journey is arduous, and pathogens rarely climb through all five stages:

Stage 1. Agent only in animals: A microbe that is present in animals but not detected in humans under natural conditions. Examples include most malarial plasmodia.

Stage 2. Primary infection: Animal pathogens that are transmitted from animals to humans as a primary infection but not transmitted among humans. Examples include anthrax, rabies and West Nile virus.

Stage 3. Limited outbreak: Animal pathogens that undergo only a few cycles of secondary transmission among humans so that occasional human outbreaks triggered by a primary infection soon die out. Examples include the Ebola, Marburg and monkeypox viruses.

Stage 4. Long outbreak: A disease that exists in animals and has a natural cycle of infecting humans by primary transmission from the animal host but that also undergoes long sequences of secondary transmission between humans without involvement of animals. Examples include Chagas disease, yellow fever, dengue fever, influenza A, cholera, typhus and West African sleeping sickness.

Stage 5. Exclusive human agent: A pathogen exclusive to humans that involves either an ancestral pathogen present in a common ancestor of chimps and humans or involves a more recent pathogen that evolved into a specialized human pathogen. Examples include HIV, measles, mumps, rubella, smallpox and syphilis.

In addition, the team examines 25 diseases of important historic consequence to humans. Of the 25 diseases, 17 impose the heaviest world burden today: hepatitis B, influenza A, measles, pertussis, rotavirus A, syphilis, tetanus, tuberculosis, AIDS, Chagas disease, cholera, dengue hemorrhagic fever, East and West African sleeping sicknesses, falciparum and vivax malarias, and visceral leishmaniasis.

Eight more imposed heavy burdens in the past but have been reined in or eradicated thanks to modern medicine and public health practices: temperate diphtheria, mumps, plague, rubella, smallpox, typhoid, typhus and tropical yellow fever. Except for AIDS, dengue fever and cholera, most of the 25 have been important for more than two centuries.

The research team considered the varied

pathologies of diseases originating in temperate (15) versus tropical (10) regions, as well as differing pathogen and geographic origins. Among the conclusions:

- Most of the temperate diseases, but none of the tropical diseases, are so-called "crowd epidemic diseases," occurring locally as a brief epidemic and capable of persisting regionally only in large human populations. Most of the diseases originating in temperate climates convey long-lasting immunity.

- Eight of the 15 temperate diseases probably or possibly reached humans from domestic animals, three more from apes or rodents, and the other four came from still unknown sources. Thus the rise of agriculture, starting 11,000 years ago, plays multiple roles in the evolution of animal pathogens into human pathogens.

- Most tropical diseases have originated in wild, non-human primates. These animals are most closely related to humans and thus pose the weakest species barriers to pathogen transfer.

- Animal-derived human pathogens virtually all arose from pathogens of other warm-blooded vertebrates plus, in two cases, birds.

- Nearly all of the 25 major human pathogens originated in the Old World (Africa, Europe and Asia), facilitating the conquest of the New World. Chagas disease is the only one of the 25 that clearly originated in the New World, while the debate is unresolved for syphilis and tuberculosis.

- Far more temperate diseases arose in the Old World because far more animals that furnish ancestral pathogens were domesticated there. Far fewer tropical diseases arose in the New World because the genetic distance is greater between humans and primates in this part of the globe.

The conclusions of the review illustrate large gaps in the understanding of the origins of even established major infectious diseases. Almost all studies reviewed were based on specimens collected from domestic animals, plus a few wild animal species.

The researchers propose an "origins initiative" aimed at identifying the origins of a dozen of the most important human infectious diseases as well as a global early warning system to monitor pathogens emerging from animals to humans.

"The initiative would help identify the closest relatives of human pathogens, improve our understanding of how diseases emerge and help create new laboratory models for studying public health threats," Wolfe said. "In addition, it may yield clues that could aid in predictions of future disease threats."

A global monitoring system, meanwhile, would track the emergence of disease threats by tracking the transfer of pathogens from wild animals in remote locations to humans.

"We continue to be bombarded by novel animal pathogens. Monitoring of people, animals and animal die-offs would serve as an early warning system for disease emergence," Wolfe said. "In addition, the data would provide a unique archive of pathogens infecting humans and the animals to which we are exposed."

Source: UCLA

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