Could HIV have been halted before it began its destructive march? He believes it could have been, and is taking steps to ensure it won't happen again.

Nathan Wolfe: "Viral Forecasting" Aims to Prevent the Next Pandemic

Nathan Wolfe ventures into parts of the world where few scientists go, for reasons that are at once simple and profound: to find the next major pandemic, and prevent it from becoming one.

HIV has infected 25 million people since it was first identified by a UCLA physician in 1981. But the virus' entry into the human population is now traced by epidemiologists as far back as a half-century earlier, when a Central African hunter is thought to have been infected by blood from his chimpanzee prey. Wolfe believes that with today's tools and know-how, HIV could have been detected and prevented before it had a chance to begin its destructive march. But the professor of epidemiology, who joined the UCLA School of Public Health faculty in January 2007, laments that virtually all of the effort at controlling emerging infectious diseases is focused on containing outbreaks after they have begun to wreak havoc. He is at the forefront of a growing movement, which he calls "viral forecasting," that seeks to be much more proactive.

"If you said to your doctor that you were interested in taking steps to prevent a heart attack and he or she told you to just wait until you had heart disease, that would be the end of your relationship with that physician," Wolfe says. "That's where cardiology was in the 1950s – just waiting for the heart attack. And that's where we are today with global disease control. In 100 years, it will be obvious that we were missing the boat in waiting for pandemics to occur and then chasing after them after they were already established."

There are currently no global monitoring systems to forecast the entry of new diseases into the human population, Wolfe explains. He is doing his part by applying cutting-edge methods from molecular virology, ecology, evolutionary biology and anthropology to study the biology of viral emergence. Wolfe's venues of choice are places where human populations come into close contact with the blood of animals – from sub-

sistence hunters in the jungles of Cameroon and the Democratic Republic of Congo (where Wolfe collaborates with UCLA School of Public Health colleague Anne Rimoin) to wet-market workers and restaurant butchers in China, to name a few. "These are populations that act as sentinels for cross-species transmission," Wolfe explains.

Wolfe's research group has been instrumental in demonstrating that viral transmissions from animals to humans are more common than was previously believed – these zoonoses are responsible for as many as three-fourths of emerging human diseases. Publishing in *The Lancet* in 2004, Wolfe and his colleagues showed for the first time that retroviruses (viruses in the same family as HIV) could cross directly from jungle primates to indigenous hunters. Last spring, Wolfe teamed with Pulitzer Prize-winning geographer Jared Diamond, another UCLA School of Public Health colleague, on a paper published in the journal *Nature* that traced five evolutionary stages in a pathogen's journey from exclusive transmission among animals to exclusive transmission among humans. The review found that animals most closely related to humans, particularly non-human primates such as monkey and apes, are disproportionately responsible for introducing what became some of the most important diseases in human history.

In 1999, Wolfe began field work in Cameroon to track "viral chatter" – the regular transmission of viruses from animals to people, usually without further spread among humans. His team of more than a dozen researchers, in collaboration with scientists at the CDC, employed a variety of techniques in their sleuthing efforts – from the collection and analysis of specimens from the Cameroonian hunters and their kills to anthropological surveys and investigations of mysterious die-offs of jungle primates.

By monitoring the habits and the blood pathologies of bushmeat hunters and their prey, Wolfe and his team identified at least three previously unknown retroviruses while also promoting 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 says.

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 forecasting sites 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 exotic sites in China, the Democratic Republic of Congo, Malaysia, Laos, and Madagascar includes source locations for such emerging diseases as SARS, avian flu, Nipah, Ebola and monkeypox. Already, Wolfe notes, the network has proven its ability to detect the entry of new viruses into humans; now, these carriers are being tracked to see whether new diseases appear and the viruses are transmitted.

Wolfe has worked in countries that are considered among the most difficult places in the world for researchers, particularly in biomedical research. The logistic and political challenges are enormous, and in many cases obvious. "If a researcher from China, Cameroon or Malaysia came to your home asking for blood, you would probably slam the door," Wolfe says. His strategy in such situations is twofold: Engage and empower the local scientists and infrastructure, and establish a long-term presence. "There is tremendous interest in these issues and substantial expertise in all of these countries," Wolfe says. "As long as people see that you are looking out for their best interests and that you're going to stick around, you can work just about anywhere."

The Pioneer funding has been critical in helping Wolfe to get the sites up and running, but he is now focusing on finding the types of long-term partnerships that will sustain the network well beyond the Pioneer funding period. Establishing a permanent system will require a substantial commitment, but Wolfe is convinced that such an investment is vitally important given the potential reward – stopping the next HIV in its tracks.

After earning his B.A. in Human Biology from Stanford, Wolfe went on to receive his doctorate in Immunology and Infectious Diseases at Harvard, where he was the recipient of a Fulbright Fellowship. He was on the faculty at Johns Hopkins University's Bloomberg School of Public Health before being recruited to the UCLA School of Public Health. "UCLA has assembled a superb group of people doing field studies in infectious disease," says Wolfe, who says he was also drawn by the potential he sees in the UCLA High Speed, High Volume Laboratory Network for Infectious Diseases, an initiative the school is spearheading.

While UCLA is his new home base, Wolfe spends close to half of his time on the road, whether it's helping to run his network's sites or setting up new projects and establishing new collaborations.

"We know incredibly little about the diversity and nature of viruses on our planet," he says, "so if you're a biologist who likes to work in the field and discover new things, there's nothing better."

"In 100 years, it will be obvious that we were missing the boat in waiting for pandemics to occur and then chasing after them after they were already established."

—Dr. Nathan Wolfe