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Finding the Next Epidemic Before It Kills

Robert Langreth, 11.02.09, 12:00 AM ET

When the swine flu outbreak hit in April, public health officials raced to contain it. But it was too late. It couldn't be stopped and quickly spread around the world.

The fact that the swine flu, so far, doesn't seem more deadly than the regular flu shouldn't reassure anyone, says 39-year-old virologist Nathan Wolfe. "We got lucky," he says. "The reality is if this had been a much deadlier virus it would still be spreading." There could have been huge numbers of casualties.

Most virologists remain within the safe confines of the lab. Wolfe is one of a swashbuckling few who travel to the jungles of sub-Saharan Africa, exotic food markets in Southeast Asia and other far-flung locales to hunt down potential killer viruses before they find us. Wolfe, a visiting professor at Stanford University, is head of the Global Viral Forecasting Initiative, a research institute he founded in 2007. With headquarters in San Francisco, Wolfe's group has 35 workers in Cameroon and smaller microbe-hunting operations with various partners in five other countries. "We want to catch viruses at the point they are just entering the human population."

Researchers don't know the most basic fact about dangerous viruses: how many there are. There could be millions. "There are lots of new and unknown diseases out there. But if you don't have good surveillance, you are never going to find them," says UCLA epidemiologist Anne Rimoin, who collaborates with Wolfe. Her own work in the Democratic Republic of Congo has shown that human cases of monkeypox, a smallpox cousin, are much more common in rural areas than anyone had thought; no one had taken the time to look before. "Nathan is an innovator and is willing to take risks. He has definitely brought new visibility to the field."

Wolfe went to grad school at Harvard, intending to become a primatologist. But while studying sick chimpanzees in Uganda in the 1990s, he became fascinated with how animal viruses spread to humans, and switched his doctorate to immunology and infectious diseases. "It has become the central driving question for my career, What can we do to interrupt the process of novel pandemics?" he says.

Animal viruses transform into human scourges in stages, he and two colleagues theorized in a 2007 paper in the journal *Nature*. At first new pathogens are contracted directly from animals. Some develop the ability to spread within clusters of people before dying out. Over time a few mutate into versions that are infectious enough to spread widely. Some, such as HIV, become exclusive to humans.

Of 335 novel infectious diseases reported between 1940 and 2004, 60.3% come from animals, most often wild ones, a 2008 study found. The aids virus originated in chimpanzees. SARS (severe acute respiratory syndrome) likely came from horseshoe bats. Ebola also may have started in bats before moving on to apes and people.

Even malaria appears to have originally been a chimp disease, Wolfe and various collaborators reported this summer in *Proceedings of the National Academy of Sciences*. They analyzed blood samples from 94 chimpanzees in Cameroon and Ivory Coast and found eight previously unknown relatives of the malaria parasite that appear to predate the human form. The chimp strains span a broad genetic diversity that encompasses the human version, providing strong circumstantial evidence that the chimp disease came first. "This answers an outstanding mystery of humanity," says Wolfe. "It is striking that in the 21st century we still didn't know where one of deadliest diseases came from."

Most disease surveillance is focused in the developed world, but the big killers often come from sub-Saharan Africa or South Asia. In these areas Wolfe's team, monitoring the flow of viruses between wild animals and humans, hopes to pinpoint potential killer viruses before they establish a big foothold in people.

Wolfe has spent much of the last decade tracking subsistence hunters in the rain forests of Cameroon, first as a young researcher at Johns Hopkins University, then at UCLA and now with his global forecasting group. In remote villages that are sometimes a daylong trip on a four-wheel drive from paved roads, men hunt porcupines, giant cane rats, small antelope and monkeys, while women often do the butchering. Roughly every six months the hunters and their families sit still for blood samples. (Village chiefs are approached first to get hunters to cooperate.) To date the virologists have collected 7,000 samples, along with thousands of specimens from the hunters' prey.

In 2004, working closely with molecular epidemiologist William Switzer from the Centers for Disease Control & Prevention, Wolfe espied a wild animal virus in the act of infecting people. He found antibodies for the simian foamy virus--a close relative of HIV that infects monkeys and apes--in the blood of ten Cameroonian hunters. In 2005 Wolfe

and Switzer found two more new viruses in Cameroon hunters, both also from the retrovirus family that includes HIV. The viruses didn't cause obvious disease, but the findings showed just how easy it was for animal pathogens to pass into people; the researchers are now watching to see if the viruses do long-term harm. It was a surprise how often the hunters got animal viruses, says Matthew LeBreton, Wolfe's ecology director in Cameroon. "There are probably unknown viruses in every sample we collect."

An animal scratch, bite or a cut during butchering may have been how HIV spread into people from chimps many decades ago. Researchers have documented HIV in blood and biopsy samples taken from African patients in 1959 and 1960, well before the disease was noticed in the U.S. The aids death toll might have been far lower if researchers had had the tools to catch it back then.

The Cameroon findings helped Wolfe land a tenured position at UCLA. Wolfe, who spends four to six months traveling abroad, soon got restless. He quit UCLA last year--raising eyebrows among his tenured colleagues--to focus on his research institute and snagged $11 million in funding from Google's philanthropic arm, Google.org, and the Skoll Foundation to expand his virus-hunting work into new countries. Besides Cameroon, Wolfe's group has projects in China, Malaysia, Congo, Laos and Madagascar. "Nathan travels to the end of the road where wild animals and people meet and tries to get one step ahead in the process," says Google.org director Frank Rijsberman. "It is quite unique."

Wolfe envisions a worldwide network of dozens of monitoring sites in emerging disease hot spots to collect body fluid samples from people who interact with wild animals. Just as weather forecasters chart storms off Africa to predict which ones could become hurricanes, he hopes to create a database of animal viruses that have the potential to cross into the human population over the next few decades. This would give researchers time to develop diagnostic tests and surveillance plans. Scientists might even have time to produce drugs and vaccines to resist the worst threats.

It could take years before Wolfe's work pays off. Spotting a new virus is just the first step, says UCLA's Rimoin; you also have to monitor it carefully to see what kind of threat it poses. How common is it? How does it spread? What is its ability to evolve into something more dangerous? Figuring out which new viruses could mutate into the next pandemic won't be easy. Says Wolfe: "If we catch just one of the next ten pandemics, the investment will be worth it."