

New findings indicate HIV/AIDS pandemic began around 1900, earlier than previously thought

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New research indicates that the most pervasive global strain of HIV began spreading among humans between 1884 and 1924, suggesting that growing urbanization in colonial Africa set the stage for the HIV/AIDS pandemic.

The estimated period of origin, considerably earlier than the previous estimate of 1930, coincides with the establishment and rise of urban centers in west-central Africa where the pandemic HIV strain, HIV-1 group M, emerged. The growth of cities and associated high-risk behaviors may have been the key change that allowed the virus to flourish.

The research, led by Michael Worobey, an assistant professor of ecology and evolutionary biology at The University of Arizona in Tucson, was cosponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, and the David and Lucile Packard Foundation. The findings are published in the current issue of the journal *Nature*.

Worobey and his collaborators screened a number of tissue samples and uncovered the world's second-oldest genetic sequence of HIV-1 group M, which dates from 1960. They then used it, along with dozens of other previously known HIV-1 genetic sequences, to construct a range of plausible family trees for this viral strain. The lengths of the tree



branches represent the periods of time when the virus genetically diverged from its ancestors.

The timing and number of these genetic mutations enabled the scientists to calibrate the probable range of rates at which the trees have grown. That is, the probable rates of evolution of HIV-1 group M. Based on this range of rates, the scientists projected back in time to the period when the trees most likely took root: around the turn of the 20th century. This marks the probable time of origin of HIV-1 group M, according to Worobey and the others.

Using newly developed techniques, the scientists recovered the 48-yearold HIV gene fragments from a wax-embedded lymph-node tissue biopsy from a woman in Kinshasa in the Democratic Republic of the Congo. The oldest known HIV-1 group M genetic sequence comes from a 1959 blood sample from a man, also from Kinshasa. A comparison of the same genetic region in the 1959 virus and the 1960 virus provided additional evidence that the common ancestor of both viruses existed around 1900. The comparison revealed that the amount of genetic divergence between these two HIV sequences took more than 40 years to evolve.

Worobey, who teaches the evolution of infectious diseases and molecular phylogenetics at the UA, has spent several years studying how to recover the fragmented pieces of viral DNA and RNA from archival specimens, to track when the virus first jumped from chimpanzees to humans.

"Previous work on HIV sequencing had been done on frozen samples and there are only so many of those samples available," Woroby said. The 1959 and 1960 samples are presently the oldest links to the HIV epidemic.



"From that point on, the next oldest sequences that anyone has recovered are from the late 1970s and 1980s, the era when we knew about AIDS. Now for the first time we have been able to compare two relatively ancient HIV strains. That helped us to calibrate how quickly the virus evolved and make some really robust inferences about when it crossed into humans, how quickly the epidemic grew from that time and what factors allowed the virus to enter and become a successful human pathogen."

Research shows that HIV spread from chimps to humans in southeastern Cameroon. Worobey said the resulting HIV epidemic among humans correlates to the growth of urban centers near this area, principally the present-day city of Kinshasa in the Democratic Republic of the Congo, which began as a colonial center for Belgium. Other countries ringing this area include the Central African Republic, Congo, Gabon and Equatorial Guinea.

By 1960 a large number of people in this region were infected with HIV, reflected by the considerable amount of genetic diversity of the virus. From there events seeded the epidemic in different parts of the world. By 1981, people started realizing that something was happening and the rest is history.

Worobey said laying the technical groundwork for analyzing samples of HIV's ancient history was extraordinarily painstaking.

"The DNA and RNA in these samples is in a really sorry state. It's highly fragmented, so instead of a nice, pearl-strand of DNA or RNA, you have a jumbled mass that's all jammed together. It's been gratifying, but a ridiculous amount of work."

Worobey said his research in the near term will be on recovering more samples and assembling the fragmented DNA and RNA sequences to



form a clearer picture of HIV's history. He said the Nature paper "does a lot to snap everything into sharp focus and allows us to understand the timing of these events and the growth of the epidemic."

"There's still a lot of interesting work we can do with these techniques. We have lots more samples to analyze and hopefully recover nucleic acids from and it's pretty exciting to be in that position," Worobey said.

"I think the picture that has emerged here, where changes the human population experienced may have opened the door to the spread of HIV, is a good reminder that we can make changes now that could help reverse the epidemic. If HIV has one weak spot, it is that it is a relatively poorly transmitted virus. From better testing and prevention, to wider use of antiretroviral drug therapy, there are a number of ways to reduce transmission and force this virus back into extinction. Our results suggest that there are reasons for such optimism."

Source: University of Arizona

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