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Tracing the Origins of HIV in Humans

### TRACING THE ORIGINS OF HIV IN HUMANS

Previous estimates trace the earlier signs of HIV in humans to Africa in the 1930s. Historical data indicates the disease made its way to Haiti, its first stop in the western hemisphere and then eventually onto the United States, but we are learning that the disease may have circulated in Africa for decades before heading west. Does this new information about the origin of HIV offer any clues about the eventual demise of the virus. You are listening to ReachMD, The Channel for Medical Professionals. Welcome to a special segment - Focus on Global Medicine. I am your host, Dr. Mark Nolan Hill, professor of surgery and practicing general surgeon and our guest is Dr. Michael Worobey, assistant professor of ecology and evolutionary biology at the University of Arizona. Dr. Worobey is the lead author of research published in the journal nature updating our estimates of when HIV emerged in humans.

#### DR. MARK NOLAN HILL:

Welcome, Dr. Worobey.

#### DR. MICHAEL WOROBHEY:

Thank you a lot Mark, good to be here.

#### DR. MARK NOLAN HILL:

Well, Dr. Worobey, tell us over the years we have seen different series and research estimating the timing of HIVs emergence. Why is that this research offers such strong evidence?

#### DR. MICHAEL WOROBHEY:

What we have done here is instead of relying on modern gene sequences which is until now been the main approach for dating these events deep in the evolutionary history, we actually kind of did the next closest thing to building a time machine and going back at time. We recovered gene sequences out of very old sample, one from 1960s, so these are HIV sequences and not allowed us to kind of step that far back in time and from that vantage point looked even further back when we think the epidemic originated.

**DR. MARK NOLAN HILL:**

And when did you think that originated?

**DR. MICHAEL WOROBEY:**

The first thing that we found when we looked at the sequence from 1960 was there was one other sequence available from a blood sample from 1959 and now that we had 2 from this early time period, we are able to put them side by side and the first thing that leads out at US those 2 sequences were very divergent, so even back in 1960, the virus had already evolved a great deal of genetic diversity. When you then plug those old sequences plus a bunch of modern sequences into one of these evolutionary tree analyses that we do, they help to elaborate how quickly what we call the molecular clock ticks along and that suggested the pandemic originated, we think somewhere around 1908 plus or minus 20 years.

**DR. MARK NOLAN HILL:**

And tell us many of the listeners may wonder well that is all and well and that is certainly interesting, but why does that information make a difference in terms of us dealing with the disease today?

**DR. MICHAEL WOROBEY:**

That is an excellent question and part of it is just pretty basic research, but with basic research, there are always angles that are important to the very sort of where the rubber meets the road and I think one of the things that this allows us to do is to realize just how slow we were to realize that we had a new epidemic on our hands, so our dating suggests it was about 70 years that this virus was circulating in humans before doctors in the United States started realizing there were clusters of people with new syndrome that did not much make sense and aside from HIV that tells us there are potentially all sorts of other pathogens that might be circulating under the radar and may be spending some more energy trying to discover those now would prevent the next HIV pandemic. Now looking with specifically at HIV, how do you translate this kind of basic understanding into knowledge that matters for people today, I think part of it is it tells you how weak this virus is in one important sense. We think of HIV as this kind of invincible, nearly invincible, but what our results suggest is that there was time when HIV could not get foothold in humans. There were conditions prior to 1908 that probably prevented HIV from spreading and then we made changes as human beings, so part of what the study does is remind us that there are also changes we can make now, not requiring any fancy vaccine development or any bells and whistles like that, but often simple changes that we can do that could potentially drive the epidemic near extinction.

**DR. MARK NOLAN HILL:**

What kind of shape were the samples in and how did you resurrect these samples?

**DR. MICHAEL WOROBEY:**

They were in pretty sorry shapes, so I mentioned that there was this one available sequence from 1959 from a blood sample, so that was from a frozen sample relatively well preserved and one of the reasons that there was a long time between that being published and our study was I think most people thought while we looked at all the frozen samples from Central Africa that have been preserved were not going to find any other old viruses. So, what we did was actually looked at non-frozen samples, paraffin-embedded biopsy and

autopsy samples of the sort that pathologist generate all over the world every day and archives and it turns out that you can get HIV gene sequences out of these things, it is just really hard, it is really damaged and fragmented, but it is there.

**DR. MARK NOLAN HILL:**

Dr. Worobey, do we still think that the origin of the virus comes from chimpanzees?

**DR. MICHAEL WOROBNEY:**

Yeah. So, HIV we think is actually multiple viruses that have crossed into humans on numerous occasions, the pandemic strain which we call HIV-1 group M and unfortunately the nomenclature is a little bit illogical with HIV, but the pandemic stream we think comes from chimpanzees, and not just chimpanzees, but a specific population, specific subspecies and we think that it crossed into humans somewhere in South East Cameroon. There are other variants of HIV that are much more minor and local, some of them come from monkeys called city mangabeys in West Africa and there is even a guerilla form of the virus we found out recently, but it looks like the chimp virus is the big one in terms of what has caused human cases worldwide.

**DR. MARK NOLAN HILL:**

How did the virus get to the United States?

**DR. MICHAEL WOROBNEY:**

Once the virus had jumped from chimps to humans and started a kind of flow burn in Central Africa, what it looks like is one of the first if not the first successful migration of the virus outside of that epicenter region, what the same virus that was discovered in the US in the early 80s and a year ago using a similar approach where we looked at archival samples of HIV, we found that there is a very strong kind of fingerprint of a migration event from Central Africa to Haiti, proceeding the US epidemic and then once the virus was in Haiti a few years later it looks like a single variant became established in the US and then it was from there that the most cosmopolitan pandemic strain kind of spread worldwide and it is kind of amazing that you can retrace these steps with gene sequences but the signal is very strong.

**DR. MARK NOLAN HILL:**

What makes the HIV virus so particularly virulent?

**DR. MICHAEL WOROBNEY:**

It is virulent in some ways and it's actually compared to other viruses, not virulent in some ways, so the main thing it does unfortunately is attacks the very cells in our immune system that we rely onto kind of have an organized and sensible immune response. So, it attacks these T-cells that in a functioning immune system will basically organize antibody responses or killer T-cell responses and if you eliminate enough of those, even though you might have other components of your immune system still functioning, it is essentially eliminated your immune response and that is why virtually 100% of people with HIV will eventually succumb to AIDS without treatment.

**DR. MARK NOLAN HILL:**

And what about the non-virulent aspects of HIV?

**DR. MICHAEL WOROBEY:**

So, often when evolutionary biologists talk about virulence, we think a bit as linked to transmission and often there is a tight link where if a pathogen breeds at a very high rate within a host, there is lot of virus particles around and that makes transmission from one host to the next easier and that high level of breeding is often linked to harm to the individual host. In terms of transmission, it looks like HIV is actually rather poorly transmitted from one host to the next, at least compared to other things like hepatitis B virus. For instances, if you come in contact with that virus, you virtually guarantee to get infected where as with HIV, it actually has difficulty moving from one host to the next which is why we think it was changes in human behavior, things like living in cities that will require to help the virus successfully move from one person to the next.

**DR. MARK NOLAN HILL:**

Why did you think that the virus started in the animals and did the animals get ill?

**DR. MICHAEL WOROBEY:**

So, that's a good question and just to zoom out and look at the rest of the picture and not just with HIV, there are all sorts of what we call zoonotic transmissions of particularly RNA viruses, so zoonotic we just basically mean jumps from animals to humans, so you could put HIV on the list with SARS, influenza from birds and all sorts of other really pathogenic viruses jump from animals to humans in all corners of the world, it just happened that the primates in Africa happened to be infected with the relative of HIV, so that particular story is linked geographically to that region.

**DR. MARK NOLAN HILL:**

No, did those animals get as ill as humans do with this disease?

**DR. MICHAEL WOROBEY:**

Right. So, it does not look like any of the naturally infected primates in Africa suffer AIDS like symptoms, which it is a very interesting question, it is probably something related to the long time that these animals have been associated with these viruses and that you have in those cases of all to a lower level of virulence either because the host have undergone evolutionary changes that help them manage the infection without becoming really ill or the viruses themselves have evolved in chimpanzees and these are the species to be less virulent over time which is something you do see in other cases. At any rate, humans as host that have not been exposed to this virus before, unfortunately get these AIDS like symptoms and interestingly, other non-African primates like Asian MAC OS X will also suffer an AIDS like syndrome which gives us a kind of model organism that we can study AIDS in.

**DR. MARK NOLAN HILL:**

Does knowledge of how the virus has spread and changed make a factor in terms of our ability to how to eradicate this?

**DR. MICHAEL WOROBEY:**

I think it does, so not only does it tell you that the epidemic has turned on this kind of chance events of changes in human ecology and migration events, the evolutionary trees tell a really strong story about how much heterogeneity there must be in terms of this chains of transmission that over and over again you looked and see that for instance virtually all of the US epidemic traces back to a single patient, so unlike influenza which every year you get lots of people traveling around the world and starting up little mini epidemics, HIV seems to trace back in a lot of cases to single events which means that if we can target the super-spreaders in the population, those individuals who do most of the spreading of the virus, whoever they are and wherever they are that you could potentially eliminate most of the transmission of the virus.

**DR. MARK NOLAN HILL:**

I want to thank our guest, Dr. Michael Worobey. We have been discussing the revised look at the earlier stages of the HIV/AIDS pandemic.

I am Dr. Mark Nolan Hill and you have been listening to a special segment - Focus on Global Medicine on ReachMD, the Channel for Medical Professionals. Be sure to visit our website at [www.reachmd.com](http://www.reachmd.com) featuring on-demand pod cast for entire library and thank you for listening.