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When H.I.V. Made Its Jump to People. (Science Desk) *Gina Kolata.*

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For several years now, Dr. Beatrice H. Hahn and Dr. George M. Shaw, AIDS researchers at the University of Alabama at Birmingham, have been well aware that the scientific evidence for the origins of AIDS had a few crucial gaps. And they intended to fill them.

But, as their new research has now shown, AIDS viruses do not always behave as expected.

The investigation began when the Alabama scientists and others argued that the AIDS virus causing the devastating human epidemic originated in chimpanzees. It jumped to humans decades ago, they said, probably when infected animals were killed and eaten.

The evidence was three captive chimpanzees, all infected with a virus closely resembling the one that causes AIDS and all of a subspecies, *Pan troglodytes troglodytes*, that lives in west-central Africa. So, scientists hypothesized, AIDS originated there.

Investigators also found a fourth captive chimpanzee that was infected with a genetically distinct AIDS-like virus. No one knew where this animal came from, but Dr. Hahn and others said it must be from somewhere other than west-central Africa -- its virus was just too different from the one in the other three animals.

"We had four chimp viruses, three that were closely related to each other and to the human strains," Dr. Hahn said. "And they were different from a fourth strain. So we said, obviously, the west-central African chimps were the likely source" of the human AIDS virus. But, she added, some scientists looked askance.

"Some said: Four chimps are not a lot. You don't know what happens in the wild," Dr. Hahn recalled. And so, she said, she and her colleagues set out to find a way to detect AIDS-like viruses in wild chimpanzees.

Dr. Hahn and Dr. Shaw were pretty certain what they would find -- widespread infection with a virus that resembles the AIDS virus but does not make chimpanzees ill. After all, they reasoned, there must be a reservoir of infected chimpanzees if the virus had passed to people. The captive chimpanzees that were infected had not become ill. And researchers have found that other animals have their own AIDS-like viruses and are widely infected with them but do not become ill.

That story began more than a decade ago, when Marlo Brown, a resident of Petaluma, Calif., who ran a shelter for cats, was astonished to see that several of them were showing symptoms that looked like AIDS. She took them to a veterinarian, who was baffled. So she took the cats to Dr. Niels Pedersen, an animal virologist at the University of California at Davis, telling him they had AIDS.

She turned out to be right. A year later, in August 1987, Dr. Pedersen and a research colleague, Dr. Janet Yamamoto, found the virus. It is a close cousin of the human AIDS virus, although it does not infect people. But where did it come from? Were wild cats infected too? And, if so, did that mean that endangered species like lions and pumas were going to get a version of AIDS, like the domestic cats, and be exterminated?

Dr. Stephen O'Brien, a cat expert who is chief of the Laboratory of Genomic Diversity at the National Cancer Institute in Frederick, Md., intrigued and alarmed, began looking for the virus in a repository of serum from thousands of wild cats, including cheetahs, lions, ocelots and pumas. To his great surprise, it was everywhere, with a vast majority of wild cats carrying the virus.

"Every cat was infected with a virus that had the potential to kill the immune system," Dr. O'Brien said. But, somehow, those animals were not even ill.

"We spent a lot of time looking for a disease, but no one could find it," Dr. O'Brien said. It seemed that wild cats had somehow learned to live with the virus and not get sick. But domestic cats, which were new victims for the virus, were defenseless and quickly succumbed.

Meanwhile, others were discovering the same pattern in primates, looking in the wild at monkeys that were not endangered, even kept as pets, and also examining captive animals. At least 20 species of African primates are infected with, but seemingly unaffected by, AIDS-like viruses. Asian monkeys, in contrast, were not infected. But when Asian monkeys in research laboratories were given the African monkey viruses -- either deliberately by researchers who were studying the viruses or accidentally because they were in cages with African monkeys -- the Asian monkeys contracted a disease that looked like AIDS.

"African primates all carry their own little viruses," said Dr. Jonathan S. Allan, a virologist at the Southwestern Foundation for Biomedical Research in San Antonio. "In some species, the viruses have been there for thousands of years. And the natural host never gets sick."

With this background, the challenge for Dr. Hahn and Dr. Shaw was to find a way to look for AIDS-like viruses in wild chimpanzees, which are a protected and endangered species. It is illegal to capture them or even to anesthetize them and take their blood.

The investigators discovered that they could find identifying traces of the virus in feces and urine. They tested their methods, first with human feces and urine and then with feces and urine from chimpanzees in captivity. (Dr. Hahn said her students rebelled after testing human feces, saying they would not spend months working with such material. But chimpanzee feces, she added, turned out not to have an objectionable odor.)

Finally, it was time to go into the wild, working with primatologists who study chimpanzees so closely that they know each animal in a colony. That allowed the researchers to trace every sample to a specific animal, to verify suspected infections by looking at more than one sample from an animal, and to observe whether infected animals were ill.

The primatologists collected urine and feces from 58 chimpanzees from colonies in the Tai Forest, a national park in Ivory Coast, in Kibale National Park in Uganda, and in Gombe National Park in Tanzania, and shipped the material to Dr. Hahn and her colleagues in the United States. None of the chimpanzee communities where primatologists spent years observing the animals included the subspecies, *Pan troglodytes troglodytes*, but the researchers expected that most chimpanzees, no matter where they lived, would be infected with AIDS-like viruses -- a situation that would resemble that of the cats and other African primates.

But, to the investigators' surprise, only one animal was infected, a healthy 23-year-old male from Gombe. And he had a virus that did not resemble the human AIDS virus. It was, instead, like the virus isolated previously from the captive chimpanzee of unknown origin. The scientists reported their results in the Jan. 18 issue of the journal *Science*.

Other AIDS experts were equally astonished.

"It's quite incredible," said Dr. Edward Holmes of Oxford University.

There are three possible explanations, he added. There may be widely infected chimpanzee populations, but they are so isolated that they did not spread their infection to other chimpanzees. Or chimpanzee populations that once harbored the virus have gone extinct, possibly because they were hunted and eaten and their habitat was destroyed by development. Or, most puzzling of all, perhaps there really is very little infection in chimpanzees.

But, scientists ask, if infected chimps are so scarce, how did the virus jump to humans? The scientists know, from looking at genetic variants of human AIDS, that the virus infected humans on at least several occasions before becoming a full-fledged epidemic.

Dr. Hahn said her group was starting to study chimpanzees that were completely wild, outside the groups where they live with primatologists, collecting urine and feces from forests where the animals live.

The group members will not be able to say which individual animals provided the samples or whether animals that may be infected are healthy or ill. But, she said, they will be able to ask whether infections are common or rare among other subspecies of chimpanzees, including *Pan troglodytes troglodytes*.

In the meantime, AIDS researchers are looking at the course of infections among wild animals and wondering what that course says about the future of human AIDS. Why, they ask, are wild cats, African monkeys, and, it seems, chimpanzees, so impervious to illness from the viruses?

Dr. Mark Feinberg, a professor of medicine, microbiology and immunology at Emory University, focused on sooty mangabeys, West African monkeys that are widely infected with a virus that is identical to H.I.V.-2, a human AIDS virus that has infected people in West Africa but has not caused a worldwide epidemic.

Researchers told him it was obvious why the monkeys remained healthy. Unlike people, whose immune systems are unable to fend off AIDS viruses, resulting in millions of viruses in each drop of blood, the monkeys' immune systems must be squelching the viruses. But that turned out to be wrong. The monkeys had huge numbers of viruses in their blood.

Then scientists said the viruses must not kill the monkeys' cells. But that too was wrong, Dr. Feinberg said. The viruses were constantly killing enormous numbers of cells. The monkeys simply replaced them.

The same is true for wild cats, said Dr. O'Brien, the cat expert. The animals have enormous numbers of viruses in their blood and tolerate the viruses' more or less constant killing of their white blood cells.

Dr. O'Brien said it was a predictable adaptation, with a clear implication for the human AIDS epidemic.

"When a virus gets into a population, like H.I.V. jumped into humans, it can kill off the species or not," Dr. O'Brien said. "If it does not, either the virus becomes weakened or the species changes."

Dr. Feinberg, like Dr. O'Brien, thinks it is inevitable that H.I.V. will alter humanity. So many are infected in some parts of Africa, he said, that future generations will have a disproportionate number of people with genetic predispositions to live with the virus. And that is how evolutionary changes occur.

"It's going to happen," Dr. Feinberg said. "The severity of the epidemic in some parts of the world is so profound that it will clearly impact human evolution."

"In the past," he added, "we've been left to infer what the impact of infection was on human evolution."

Now, he said, "We will have the opportunity to observe it."

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