Out On A Limb

Recent scientific findings have spawned a renewed commitment to conducting biomedical research on primates. But the questions remain: Do chimps hold the secret to stopping AIDS? Or are we barking up the wrong tree and torturing our close relatives unnecessarily to find out?

January 1, 2009 By Lucile Scott

Carole Noon has spent the last several years planning road trips for nearly 300 chimpanzees in a bus that she customized to ensure that each hairy passenger can have a window seat. She wants the travelers to be comfortable on the long journey from their home at the former Alamogordo biomedical laboratory in New Mexico—notorious for its inhumane treatment of animals—to their new digs at Noon's chimp sanctuary in Fort Pierce, Florida.

Noon has dubbed the travels the Great Chimp Migration.

Noon, a PhD, and now the head of the Save the Chimps sanctuary, has worked with chimpanzees since 1984—the same year scientists began researching various potential vaccines and cures for HIV in our closest relatives. Chimps share 98 percent of our DNA and are the only other species that can be infected with HIV and its primate predecessor, simian immunodeficiency virus (SIV).

Chimps not only can carry HIV, but are also believed to be its origin. Beatrice Hahn's research team spent years collecting feces and urine from wild chimps to trace what they believe is the origin of HIV-1 back to chimps found in southeastern Cameroon. SIV and HIV do not progress in primates, including chimps and monkeys like mangabeys, who naturally carry it in the wild. Only species such as humans or macaques that were introduced to the virus more recently—humans possibly through ingesting bush meat, and macaques because it is injected in them in labs—cannot suppress the virus. "Naturally infected primates have been infected for a very long period of time, and this co-evolution with the virus has prompted them to do something different and we need to understand that," Hahn says, adding, "But I am personally against any invasive studies in chimpanzees. They are not furry test tubes. They are 98 percent genetically identical to us, and it is unethical."

"The fact that they are our next of kin can go two directions; either that we must use them in research or that it forbids us," says Noon, dressed casually for fieldwork, with a flimsy baseball cap perched on her head. She sits proudly on one of the 12 large islands she has designed so Save the Chimps' residents can live a largely bar-free life after spending decades caged in a lab. She points affectionately at the chimps, who are swinging and lounging on the islands in the distance, calling

out to them by name and describing their various mental and physical ailments. When asked about her opinion of biomedical testing on chimps and other primates, she says, “I’m just a primatologist,” with a knowing glint in her eye that causes the statement to sound more than a little like, “I plead the Fifth.”

While biomedical research on chimps still occurs in the United States, HIV research in them has steadily dwindled since the early ’90s when it became clear that the disease does not progress in chimps, meaning little could be learned about the virus’s effects on humans by injecting it into primates. Also, chimps are extremely expensive to care for, and invasive research on them is politically and ethically controversial because they’ve been endangered since 1976 and are highly intelligent and sensitive creatures. In fact, many countries ban such research.

However, more than 1,200 chimps remain in U.S. labs. Many were bred for research in the ’80s when scientists first wondered if they held the key to curing AIDS. Now, even if their owners want to retire them to a better life after their years of serving science, they have nowhere to send the primates. “There are some chimps waiting for retirement who can’t live in most local sanctuaries or in a zoo because they are HIV positive [or SIV positive] and are considered a risk,” says Gloria Grow, who in 1997 became the first person to give retired HIV-positive lab chimps a home at her Montreal sanctuary called the Fauna Foundation.

Today, most biomedical HIV vaccine research uses macaque and other monkeys as its “animal models” since they can be infected with SIV or scientifically engineered hybrids of HIV and SIV known as SHIV. But SIV is not HIV, and monkeys are not humans, and many working with AIDS are asking why we continue to invest money and expend animals’ lives in this research especially as animal models, even those that nearly replicate our bodies, do not accurately reflect the progression of a given disease or the efficacy of its treatment. Especially when there have been no significant advances in vaccine or cure research after 25 years and billions of dollars spent on research in primates. After the high profile failure of human trials of Merck V520 last year—which worked in macaques infected with SHIV but actually increased the risk of infection in some people—a growing chorus of physicians and scientists began calling for a change in our approach to ending AIDS.

Several candidate vaccines tested on primates since the dawn of AIDS have failed, and some animal-rights-conscious scientists see that as a reason to scratch research on chimps completely. They advocate funding research of new technologies and other approaches instead. “We know very intricately what happens when we inject SIV or SHIV into non-human primates. The problem is that it has no relevance to what happens with people and HIV and AIDS,” says John J. Pippin, MD, of the Physicians Committee for Responsible Medicine, adding that many drugs that work in primates do not work in humans and vice versa. The current research model, he says, costs millions to test drugs that seem to work in monkeys but end up ineffective in humans. What’s more, research on drugs that are ineffective in monkeys is delayed or even shelved—and that could be a huge mistake. Theodora Capaldo, EdD, president of the New England Anti-Vivisection Society, points out a provocative parallel situation: “Penicillin was delayed for 20 years because it killed lab animals.”

Most researchers do not take such an all-or-nothing approach, however. They agree that the Merck trials and other failures demonstrate that knowledge of HIV and the human immune system is currently not advanced enough to develop an effective vaccine or cure. Instead of cranking out candidates for human trials, researchers must return to basics: understanding HIV.

What scientists do debate is the role primates should play as researchers head back to the drawing board. “Monkeys are very good [subjects for] asking questions [about immune responses and the virus], but they can never tell us if a vaccine works,” says David Weiner, PhD, of the University of Pennsylvania School of Medicine. Like Pippin and Capaldo, he doesn’t think monkeys should be used as the gatekeepers for human clinical trials, though he believes they are necessary for other studies to better understand HIV. Critics have suggested that scientific advancements during the past 25 years could allow us to do AIDS research without animal models. Not true, Weiner says. “We are as far away from that as we are from landing on Mars.”

Pippin, however, contends that if the National Institutes of Health (NIH) would direct more of its $490 million annual AIDS vaccine budget into developing new strategies, the state of new technology might change quickly. He offers this analogy: “If you went to the car and you put the key in the ignition and you realized that you have the key to someone else’s car, would you keep fiddling and trying to make it work or would you go back in the house and find the right key?”

Anthony Fauci, MD, director of the National Institute of Allergy and Infectious Disease at the NIH, believes increasing funding and resources for testing in primates is the best path to better understanding basic immune responses to the virus. He has begun expanding primate research facilities and setting up workshops to improve primate testing. “We came to the realization painfully that the body does not develop an adequate immune response to HIV after seeing more and more trials fail,” he says. “What about HIV is not capable of inducing that response? How can we then induce the body to make the response that is necessary for protection? These are questions we have never had to ask with other vaccines. We are perfecting animal models to make them more predictive.” He believes that all the past failures have revealed a better road forward and that while a 25 year wait is far from ideal, in the scientific scheme of things, it is not so long. It took more than 47 years to develop the polio vaccine and 42 years to develop one for measles.

Paul Bieniasz, PhD, of the Aaron Diamond AIDS Research Center, agrees with Dr. Fauci. He is working to develop a new strain of SHIV that he hopes will be much more reflective of human HIV. While most past SHIV viruses have been at best 30 percent HIV and 70 percent SIV, this new strain is 90 to 95 percent HIV, a development he believes shows that vaccine research is and always has been advancing. Like other new developments popping up, it will allow scientists to better study and understand the disease. “We’ve learned a lot using the SIV model, and we are developing new models that guide new vaccine research,” he says. “Calling previous research not worthwhile is not appropriate.”

Of course as with any changes within established technology or science—such as a shift from oil to

clean energy—some contend that the main players are too entrenched in the existing model of funding, grants and lobbies to make any kind of radical shift. “They want to return to monkeys because it is a business with multibillion [dollars] in profit,” says Capaldo. For example, Charles River Laboratories Inc. received a $42.8 million, 10-year contract from the NIH to house primates in 2001. Charles River is a multinational corporation and the world’s largest supplier of lab animals. With more than $1 billion in assets, Capaldo says, it proves a powerful lobbying force. Indeed, the government contract with Charles River persists despite three charges for alleged animal cruelty in 2004 that came after several of its resident chimpanzees died. Rick Lee, DVM, and director of the Alamogordo Primate Facility at Charles River, says only, “The facility is highly regulated to ensure the highest quality of care for the chimpanzees. Thank you for your concern for their well-being.” (The charges were later dropped because New Mexico’s cruelty statutes contain an exemption for the practice of veterinary medicine and the judge ruled that the lab chimpanzees fell into that category.)

Of course the questions remain: Is primate research necessary and will the science resulting from primate research prove useful for stopping HIV? Most researchers say they would scrap primate research immediately if something better came along, but that for the time being it is a necessary evil. World-renowned bioethicist and primatologist Jane Goodall, DBE, has suggested that alternatives to animal research be encouraged—and funded. She has recommended that a Nobel Prize be given for it.

Some fear Fauci’s call will cause a return to chimp research to further study the virus and why it does not progress in chimpanzees, despite the more costly ethical and monetary considerations. While chimps are no longer a popular HIV research animal model, many sacrificed much to the cause in the past, and many are still being used for other non-HIV related tests, including tests related to hepatitis.

Still others believe the unflagging dedication to developing a vaccine and cure is a relic from the ’80s, before we had any idea how to fight HIV and assumed it could be dealt with like other viruses. In March 2008, after a string of vaccine failures—including the Merck trial—Michael Weinstein, president of the AIDS Healthcare Foundation, one of the world’s largest AIDS organizations, called for a moratorium for federal funding of AIDS vaccine research. “We’ve been looking for an AIDS vaccine for more than 25 years; not only have we not made progress in finding one, we have actually done harm to patients,” he says. “I consider it a waste of money when half of the HIV-positive people in the United States are not in regular treatment and other programs are hurting. You need to distribute condoms, do mass testing and give access to ARVs [antiretrovirals].”

Weinstein claims that the U.S. government has spent six times more on researching a vaccine than on HIV testing despite the fact that we know that people who are aware of their status are much less likely to infect others and are much more likely to get the treatment that saves lives. “Everything that can be imagined isn’t possible,” he says of an AIDS vaccine or cure. “There is no perpetual motion machine. No cold fusion. We didn’t anticipate that we would have one pill once a day that could keep people alive, but we do.” Like Capaldo, he believes that the status quo

persists because “commercial interests and lobbies perpetuate it. And it’s politically correct to want an AIDS vaccine. Plus, it’s harder work to provide ARVs than to promote vaccine research. You can’t do that in an arm chair in Washington or New York.”

As the treatment of the animals goes, macaques and other monkeys that are infected with SIV and SHIV live in cages and undergo many tests and procedures as their disease progresses. Most are euthanized after they develop full-blown AIDS. The chimps at the Fauna Foundation and Save the Chimps display many emotional and physical scars from their years in labs.

“If they spent 40 years in a cage with all the government did to them and it wasn’t of any use…” says Noon, trailing off.

Noon’s chimps appear healthy and surprisingly human as they romp about in the sun, making probing eye contact, their opposable thumbs latched around a fence. A chimp named Arthur smiles and pets his belly and tries to engage any onlookers with a reserved, dry humor. His gangly build is reminiscent of David Letterman’s. Chaka is stockier and struts about, kicking the fence and spitting water, before settling down to chow on an apple with the self-satisfied macho cockiness of a high school quarterback in a new sports car. Pepsi points at passersby’s feet, hoping they will show her their toes.

But despite their spry behavior, Grow’s and Noon’s chimps have life expectancies much shorter than other chimps. Autopsies reveal that many of them die not from AIDS, but from years and years of untreated infections caused by darts shot to anesthetize them for procedures (this is required often because a full-grown chimp has the strength of several men). Many of the chimps underwent incredibly painful procedures under the effects only of Ketamine, known on the street as Special K, which immobilizes them but allows them to feel the pain. Many suffer from full-on flash backs, their eyes rolled back in their heads as they relive the episodes. Others chew off their fingers or rip out their hair in response. “It’s like working in an abuse center,” says Grow. “We have self-mutilators and chimps who suffer depression and all those things.”

Chimps can use tools, express love, get embarrassed, laugh, speak sign language and eat spaghetti with a fork. They suffer psychological damage from solitary confinement in cages not much larger than they are.

Grow says her chimps’ experience with HIV does mirror the human experience in one significant way: stigma. When her Canadian neighbors discovered she was bringing HIV-positive chimps to town, there was an outcry. She had to fight through thicker and thicker red tape to get the requisite permits, and she had to build a tall electric fence around her property.

“At first, we kept the HIV-positive chimps separate from the others and treated them like they were biohazards like everyone had told us to. Then I was like, This is stupid. The disease doesn’t progress in chimps. And they aren’t returning to the wild. And people would have to have sex with a chimp or share a needle [with one] to get HIV.” So Grow ditched the gloves and other extreme precautions she had taken with the positive chimps and allowed all her residents, positive and

negative, to live and frolic together. And when her positive chimps die—from heart failure or other side effects of lab life, not HIV—labs refuse to take them to perform a proper autopsy.

No matter if you are talking dollars, human lives or suffering primates, the cost of 28 years of fighting HIV has been high—and is far from over. When asked why she has dedicated the past decade of her life to building Save the Chimps, Noon quips, “Oh no reason. I’m just an eccentric old woman,” then pauses and continues: “Because Carlos sat in a cage for 40 years, and when he was heading out into the open for the first time and he had no idea what was out there, he had the courage to move toward it. I would have stayed in the cage and said, Call me in three weeks.”

No one knows when, how or if we will end AIDS, but everyone involved in the fight should agree that Carlos is a role model we can all follow.

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http://beta.docker.poz.com/article/chimps-hiv-biomedical-15887-1281