



Chimpanzees at the New Iberia Research Center in Louisiana are some of very few remaining worldwide that are still being used in invasive research.

CHIMPANZEE RESEARCH ON TRIAL

As pressure from activists builds, the United States is considering whether it should end invasive experiments in chimpanzees.

BY MEREDITH WADMAN

The unusual meeting was held in a conference room, but it might have been called a war room. Gathered inside a little-known research centre in southern Louisiana, the people who oversee chimpanzee research in the United States were preparing to battle for the survival of their enterprise.

Although no other country besides Gabon carries out invasive experiments with chimpanzees, the United States continues such work at three major research facilities. Louisiana's New Iberia Research Center (NIRC) is the largest, with a population of 360 chimps, used by investigators from pharmaceutical companies and federal agencies to test new drugs and study diseases such as hepatitis. During the meeting, Thomas Rowell, director of the NIRC, stood up, surveyed the audience, and launched into a presentation about possible strategies to build public support for their work.

"How do we get industry to be forthcoming about their use of chimpanzees?" a slide read.

"Could we get at least a few solid examples of how the use of chimpanzees has truncated the time to discovery?"

And "When we talk about time and lives saved by using chimpanzees,

can we provide actual time span data or numbers?"

Another slide went on to note that the National Institutes of Health (NIH) spends about US\$12 million a year caring for the chimpanzees it supports (currently totalling 734), versus the billions in health-care costs for the human diseases that can be studied through experiments on chimpanzees. One of them, hepatitis C, currently affects at least 170 million people globally. If researchers don't have access to the chimp model, said Rowell, people afflicted with hepatitis C will suffer. "Their lifespans are going to be shortened. They will not have a proper quality of life." He called them a "silent voice".

Rowell's pep talk in April was partly for the benefit of some visitors at the meeting: representatives from the Food and Drug Administration, the National Institute of Allergy and Infectious Diseases, the drug industry and, most importantly, the Institute of Medicine (IOM). The IOM, the medical branch of the independent National Academy of Sciences, was asked by the NIH in January to examine whether the government should keep supporting biomedical research on chimpanzees — the closest living relatives of *Homo sapiens*.

The NIH called for the study after the agency sparked a storm of

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opposition last year, when it announced plans to move 186 semi-retired chimps back into active research¹. After protests by the Humane Society of the United States (HSUS) in Washington DC, famed primatologist Jane Goodall and others, the NIH changed course and said that it would make no decision on moving the chimps until the IOM study is complete. The study, it announced, would be “an in-depth analysis to reassess the scientific need for the continued use of chimpanzees to accelerate biomedical discoveries”.

Proponents say that the research is necessary for continued progress towards a hepatitis-C vaccine; for developing more effective drugs against hepatitis B and C; for testing monoclonal antibody treatments for a variety of conditions; and for research to develop a vaccine against respiratory syncytial virus, a seasonal virus that kills more than more than 66,000 children under the age of 5 each year across the globe². For many of these conditions, backers argue, the chimpanzee is either the only available model, or by far the best one.

But chimpanzee research in the United States is facing growing public and political opposition. Animal-welfare activists have stepped up their efforts to end the work, arguing that it is inhumane, ineffective and a waste of taxpayer money. The day after the meeting, activists held a press conference on Capitol Hill to mark the introduction of the Great Ape Protection and Cost Savings Act. The act would make all invasive chimpanzee research illegal, including private-sector work conducted at the centres and paid for by drug companies. The bill's lead sponsor in the House of Representatives is Roscoe Bartlett (Republican, Maryland), who trained as a physiologist and conducted primate research with NASA and with the military in the 1960s.

“There's just no valid argument to continue to keep these great apes as they're now being kept,” Bartlett told the news conference. “Very few of them are used in research and I'm not sure that any of them need to be used.”

The scrutiny this year adds to the tension felt by researchers who work with chimpanzees. That stress is particularly intense at the NIRC, which has been on the defensive ever since a television documentary two years ago showed footage of employees there mistreating and neglecting chimpanzees and macaques. The NIRC, which is part of the University of Louisiana at Lafayette, later paid a fine and has since passed numerous inspections, but the exposé helped to propel the activism. In the contest for public support, says Rowell, “our backs are up against the wall”.

A STUDY UP CLOSE

On the same day that the chimp-protection measure was introduced in Congress, staff at the NIRC prepared to start a drug-company trial that used two chimpanzees to test the absorption, metabolism and excretion of an experimental medication. One of the animals was Simba, an 88-kilogram male around 40 years old. That morning he was coaxed

from his outdoor enclosure, where he lives in a large social group, into an individual cage. A technician used a needle and syringe to sedate him. He was then strapped to a stretcher and transported by ambulance to Building 52 to receive a pre-study physical examination.

At 9:27 a.m., Simba was slid off the stretcher — where it became clear that he had defecated — and onto a stainless-steel gurney. His fleshy pink gums were relaxed and prominent. He was drooling.

“I need to do a dental on him,” said Dana Hasselschwert, head of the veterinary-sciences division and one of nine veterinarians on the NIRC staff. The veterinarians care for the centre's chimps, along with its 6,500 macaques and other monkeys. Today, three technicians are assisting Hasselschwert with the physical. Speed is important, because the sedative is short-lived. Fully alert chimpanzees are strong and sometimes violent.

One technician quickly shaved Simba's forearms, armpits and groin. On the skin of his right groin, a tattoo identified him as chimpanzee number xo19. The other technicians placed electrodes on his body;

his electrocardiogram revealed a regular heart rhythm. Simba's blood pressure was 143/87 millimetres of mercury — normal for him, Hasselschwert said. Blood was drawn from Simba's left femoral vein; his rectal temperature was taken and was normal, at 37.3 °C. His pulse was 104 beats per minute; his respirations 32.

Hasselschwert palpated his liver and kidneys and found nothing abnormal. But one of the technicians was having trouble

catheterizing Simba to collect a urine sample. Hasselschwert placed an ultrasound paddle on Simba's lower abdomen and located his bladder on a nearby screen. An assistant quickly shaved the overlying area.

“It's undignified, a male having bikini marks,” Hasselschwert declared. She inserted a needle through Simba's abdominal wall and withdrew three millilitres of pale yellow urine.

Simba's breathing was speeding up, a sign of growing wakefulness. “Y'all, we need to move,” Hasselschwert said. She wiped Simba's drooling gums with paper towels, and patted his open palm. His hand was half again as big as hers. “He looks good,” she declared, and, at 9:40 a.m., Simba was wheeled away on the gurney and placed in a wire cage that measured 2 metres long by 1.5 metres wide by 2.2 metres high. The cage is one of many in the room, and it can be compressed if an animal refuses to present an appendage for injections or blood withdrawal — a procedure that staff call “squeezing up”. Three days later, Simba would be injected with the experimental drug. After that, for 72 hours, at regular intervals, his blood would be drawn and his urine collected from a pan beneath the cage. He would then be returned to his outdoor enclosure.

Last year, the NIRC conducted 23 chimpanzee studies, which typically involve between two and six animals. On the day of Simba's physical, ten chimps were in experiments. The remaining chimps are kept in the outdoor cages. To keep the chimps prepared for being research subjects, trainers reward them with fruit in exchange for presenting their legs for mock injections, or for urinating in a cup. The chimps are wary of strangers, at whom they are wont to hurl gravel or faeces.

Chimpanzee studies are expensive, costing anywhere from \$20,000 to \$250,000. And roughly 85% of the revenue for the NIRC comes from a score of pharmaceutical companies that are regular customers. (Other centres tilt more towards academic and governmental clients.) As well as conducting drug and vaccine trials, the NIRC breeds macaques for several companies, and is a registered importer of the monkeys.

The other 15% of the centre's revenue comes from government agencies, mainly the NIH. The biomedical agency owns 124, or roughly one-third, of the NIRC chimpanzees, and pays the centre to maintain two breeding colonies of macaques. The centre also conducts chimpanzee research under contract for the Centers for Disease Control and Prevention. It owns 11 more chimps, which are kept at Bioqual, a company in Rockville, Maryland, where young animals are used in

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Thomas Rowell directs the New Iberia Research Center in Louisiana.

hepatitis-C studies run by the NIH's infectious-diseases institute.

If the IOM were to recommend that the NIH stop supporting chimpanzee research, and if the NIH were to comply, this would, theoretically, not affect the drug-company funded research at the NIRC and the other centres. But in practice, the directors say, it would hobble their enterprise, not least because some two-thirds of the chimpanzees available for research in the United States are owned or supported by the NIH (see 'Chimpanzee Research in the United States'). What is more, they say, the per diem fees and user fees paid by companies for individual experiments do not begin to cover the long-term care of the animals, which is supported by NIH infrastructure grants.

"The lifetime maintenance of chimpanzees requires a long-term commitment of financial support that individually sponsored studies do not provide," the directors wrote in a jointly authored statement to *Nature*.

INSPIRED WORK

Rowell, who is 52, has been working with chimps most of his life, ever since he took a job cleaning cages at the NIRC when he was 17. He quickly got a taste of the value of chimpanzee research, when Carleton Gajdusek shared the 1976 Nobel Prize in Physiology or Medicine for discovering that neurodegenerative disorders such as kuru and scrapie are transmitted by infectious agents³. As part of his research, Gajdusek injected infected human brain tissue into chimps from the centre.

The thrill of Gajdusek's work rubbed off on Rowell. "This is what was so exciting — a teenager off the street working at the level that I was — and being involved with something so huge." Rowell chose his career at that point, and earned a degree in veterinary medicine at the Louisiana State University School of Veterinary Medicine. Hired by the NIRC in 1990, he became its director in 1998.

Rowell has expanded the centre significantly, from about 170 employees in 1998 to 249 today, and from 4,560 primates in 1998 to 6,860 today. He also strengthened the NIRC's experimental credentials and abilities, which has made the centre highly attractive to the pharmaceutical industry.

In the years since Rowell first started working at the facility, support for chimp research has slowly eroded around the world. The United States stopped importing chimpanzees after signing a 1973 treaty banning trade in endangered species. When the AIDS epidemic hit, the NIH launched a breeding programme for chimpanzees, but the agency declared a moratorium on breeding in 1995, after it became clear that chimps were a poor model for the disease.

Soon, countries started to outlaw chimp research completely. In 1997, the United Kingdom took that step. Another eight countries followed suit in the next decade, and last year, the European Union outlawed great-ape experimentation.

Only one pharmaceutical company, GlaxoSmithKline, has dropped chimp research, at least publicly. It announced in 2008 that "the case for using great apes in the future is less clear than it may have been previously".

Opponents of chimp research have painted the United States as an outlier for continuing to allow such experiments. That charge irks the directors of the chimpanzee centres. Responding to a request from *Nature*, the directors catalogued 27 chimpanzee studies carried out at their centres by foreign companies or scientists since 2005.

"The Europeans did not ban their companies from coming to the United States," says John VandeBerg, director of the Southwest National Primate Research Centre in San Antonio, Texas, another of the centres that conducts chimp research. "And I can assure you they are not going to ban the importation of drugs into their countries that are developed using chimpanzees."

In the United States, public pressure to shut down the research intensified after the television exposé. The show contained video

footage obtained surreptitiously by an HSUS investigator who infiltrated the NIRC and worked there for nine months.

In one scene from the resulting documentary, aired by the ABC news show *Nightline*, a sedated chimp fell several feet from a bench to the cement floor of a cage. In another scene, a sedated chimp is carried by its arms and legs, not on a stretcher.

Footage of some of the centre's monkeys was equally damaging. A technician hit a baby on the head after it bit her, and another employee rapped a monkey's teeth with a metal pole. In a different scene, an anaesthetized monkey was allowed to fall from a chest-level counter to the floor of a lab room.

The show drew strong reactions. Jane Goodall issued a statement saying: "In no lab I have visited have I seen so many chimpanzees exhibit such intense fear." And agriculture secretary Tom Vilsack ordered an investigation of the NIRC's animal-welfare practices. In the following 14 months, the centre underwent inspections by two units of the US Department of Agriculture (USDA), the NIH's Office of Laboratory Animal Welfare in Bethesda, Maryland, the Association for Assessment and Accreditation of Laboratory Animal Care International in Frederick, Maryland, and auditors from every one of the NIRC's pharmaceutical clients. The government agencies also paid surprise visits to the other facilities conducting chimpanzee research.

THE CASE FOR RESEARCH

In May 2010, the NIRC paid \$18,000 to the USDA to settle six alleged violations of the Animal Welfare Act, such as leaving sedated adult chimps unattended with nursing infants. As part of the agreement, the centre neither admitted nor denied that the violations took place, or that they were, in fact, violations. But the NIRC has since retrained employees in, for instance, keeping animals safe when they are sedated.

Rowell says that he watched all ten hours of undercover video footage that the HSUS turned over to the NIH. He concedes that there were moments of carelessness and one case of inappropriate behaviour, when the technician hit the infant monkey. But he says that the undercover operative — who was working as an aide — bears responsibility for the fall involving the sedated monkey. It was her job to protect the animal, but she had stepped away to film the room from a distance. Overall, he says, "I was proud of what I saw".

Now, focused by the IOM study, he is going on the offensive. Others are also speaking up, such as Christopher Walker, a hepatitis-C researcher based at Nationwide Children's Hospital in Columbus, Ohio, who is the main academic customer at the NIRC. Walker is part of a team funded by a five-year, \$12.5-million grant from the Bill & Melinda Gates Foundation in Seattle, Washington, to try to develop a drug for hepatitis C that reinvigorates exhausted immune-system cells called T cells; he also relies on NIH grants.

Walker has not spoken to the press before about his work with

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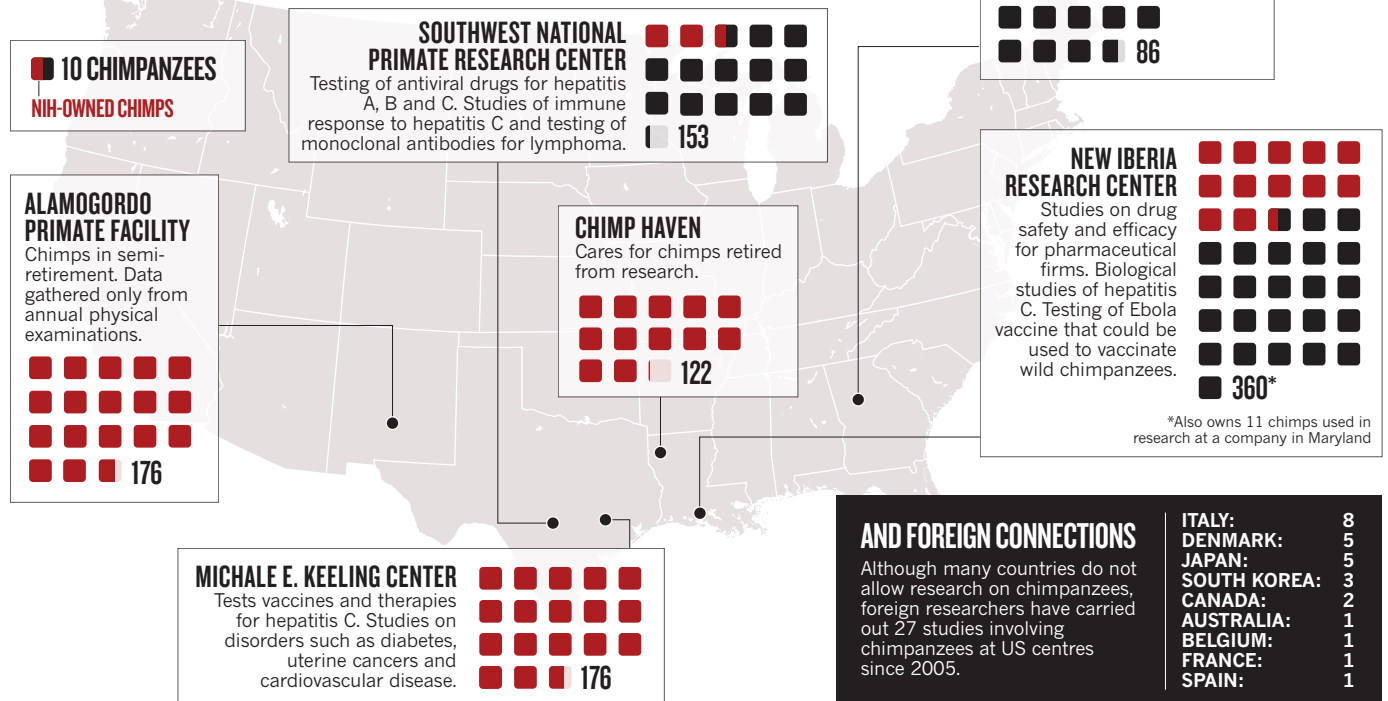


Outdoor enclosures at the NIRC house chimps in social groups.

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CHIMPANZEE RESEARCH IN THE UNITED STATES

This year, the US National Institutes of Health (NIH) will spend US\$12 million maintaining chimps for research and providing care for retired animals. Three centres conduct invasive research, one does behavioural work and two care for chimps not currently involved in research. The \$12 million does not include extramural grants.



chimpanzees; he has been afraid of being targeted by animal-rights activists. But he is talking now, he says, “because we are reaching a critical decision point”. Walker’s work focuses on unravelling the role of cellular immunity in hepatitis-C infection, which often leads to liver cancer, a disease that is almost always fatal without a liver transplant. While working at a firm called Chiron in Emeryville, California, in the 1990s, Walker did the scientific groundwork^{4,5} in chimpanzees that led Merck to develop a hepatitis-C vaccine programme. Several Merck employees then spun off Okairos, a Rome-based biotech, which has since moved a vaccine into human trials, after publishing proof-of-concept work in chimpanzees⁶.

“The chimpanzees were absolutely critical,” Walker says, in establishing that immune-system cells called T-cells have an important role in controlling the hepatitis-C virus, and that any successful vaccine would need to generate a T-cell response.

Walker is a strong believer that chimpanzee studies continue to be needed not only for developing a hepatitis-C vaccine, but also for testing the safety of new, and potentially risky, medicines to treat both hepatitis C and B. He points, for instance, to research published in 2009 that showed RNA silencing to be effective in controlling hepatitis-C infection in chimps⁷.

Some others who use chimpanzees see few remaining justifications for experiments on the animals. Michael Houghton, a virologist at the University of Alberta in Edmonton, and a co-discoverer of the hepatitis-C virus, says that in research related to that virus, “we do not need the chimp any more for diagnostic development or for antiviral-drug development as we have the infected human available”. The risk-to-benefit ratio for infected people in such studies is low enough to justify testing in humans, he says.

Still, Houghton supports chimpanzee use for hepatitis-C vaccine development, because vaccines must be tested in uninfected individuals. He also supports studies in chimpanzees for the development of riskier immunotherapies against the disease. “As inconveniencing tens of chimpanzees impacts the health

of millions of humans, it is unethical not to use the chimp model for certain indications,” says Houghton. He also believes that it would be unwise not to keep humanely treated chimps available in sanctuaries in case of bioterrorist attacks; the animals could be used to study the transmission of infectious bioweapons as well as vaccines and therapies, he says.

Activists, though, see no rationale for continuing tests on chimps, partly, they say, because ever-more sophisticated *in vitro* methods make it unnecessary⁸. They also argue that, despite the genetic similarities between chimps and humans, they have relevant differences in, for instance, immune-response genes⁹, and that differences in gene expression make chimps weak as a biological model. “Stop using the excuse that chimps are essential to this research,” says John Pippin, a physician who is senior medical and research adviser for the Physicians Committee for Responsible Medicine in Washington DC.

By the end of the year, the IOM committee will offer its own analysis of whether chimp research is scientifically warranted. The committee’s report will be the most weighty pronouncement on the issue so far in the United States, but it may not settle the debate.

The ongoing controversy has taken a toll on some of those who work with chimpanzees. Rowell says he does not take the same amount of pleasure in his work that he did five years ago. “I’m exhausted,” he says. Still, he vows to stay in the job. “It’s not something that I do. It’s who I am.” ■ [SEE EDITORIAL P.251](#)

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For more on chimp science, see: go.nature.com/5uuv2