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Alternatives Sought to Save Lab Animals

Jim Detjen

In a high-tech laboratory in New York City, a scientist inserts a small plastic rectangle honeycombed with 96 holes into a machine. Click ... click ... click, the machine reverberates as it analyzes mouse tissue inside each of the holes. Within minutes, the machine spits out a strip of paper that details how toxic chemicals have damaged the tissues, which were grown in a test tube.

Scientists at Rockefeller University are engaged in a search, but it is not to find a cure for cancer or some other dreaded disease. Instead, they are seeking to find new ways to do science itself, ways that would greatly reduce both the number and the suffering of laboratory animals.

The Rockefeller researchers are seeking to replace lab animals with cells and tissues grown in test tubes. Scientists in Philadelphia, Boston, Baltimore and other cities also are testing computers, chicken embryos, garden slugs, horseshoe crabs, human placentas and even the discarded foreskins of circumcised babies as possible replacements for the millions of cats, dogs, rats and other mammals killed each year in scientific experiments.

Some scientists have even proposed using "neomorts" –the bodies of brain-dead people whose other organs have been kept alive by medical technology—for drug testing, surgical training and biomedical research.

It is all part of a relatively small, but determined, effort to find alternatives to killing animals in the name of science, efforts that have been spurred on by the angry protests of animal-rights activists at cosmetic companies, universities and research laboratories during the last six years.

At Rockefeller University, the scientists are searching for an alternative to the controversial Draize test, in which chemicals are placed into the eyes of rabbits. The test is used by industry as a way to make sure chemicals sold to the public do not damage people's eyes. Tens of millions of rabbits have been blinded or killed during the last four decades because of this test.

"In the past, (a particular application of) the Draize test would have required us to use 96 rabbits that would have filled up two rooms just to house them," said Harvey Babich, a senior research associate at Rockefeller University. "But with this new technique we are developing, we can save lab space, time, money and the suffering of 96 animals. And we believe the results of this and other tests will be much more accurate in predicting the effect of chemicals on people."

At stake are the lives of the 17 million to 70 million animals – the precise figures are not known -- killed each year in the United States in scientific laboratories. Among these are rats, mice, dogs, cats, rabbits, birds, pigs, hamsters, gerbils, guinea pigs and primates.

Alexander Rowan, an assistant dean at Tufts University School of Veterinary Medicine in Boston, estimates that 5.7 million animals are used each year in education; 14 million are employed in product-safety testing, and 50 million are used in biomedical research.

Nobody knows for sure how many of these animals can eventually be replaced by other scientific methods, although Rowan estimates that there has been a 25 percent reduction in animal use during the last decade as a result of the protests and the increasing costs of laboratory animals.

Animal-rights advocates say that 80 percent of the animals used could be set free overnight without harming public or scientific research. Most scientists disagree, saying that some animals always will be needed and that the development, testing and acceptance of possible non-animal alternatives are still years away.

And the federal Office of Technology Assessment said in January that an outright ban on the use of animals in scientific research would have "dangerous" consequences for the nation's health and would "effectively arrest most basic biomedical and behavioral research and toxicology testing."

Despite these arguments, the search for alternatives is being taken seriously by the scientific community.

Henry Spira, a New York City activist who is credited with forging the animal-rights movement into a potent social force during the 1980s, said that finding alternatives has moved from "being a humane, but flaky, idea into one that is now in the scientific mainstream."

"Scientists realize now that alternatives can be found that are faster, cheaper and more humane than using animals," said Spira, a former merchant seaman, schoolteacher and union organizer, "and that many of these alternatives will be more accurate than the animal tests in use today."

Alternatives

Among such alternatives:

At the University of Texas, Dr. James Walker has developed a computer model that can simulate the effect of drugs on dogs. This program, which medical students used instead of live animals, has saved the university \$18,000 over the last five years and saved the lives of about 240 dogs.

At the Medical College of Pennsylvania, Dr. Joseph Leighton has developed a test in which the membrane of a chicken embryo replaces the Draize product-safety test as a way to determine if substances are harmful to the human eye. Scientists at Colgate-Palmolive are conducting further tests on this technique.

At Johns Hopkins University, researchers have developed a test using the blood of a horseshoe crab that can determine whether drugs injected into people would cause fever. The test does not harm the crab and is beginning to replace an older test that killed at least three rabbits each time it was performed.

At Cornell University, veterinary students are using "resuscidog," a realistic electronic model of a dog, to practice cardiopulmonary resuscitation. This model replaces 10 to 15 live dogs a year at a savings of \$3,000 to \$5,000 annually. The University of Pennsylvania's Veterinary School has a similar dog model and will begin teaching with it this fall.

The University of Pennsylvania became the center of a nationwide controversy in 1984 when animal-rights activists broke into the medical school, vandalized equipment, destroyed records and stole videotapes showing the treatment of baboons used in head-injury research. The publicity ultimately resulted in a federal probe and the suspension of federal funds for the baboon project.

Since then, Penn has spent \$5 million improving animal care and upgrading its animal facilities, and it plans to spend an additional \$17 million to build more laboratory animal facilities during the next five

years. It also has set up a university-wide committee to oversee animal care and is in the process of hiring a veterinarian who would be responsible for administering animal laboratory care throughout the university. In addition, the university has established the nation's first endowed professorship in humane ethics and animal welfare, using a \$1.25 million donation from a Virginia woman.

Efforts to minimize the suffering of animals date to the mid-19th century, when animal lovers in Britain began protesting cruelty to farm animals. Britain enacted a strong law against cruelty to animals in 1876, and its laws have been made progressively tougher since.

In the United States, a federal law was passed in 1966 requiring humane treatment of animals in scientific laboratories. Amendments, most recently in 1985, have strengthened it.

The early animal-welfare protesters demanded that animals be treated less cruelly. With the publication of Peter Singer's *Animal Liberation* in 1975, the movement gained a strong philosophical underpinning and more militant followers.

Singer, chairman of the philosophy department at Monash University in Australia, attacked "speciesism," which he defined as a "bias towards the interests of members of one's own species and against those of members of other species."

His book has spurred the growth of the animal-rights movement, which insists that animals, like human slaves, are not chattel. Militant animal-rights activists say that animals should not be raised to be eaten, experimented with or used in sporting events such as horse racing.

"Singer's book was a watershed said John McArdle, director of the laboratory-animal welfare department of the Humane Society of the United States. "It gave the movement a strong philosophical basis. It has brought many professionals such as lawyers, teachers and veterinarians into the movement."

During the last two years, the Humane Society says, its constituency has doubled to 500,000. The membership of People for the Ethical Treatment of Animals, a more militant group founded in 1981, has tripled to 135,000.

Spira, who was drawn into the animal-rights movement after reading Singer's work, organized a protest against Revlon Inc. in 1980, widely considered a turning point in the modern animal-rights movement. Spira pulled together a coalition of more than 400 groups to oppose the company's use of the Draize test. Protesters marched in rabbit costumes outside Revlon's corporate offices in New York and ran full-page ads in major newspapers featuring a white rabbit with tape over its eyes asking, "How many rabbits does Revlon blind for beauty's sake?"

Revlon later donated \$750,000 to Rockefeller University to help look for possible alternatives to the Draize test. The Cosmetic, Toiletry and Fragrance Association gave \$1 million to create the Center for Alternatives Testing at Johns Hopkins University in Baltimore. And animal-rights groups also have raised funds for research into alternatives.

The amount spent specifically on this research in the United States remains small—perhaps \$1 million a year, experts say—but researchers are optimistic that progress is being made. Centers for research into alternatives also have been set up in Switzerland, West Germany and Canada.

In their attempt to reduce animal research, scientists are seeking what has become known as the "three Rs" of alternatives: replacement, refinement and reduction. They are trying to replace animals with computers, cell and tissue cultures and lower organisms. They are attempting to *refine* scientific

techniques to reduce the pain and suffering of animals. And they are trying to *reduce* the number of animals used.

Efforts to replace the Draize test have focused primarily on cell and tissue cultures that are grown in test tubes. Scientists have found that these cultures can be good indicators of whether a chemical is toxic to people.

Marcia Jumblatt and Arthur Neufeld of the Eye Research Institute of Boston have taken tissues from the cornea of a rabbit's eye and successfully grown additional tissues *in vitro*, or outside of the body in a container such as a test tube.

Testing tissues

Using time-lapse photography and other techniques, they have studied what happens to the tissue's ability to repair itself when toxic chemicals are placed on it. They have found that the slower the healing, the more toxic the substance.

Neufeld said that the tissue from one rabbit can provide tissues for 48 different tests, thereby eliminating the need to experiment on 47 other rabbits. He said that his test was more accurate, far less expensive and much more humane than the Draize test "Not only is the Draize test a poor way to treat animals," Neufeld said, "but the *in vitro* method appears to be far more sensitive and far more relevant."

Dennis Stark, director of Rockefeller University's laboratory-animal research center, said that Rockefeller researchers were developing a number of tests using connective tissue from a mouse's skin. He said that eventually a battery of tissue culture tests probably would be used to replace the Draize test.

Joseph Leighton, chairman of the pathology department at the Medical College of Pennsylvania, also is working to develop an alternative to the Draize test. He believes that a chemical's effect on the human eye will be more accurately predicted by the exposed membrane of a chicken embryo.

The particular membrane he uses acts as a lung for the developing chicken. The membrane responds to chemical irritants like a living tissue which it is, but because it lacks nerves, the embryonic tissue feels no pain. After the 17-day procedure, the fertilized egg is discarded.

Leighton said that although the chicken embryo test and other alternatives are promising, they still must be validated against existing tests. It probably will take about five years before these tests are adopted by industry as replacements for the Draize test, he said.

Computer programs offer another hope of reducing the number of animals in scientific research.

Kurt Enslein and his colleagues at Health Designs Inc., a private firm in Rochester, N.Y., specializing in the use of computers in product testing, have compiled a computerized testing of more than 6,000 chemicals already known to be toxic through animal tests. They correlated the chemicals' structure, molecular weight and other characteristics with their toxicity and developed a program that can help predict whether a new chemical is likely to be toxic to people.

Enslein said that for certain tests, his computer program can predict with an accuracy of 95 percent to 98 percent whether a chemical has been shown to be toxic in animal tests. "No longer does industry have to test willy-nilly with animals," Enslein said.

Another program, developed by a team of 30 biologists and computer scientists at the Los Alamos National Laboratory in New Mexico, predicts how different chemicals would affect people. The program,

known as HUMTRN for "human transport," uses more than 10 million pieces of information about the body's physiological system and has been described as the "research rat of the future."

Anthony Gallegos, a dean at Highlands University in Las Vegas, N.M., and one of the developers of the system, said the program already has reduced the need for laboratory animals. He said it can be used to predict how nuclear accidents, such as the one that occurred at the Soviet nuclear plant at Chernobyl, would affect people's health. Ronald Wolfe, vice president of product research and development at Avon Products Corp., the world's largest cosmetics company, said computers had played an important role in helping Avon reduce its use of animals by two-thirds since 1981.

"Basically, we've used a sophisticated data management system, made possible by computers, to cross-access and reference all our prior testing," he said. "We've found that 87 percent of all product formulations can be cleared without ever doing any animal testing."

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