ANIMAL
RESEARCH

BY JOHN F. LAUERMAN

EVERY YEAR, SCIENTISTS USE MILLIONS OF ANIMALS—MOSTLY MICE AND RATS—IN EXPERIMENTS. THE PRACTICE PROVOKES PASSIONATE DEBATES OVER THE MORALITY AND EFFICACY OF SUCH RESEARCH—AND HOW TO MAKE IT MORE HUMANE.

"What is man without the beasts? If the beasts were gone, man would die from a great loneliness of spirit. For whatever happens to the beasts soon happens to man."

~CHIEF SEATTLE

Frederick Banting would never have begun his research without access to research animals. Before he had even spoken of his ideas, his first note to himself on the subject read: "Ligate the pancreatic ducts of dogs." The quiet Ontario doctor envisioned that severing the connection between the pancreas and the digestive system in a living animal would allow him to isolate the mysterious substance that would control diabetes.

During the first week in the laboratory, Banting and his assistant, Charles Best, operated on 10 dogs; all 10 died. Finally, in 1921, after months of experimentation, Banting and his colleagues isolated a material that kept a depancreatized dog named Marjorie alive for about 70 days. Exactly what information was gained from using dogs, and how many dogs were absolutely needed, is not clear. Work previous to Banting and Best's; some of it in humans, had indicated the presence and importance of a hormone involved in glucose transport. Many more experienced scientists in the diabetes-research community believed that Marjorie had never been fully depancreatized, and thus may have never been diabetic. More likely, they said, the dog died of infection caused by her pancreatectomy. It's possible that even the death of the famous Marjorie was unnecessary for the great discovery.

But the two Toronto researchers had isolated insulin, providing the first step toward producing it from pig and cow pancreas, available in bulk from slaughterhouses.

The result—that Banting and Best "saw insulin"—appears to have justified all sacrifices. What's the life of a dog, 10 dogs, a hundred? Before Banting and Best operated on dogs, we had no insulin; afterwards, we did.

Stories such as these are the reason our society and the vast majority of societies in the world accept the use of animals as a vital component of medical research.

Deeply entrenched traditions support the notion that animal welfare must bow to the best interests of humans. Animal de- domestication was among the first labor-saving devices. Humans have experimented with animal breeding, feeding, and disease control for thousands of years—not to benefit the animals themselves, but to insure that the owners obtained a maximum yield.

Today, these traditional practices have evolved into a scientific institution, the appropriateness of which is subject to perennial debate. In the United States alone, there are an estimated 7 million to 22 million animals in laboratory research facilities. To many people, animal research represents a doorway to the medical treatment of tomorrow, but to animal protectionists, and a growing number of other Americans, animal experimentation is a barbaric, outdated practice that—on the basis of a few notable past successes—has somehow retained its vestigial acceptability.

"Let's say that it's true, that animals were indispensable to the discovery of insulin," says Ned Barnard, M.D., of the Physicians
rated, and that their pressure has exposed prolifugacity among experimenters.

In February 1997, a highly controversial collection of articles appeared in Scientific American on the subject of laboratory-animal research. The first, written by Barnard and Stephen Kaufman, M.D., of the Medical Research Modernization Committee, another protectionist group, advanced the view that data collected from animal experimentation are almost always redundant and unnecessary, frequently misleading, and by their very nature unlikely to provide reliable information about humans and their diseases. "Animal 'models' are, at best, analogous to human conditions," the authors wrote, "but no theory can be refuted or proved by analogy. Thus, it makes no logical sense to test a theory about humans using animals."

A rebuttal in support of animal research followed, by Jack Botting, Ph.D., former scientific adviser to the Research Defense Society in London, and Adrian Morrison, Ph.D., D.V.M., of the University of Pennsylvania School of Veterinary Medicine. Their reply cited examples of scientists from Louis Pasteur to John Gibbon, a twentieth-century pioneer in open-heart surgery, who made important breakthroughs in the treatment of human disease through animal research.

Many scientists—both supporters of animal research and advocates for its diminution—simply refused to discuss the difficult topic, recalls Madhusree Mukerjee, the editor who proposed that Scientific American explore the controversy and who wrote a third article, reporting on the overall state of animal research in the sciences. (Similar difficulties were encountered in researching the present article.) Mukerjee suspects that possible interviewees feared the criticism of their colleagues.

Reader response, on the other hand, was overwhelming, both pro and con. "We got a huge amount of flak for dealing with the subject at all," recalls Mukerjee. "Some of it was fairly frightening." To many animal-research supporters, it was as though the floodgates had been opened. "I am simply stunned that Scientific American, a paragon of promotion of scientific research, would actually offer up for debate whether animal research should occur," wrote one reader. "Please leave this question of animal research to animal-rights activists, and stop yourselves from turning into scientific wimps." A lot of the scientific community felt [Scientific American's editors] had overstepped their bounds and compromised their values by printing the Barnard-Kaufman article," says Joanne Zurlo, associate director of the Johns Hopkins School of Public Health Center for Alternatives to Animal Testing and a specialist in chemical carcinogenesis.

Those researchers who supported animal use and wrote in said

Arthur Lage makes sure that Harvard laboratories comply with animal-welfare laws.

Committee for Responsible Medicine, an animal-protection group. "That was a long time ago. I think to say, 'It was done this way and there's no other way it could have been done' is a bit of a leap of faith, but let's say that at the time there was no other way. You could also say that you couldn't have settled the South without slavery. Would you still do it that way today? Just because something seemed necessary or acceptable at the time is not to say that we should do it in our time."

THE ANIMAL DEBATE

The legitimacy of the animal-research debate challenges one of the most important and widely used scientific approaches to discovery about the human body and its diseases. Animal experimentation is often considered as much of a sine qua non to research as the Bunsen burner. But animal protectionists reply that the importance of animals to research is over...
the animal-protectionists' side of the Scientific American debate was fraught with misstatements and scientific errors, although Mukerjee maintains that all the articles were painstakingly fact-checked. "We annoyed a lot of influential scientists," she says. "Our publication has spent more than a century describing advances in medical research, including some by falsely controversial figures. We'd never addressed the question of research on animals before, and in a sense it was a necessary thing to do. We probably lost some subscriptions because of it. But we are a bridge between the researchers who write for us and the public who read us, and we decided to let our readers decide for themselves."

ANIMAL WELFARE

Animal protectionists date their movement back to the times of Leonardo da Vinci and even Pythagoras, who are alleged to have been vegetarians. Numerous essayists and animal lovers have detailed their objections to the misuse of animals. Yet not long ago, virtually anyone who wanted to conduct experiments on animals. In the 1860s, it was not uncommon to walk into a laboratory and find mice, dogs, cats, even monkeys, housed on the premises in whatever conditions researchers saw fit to provide. Banting himself frequently bought pound dogs and may even have caught dogs on his own, his collaborators recalled that he once arrived at the lab with a dog he had leased with his fee.

Only in the nineteenth century did animal research begin to draw explicit objections from protectionists. A pivotal event occurred in England in 1874, when a lecturer at the University of Norwich demonstrated how to induce epileptic symptoms in a dog through the administration of absinthe. Objections were raised by students in the audience, and the dog was set free. Later, charges were filed against the lecturer under Dick Martin's Act, an 1822 law that called for a fine of 10 shillings from anyone committing acts of cruelty against animals. Two years later, in 1876, Parliament passed the Cruelty to Animals Act, requiring a license for animal experimentation and placing restrictions on some painful forms of experimentation.

In the United States, minimal restrictions on animal experimentation prevailed until 1966, when the first Federal Laboratory Animal Welfare Act (now known as the Animal Welfare Act, or AWA) was passed by Congress. In 1970 the AWA was broadened to require the use of appropriate pain-relieving drugs, and to include commercially bred and exhibited animals. Six years later, provisions were added covering animal transport and prohibiting animal fighting contests. In 1985, Congress passed the improved Standards for Laboratory Animal Care, and since then, inspectors and enforcement of U.S. Department of Agriculture (USDA) standards, enforced by U.S. Department of Agriculture (USDA) inspectors, and also aimed to reduce unnecessarily duplicative animal-research experimentation.

In 1976, however, the AWA was amended in a rather curious way; rats, mice, birds, horses, and farm animals were specifically excluded from its purview for reasons that are not fully clear, although the USDA's limited resources—along with political pressure from interested parties—are likely to be among them. Since rats and mice make up more than 95 percent of all research animals in this country, the amendment effectively put the vast majority of laboratory animals outside the reach of the USDA. Since then, at least one court has ruled the 1976 amendment "arbitrary and capricious."

THE MOUSE WAREHOUSE

A. S. Associate Professor of Surgery Arthur Lage, D.V.M., walks through the doors of Harvard Medical School's Alpert Building. People recognize him, smile, and let us pass without showing identification. He is director of the Center for Animal Resources and Comparative Medicine and the Center for Minimal Invase Surgery at the medical school and director of the Office of Animal Resources for the Faculty of Arts and Sciences as well. We take an elevator down to a basement, where Lage-swipes a card through a reader, unlocking a door to a hallway, where he speaks into a phone. A minute later, a young man clad in blue scrubs opens the door. Lage explains that he's bringing in a reporter in for a tour and that we'll need keys to see certain rooms. The young man hands over the keys and closes the door.

At the other end of the short hallway are two doors, each leading to a small changing room. When you turn the lights on in the changing rooms, the doors at either end lock automatically. After we've pulled blue scrubs over our clothes, Lage douses the lights and we step out of the room into another brightly lit hallway.

We're in one of Harvard's 36 animal facilities now, a moderately "clean" facility—meaning that it requires only minimal preparations for entry. Some laboratories would require us to remove our clothes and shower before entering, others don't even stock scrubs. But this facility is full of mice—transgenic mice. A stray pathogen in one of the animal rooms could wipe out millions of dollars' worth of experiments or, just as disastrous, infect a colony of mice with viruses or bacteria that might confound the results of a study.

Of course, the security isn't intended only to repel microbes. Perhaps in frustration with perceived shortcomings in the oversight of animal experimentation, some animal-protection groups have gained a reputation for tactics that are rash and often destructive. On several occasions, animals have been "liberated" from laboratories, terrorizing potential results and sometimes careers. In 1989, the Animal Liberation Front took credit for the release of more than 1,100 laboratory animals, some of them infected with cryptosporidium, which can be harmful to infants and immuno-

YOU COULD ALSO SAY THAT YOU COULDN'T HAVE SETTLED THE SOUTH WITHOUT SLAVERY. WOULD YOU STILL DO IT THAT WAY TODAY? JUST BECAUSE SOMETHING SEEMED ACCEPTABLE AT THE TIME IS NOT TO SAY THAT WE SHOULD DO IT IN OUR TIME."

NEAL BARNARD
compromised people. The total damage was estimated at $390,000. In 1987, a laboratory under construction at the University of California at Davis was burned; the loss was estimated at $3 million.

Although there is little evidence of violence toward animal researchers here in the United States, in Europe, where the animal-protection movement is more firmly entrenched, activists have taken aim at individuals, sometimes with disastrous results. In 1990, the infant daughter of a researcher was injured by a car bomb believed to have been set by animal protectionists. In separate, related incidents, a terrorist and a breeder of cats used in experimentation were injured by letter bombs. Responsibility for the mail bombs was assumed by "The Justice Department," a militant, underground, animal-protection organization.

Even today, animal-protection groups find ways to gain access to research and testing facilities. In 1993, Michelle Rockefeller of People for the Ethical Treatment of Animals (PETA) infiltrated Huntington Life Sciences, a drug- and cosmetic-testing firm in East Millestone, New Jersey. Using a surveillance camera embedded in her eyeglasses, Rockefeller spent hours of films that PETA claimed showed animals being slammed into cages and roughly handled. PETA president and co-founder Ingrid Newkirk said their investigation also revealed that young beagled legs were broken for another study at Huntington. Movie star Kim Basinger gave a press conference on Huntington's lawn in April 1998, the USDA fined Huntington $50,000 for AWA violations.

In the basement of the Alpert building, there is no evidence of such fury. Each room holds literally hundreds of mice in shoebox-sized cages, and there are so many of them it looks like a shoe warehouse. There are about 35,000 mice involved in research at Harvard at any one time, but that number is growing constantly. In 1997 it was closer to 50,000; by the end of 1998 it approached 56,000. By comparison, the numbers of other animals are almost negligible: about 1,300 rats, 145 rabbits, 115 hamsters, 70 guinea pigs, 67 primates, 33 pigs, 39 gerbils, 26 ducks, 26 dogs, 18 sheep, 6 cats, and 1 ferret. In addition, the New England Regional Primate Research Center in Southborough, Massachusetts, houses another 1,000 monkeys and other primates. Established at Harvard in 1966 with a grant from the National Institutes of Health, the NERPRC is one of seven such centers created by Congress in the early 1960s to serve as regional resources for scientists.

Surprisingly, there is no hint of animal smell within the basement facility. Temple Grandin of Colorado State University, a specialist in the behavior of captive animals, says that what mice really crave is some form of bedding—wood chips, paper, or shavings—which not all these animals have. Still, these laborato-

"I'M SURE SOME OF THE PRINCIPAL INVESTIGATORS RESIST THESE REGULATIONS. IT DOESN'T HAPPEN THAT OFTEN, BUT THERE ARE RARE OCCASIONS WHEN I RUN INTO RESISTANCE FROM AN INVESTIGATOR."

JULIE MEDLEY

ory animals, born and bred under fluorescent lights, are comfortable enough to live out their lives, they would never approach in the wild and, of course, to reproduce. And since almost all of them are involved in genetic studies, making sure they're happy and healthy enough to reproduce is of vital importance. Keeping these buildings clean and free of infection is a triumph of research design. All the soiled animal cages are shuttled to one end of the laboratory where, before they are sent, they pass through an enormous autoclaving machine that sanitizes the cages as well as the carts they sit on.

Amid the towers and technology of the medical area, animals once normally associated with a farm are ajar many. But Lige (pronounced Lay-gee) led me through animal laboratories in the basement of the Science Building where we saw pigs, sheep, and rabbits held in small, clean pens. At one point, we watched eight sheep slated for experimental surgery flash around a room that looked almost exactly like an office. If the straw were swept away, one could easily have moved in a desk and gone to work.

"We care for all these animals just as though they were covered by the Animal Welfare Act," Lige says proudly. "I think most of us believe that the act should cover rats and mice."

Although the Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC), like the USDA, inspects laboratory-animal facilities, including those of rats and mice, AAALAC accreditation isn't legally required to conduct animal research. AAALAC conducts something like a "peer review" assessment," Lige says. "It's a voluntary process, subscribed to by many, many research organizations. If you decide not to go through accreditation, you have to describe your entire program every time you apply to the government for funding for animal research."

Many laboratories and commercial drug-testing companies that receive no funding from federal sources and use only rats and mice proceed with only minimal oversight from their own institutional animal care and use committees (IACUCs). But restrictions on animal research are, if anything, increasing, not abating. Not content with the level of state and federal regulation, for example, the city of Cambridge in 1989 passed its own law creating an inspector's office with the power to make USDA-type inspections of all research facilities housing vertebrate animals, including rats and mice.

Cambridge's current commissioner of laboratory animals, Julie Medley, DVM, annually inspects 34 laboratories, makes follow-up visits to some facilities (sometimes unannounced), and reviews "hundreds and hundreds" of research protocols to ensure that all experiments meet federal standards for pain control. Investigators readily comply with Medly's suggestions for better animal care and pain control, she says, but she perceives an undercurrent among some researchers who chafe under what they perceive as excessive government intervention in the work. "I'm sure some of the principal investigators resent these regulations," she says. "It doesn't happen that often, but there are rare occasions when I run into resistance from an investigator."

Still, for animal protectionists, the intentions of the Animal Welfare Act, AAALAC, and state inspectors are not enough. Sandi Larson, a scientific adviser to the New England Anti-Vivisection Society, who has a master's degree in microbiology, concurs that "not all researchers are Dr. Frankensteins. But," she
adds, "they have been trained to look at animals as tools. It's ingrained in them to shut off their compassion and act like scientists. They think there's no room for emotions." A significant portion of the animal-protection movement believes that most experimentation on animals is without merit. If animals are different enough from humans that we can dismiss their suffering as inconsequential, isn't it just a little too convenient that they resemble us enough to be considered a source of reliable information about human physiology?

ANIMAL LIBERATION

Peter Singer was an Oxford philosophy student who had little interest in animals, domesticated or otherwise, until he had lunch with a vegetarian friend one day and they began talking about the use and abuse of animals. Singer was quickly converted to the cause, and within a few years became its champion. One of the pivotal events in the treatment of laboratory animals in this country and throughout the world was the publication of his manifesto, Animal Liberation, in 1975.

Just 25 years ago, some proponents of animal experimentation still held that animals' intellectual inferiority to humans meant that they could not be accorded the same rights as humans. Some argued that animals had no consciousness or memory, that they did not think as humans did. The quality and intensity of the pain felt by animals was still subject to debate. Singer, recently appointed DeCamp professor of bioethics at Princeton University's Center for Human Values, refuted the assertion of animals' inequality, pointing out that our society grants equal rights to all humans without regard to IQ or ability to function. "If the demand for equality were based on the actual equality of all human beings, we would have to stop demanding equality," he wrote. "...[T]he claim to equality does not depend on intelligence, moral capacity, physical strength, or similar matters of fact."

As for consciousness and the ability to feel pain, Singer pointed out that we have no reason to believe animals lack either one. Some of the experiments he recounts make their emotional vulnerability all too clear. In the late 1960s, for instance, psychologist Harry Harlow of the University of Wisconsin embarked on a series of experiments in which he deprived young rhesus monkeys of contact with their mothers. Young monkeys who were most completely deprived of parental contact developed very bizarre behavior, and would cling to objects that supplied the most minimal comfort, such as a scrap of terry cloth. Many of his fellow researchers considered Harlow a genius for having established the importance of interpersonal contact to normal childhood development. Singer, on the other hand, pointed out that the experiments demonstrated just how much like us monkeys really are, and he condemned the inhumanity of torturing them to obtain information that could have been elucidated in many other ways, perhaps through epidemiological studies of children who had been separated from their mothers at critical periods of development.

"You can't have it both ways," says biochemist Karin Zupko '77, an animal-rights advocate formerly with the New England Anti-Vivisection Society. "You can't say that animals are different enough from people so that it's acceptable to experiment on them, but enough like people so that the results of the experiments are valid."

MODELS FOR MEDICINE

Scientists, however, counter that you can, in fact, gather useful information about humans from animals that seem vastly different from us. They point to the many surgical experiments performed on pigs, dogs, and monkeys that have led to advances in transplantation, heart-valve replacement, and coronary artery bypass graft surgery.

"Research on live organisms is essential for medical advance," asserts Francis D. Moore '35, M.D. '39, S.D. '82, Moseley professor and surgeon-in-chief emeritus at Harvard Medical School and Brigham and Women's Hospital, respectively. As Moore has pointed out in testimony to the Massachusetts legislature and in
his autobiographical book, A Miracle and A Privilege, the first successful human kidney transplant, in which Moore played a pivotal role in 1963, would not have been possible at that time without an understanding of immunology based on experiments in rats and mice. Important aspects of the surgery were developed in larger animals. “There’s no substitute for it,” says Moore. “Some people say you can set up a computer program to act like a dog. Well, forget it. All animals have responses that we don’t understand, and there’s no way to set that up on a computer.”

A great deal of our understanding of basic human physiology comes from experiments in large animals, like dogs and chimpanzees. Harvard physiologist Walter B. Cannon, A.B. 1896, M.D. ’00, S.D. ’37, for example, performed experiments on dogs for many years to understand the basic dynamics of digestion. Different animals may be selected for different purposes. A dog’s prostate differs from that of a human in having only two lobes, yet dogs, like humans, can develop benign prostatic hyperplasia.

“Not all animal models are ideal, but some cases are a perfect fit,” says Arthur Lage. “Mice are certainly a very good model for studying human genes. Much of the genetic makeup of the mouse is very similar to that of a human; there are large regions of shared identity.” That’s why, Lage explains, Harvard will probably double its use of mice over the next five years—to about 100,000 mice annually. The chief reason for this is transgenic-mouse technology—which allows the insertion and deletion of key disease genes into the mouse genome. These techniques allow researchers to study the impact of both subtle and drastic changes in the genome, and to make key predictions about how similar changes would affect humans. Mice can be bred, for example, with varying ability to express the j53 gene, which has been implicated in a wide variety of cancers. Understanding how the activity of such genes affects cancer development promises to vastly increase our knowledge of treatment and prevention.

Philip Leder ’56, M.D. ’60, Andrus professor of genetics and head of the medical school’s department of genetics, who pioneered the technology, points out that transgenic mice have been used to test the safety and efficacy of new therapeutics; to detect biohazards; and to advance our knowledge of cancer. Yet he concedes this widely embraced methodology has yet to produce new therapies itself. “It’s impossible as yet to bring it home to lives of patients,” he says, “because the development of diagnostics and therapeutics takes time.”

There are many areas, however, where a direct connection between animal research and patient welfare can be argued. In the field of AIDS, for instance, research on animals has been making important contributions to the basic understanding, prevention, and treatment of this life-threatening disease.

In 1981, Norman Letvin ’71, M.D. ’75, received a call that would change his life. It concerned an epidemic of mysterious deaths, all caused by unusual pathogens and cancers, such as pneumocystis carinii pneumonia, cytomegalovirus, and rare lymphomas. But the patients suffering from these infections were not humans, but laboratory monkeys.

We now recognize these so-called “opportunistic infections” as signals of the presence of the human immunodeficiency virus (HIV) that causes AIDS. But at that time, the disease was just being recognized in humans, the term “AIDS” itself was unknown, and the cause of all these infections was still a frightening mystery.

Letvin, now professor of medicine at Harvard, says HIV probably began as a relatively harmless virus that infected some species of African monkeys. When it crossed species lines, it did so in several directions, spreading simultaneously into both human and additional non-human primate populations. In these new populations, the infection had much more serious consequences than in the African monkeys; it was lethal. But to Letvin, the realization that a parallel syndrome was occurring in man and monkeys was a tremendous opportunity.

“A great deal of effort has been expended on trying to find rodent and rabbit models for studying HIV infections, but they have not proven terribly useful,” Letvin notes. “The only way we can see what happens in the first few minutes, hours, and days after infections—questions that are essential to answer in order to develop an HIV vaccine—is by working in animal models. We are forced
to work in these models if we want to answer these questions.”
(The number of monkeys needed for such an experiment, he hastens to point out, is relatively small—usually about six.)

In Levtin’s experiments, monkeys are inoculated with candidate vaccines against HIV. After a brief period during which the vaccine draws a response from the host monkeys’ immune system, the animals are inoculated with a strain of immunodeficiency virus that brings on an AIDS-like disease. Periodic blood samples are taken to monitor their white blood cell counts and viral replication. An experimental model that causes the monkeys to get sick is more informative, Levtin explains, because even if the vaccine doesn’t prevent infection, it may slow the course of the disease enough to be useful.

“There’s little question that exciting animal data is a major drive for the initiation of human studies,” Levtin says. “It’s not a gatekeeper, but an important piece of a complex puzzle we use to determine whether to go forward with the long march into humans. There are hundreds of approaches one could take. If a strategy does look promising, an animal trial makes it easier to determine whether it’s worth spending millions of dollars to measure its safety and efficacy in humans.”

Levtin points out that an AIDS vaccine would save millions of human lives, particularly in populations where expensive treatment is not available. Thus the use of animals in research on diseases such as AIDS seems fated to continue for years to come. If the past is any indication, it will probably yield a rich crop of new medical information.

Perhaps the more accurate question then—under the circumstances—is, how much do we care about animal suffering? Is it worthwhile to consider that issue in our quest for better treatment for diseases?

THE THREE R’S

Since Peter Singer formulated his ideas, the animal-protection movement has gone from a series of scattered eruptions to a steady influence on the course of medical research. Everyone involved in the animal-research debate admits that the situation has changed considerably during the last 25 years. Ernie Prentice, a nationally recognized expert in the regulation and ethics of animal research and a member of the institutional animal care and use committee at the University of Nebraska Medical Center, can remember a time when animals were routinely subjected to painful measures without pain control. In one well-publicized experiment, pigs were burned without anesthetic; in another long-running research project, monkeys were subjected to traumatic blows to the head without analgesics. Animals progressed to the end stages of artificially induced malignancies, renal failure, and heart disease, all without any form of pain control.

“Those kinds of projects would not be permitted now. They would be unacceptable for at least two reasons,” says Prentice. “One is that we now have regulations that clearly ban this kind of experimentation, and those regulations are adequately enforced to make sure that they’re followed. At the same time, there is heightened ethical sensitivity among both researchers and IACUCs. If you had sat in on a meeting of an

IACUC in 1985 and were able to compare the level of discussion back then with what goes on today, you would see a tremendous difference.”

Increasingly, members of the protection community are taking legal steps to gain input into animal-treatment guidelines, and have found more conventional ways to exert pressure. Marc Jurnove, a member of the Animal Legal Defense Fund (ALDF), is suing the USDA for “aesthetic and recreational injuries” that he suffered when seeing the living conditions of chimpanzees and apes at a Long Island zoo. Jurnove charged that the USDA failed to adopt and enforce adequate standards for the animals’ well-being, as is required by the AWA. This past September, the U.S. Court of Appeals for the District of Columbia Circuit, the nation’s most influential circuit court, upheld Jurnove’s right to sue. Recently, the ALDF also led animal-rights groups in successfully suing the National Academy of Sciences for access to records and to committee meetings pertaining to a guide on the care and use of laboratory animals.

Some major funding organizations have also embraced the animal-rights movement. The Doris Duke Charitable Foundation, with assets of $1.25 billion, is one of the 25 wealthiest philanthropies in the country. Although it funds medical research, one of its restrictions is that animals not be used as subjects. This creates a sticky situation for the board, which hopes to fund research on AIDS, cancer, heart disease, and sickle-cell anemia, areas heavily dependent on animal research in the past.

Scientists, Says Sandi Larson, “have been trained to look at animals as tools.”
But the effort to occupy a middle ground, supporting the principles of reduction, replacement, and refinement of animal research while acknowledging its necessity, has been extremely frustrating.

Several research institutions have established centers of animal-rights advocacy. The Center for Animals and Public Policy at Tufts University and the Center for Alternatives to Animal Testing at Johns Hopkins University, for example, have tried to establish liaisons with both protectionist and researchers. "I wasn't running around throwing bombs," says Andrew Rowan, Ph.D., former director of the Tufts Center and now senior vice president of the Humane Society of the United States. "I was engaging colleagues in scientific debate without being obnoxious. People were shouting past each other." Veterinarian Peter Them, vice president of the health and hospitals division of the Massachusetts Society for the Prevention of Cruelty to Animals and director of the MSPCA's Center for Laboratory Animal Welfare, says that his group has had to walk a fine line. "We try to maintain a rapport with both sides," he stresses. "I hate to say that we often don't agree with some of the more aggressive groups, like PETA. But there's a tendency to paint the animal-welfare community with a broad brush. And that makes dialogue extremely difficult."

"When you say you're for animal welfare, you're perceived as rabid," says Joann Casulo of the Johns Hopkins center. "At the same time, we can't deal with groups like PETA because they believe in abolition of animal use. When we organized the first World Congress on Alternatives and Animal Use in the Life Sciences in 1994, we invited representatives from every organization to sit at the table. PETA would not join. Even the American Anti-Vivisection Society sent a representative, but members of the hard-line groups who were picketing outside hounded her and called her a murderer."

"IT IS VERY EASY TO SAY IT IS WRONG TO CAUSE THE DEATH OF ANOTHER LIVING ANIMAL, THE DIFFICULTY COMES IN SAYING, 'I UNDERSTAND THAT WHAT I'M DOING IS CAUSING THE DEATH OF A LIMITED NUMBER OF ANIMALS, BUT I'M MAKING A JUDGMENT THAT THE RESULTS WILL JUSTIFY DOING THE STUDY.'" NORMAN LETVIN

"The growth of the animal-protection debate has been fraught with legitimacy. The results, however, go beyond the additional credibility that has been afforded animal protectionists. Scientists, too, find that they can be more open about the feelings they have or may have had for the creatures in their care, and are more free to explore alternative methods of experimentation.

"All of us, whether we're doing research on animals or not, recognize that this is something that is not optimal," Andrew Rowan says. "If society didn't feel that we needed the information, we wouldn't do research on animals. But society feels we do, and so do scientists. There's a tension between our concern about causing pain and distress and killing animals and our need for new knowledge. No one would say that the animals in research benefit from it, and in a world that was perfect we wouldn't be doing this. We're engaged in encouraging people to make animal-welfare a higher priority without compromising their ability to gather information."

Neal Barnard, of the Physicians Committee for Responsible Medicine, argues that the route away from animal research should carry us toward population-based efforts like the Framingham Heart Study, in which heart researchers have closely followed the health habits and outcomes of 5,200 adults for just over 50 years. That study was a key factor in galvanizing current national efforts to lower cholesterol, combat hypertension, and encourage proper diet and exercise to reduce mortality from heart disease.

"Those areas where we struggle the most, clinically, are those where we haven't exploited good clinical research and are relying on animal models," Barnard says. "Look at cardiac defects. We don't know how they're caused because no one has done the equivalent of the Framingham study for heart defects, even though it's quite feasible. The Centers for Disease Control and organizations study these congenital abnormalities only in a very hap hazard way."

"Of course," he continues, "there have been some brilliant exceptions, such as the research on neural tube defects. It was found through observation of humans that these defects were associated with deficiencies in folic acid, and that by taking vitamin supplements you can reduce the risk. The same with fetal-alcohol syndrome: the breakthroughs came in studying humans, not animals."

Politics frequently obscures our view of research bias, Barnard says. He has called for a Framingham-style study of the health implications of cows' milk consumption, which has been implicated in some studies as a possible cause of Type 1 diabetes in children. Barnard believes that the political strength of the dairy industry has kept such a study from becoming a reality even though some 700,000 Americans suffer from Type 1 diabetes.

Even within the scientific community, there is an increasing willingness to admit that current research methods can be improved upon. A wide variety of in vitro tests have been proposed (among them, the use of human tissue culture and in vitro cell-culture assays), as well as increased reliance on computer modeling and the creative application of human epidemiological studies. Both government and industry experts agree that new techniques eliminate or reduce the use of animals, so much the better. "[The current rodent bioassay for assessing carcinogenicity costs $1 million to $3 million and requires at least 3 years to complete," reads the summary of a January 1997 meeting of the Scientific Group on Methodologies for the Safety Evaluation of Chemicals. The main topic of the meeting was the development of alternatives to animal research, and the report continues. "More-efficient testing methods may reduce the time required to bring new products to the marketplace and increase..."
the amount of useful information that can be obtained.

Most researchers recognize that the humane treatment of animals isn't only compassionate—it's also good science. Imagine trying to measure the effect of blood-pressure medication on a dog that hasn't been walked in days. We now know that animals' feelings, behavior, and emotions have a profound effect on their physiological functioning—as is the case with humans. Consequently, after strong initial opposition to the Animal Welfare Act, most researchers have come to support it.

The Humane Society of the United States represents one example of how animal protectionists can set reasonably limited goals that promote animal welfare in ways that better serve both animals and humans. “We've contacted animal care and use committees and asked them to work with us to identify techniques that cause pain and distress and figure out ways to share ways to eliminate that in research,” says HSUS's Andrew Rowan. “Some of the committees are rather suspicious; they see a hidden attempt to stop all animal research. The response has been slight so far. But we think that most researchers are bright people and will understand that our primary goal is just to eliminate animal suffering wherever possible.”

Norman Levin, who frequently debates animal protectionists, knows that there are many who would like to end the practice of animal research for good. Although he is ready and willing to discuss the morality and ethics of his work, he thinks that calling an end to the practice would hurt society enormously.

“It is very easy to take an absolutist position and say it is wrong to cause the death of another living animal,” Levin says. “The difficulty in what researchers do comes in saying, 'I understand that what I'm doing is causing the death of a limited number of animals, but I'm making a judgment that the information gained from this limited, focused experiment will yield results that will justify doing the study.' Many humans infected with viruses or suffering from cancer or heart disease enter into studies that allow the development of new therapeutics. Every day, thousands of humans say, 'It is worth it for me to be involved in those studies because, even though I probably won't benefit, others will.' In the end, the decisions I'm making with respect to experimental animals are not dissimilar.”

As we walked to a new facility on Longwood Avenue, Arthur Lage reminded me that it was the former site of Angell Memorial Animal Hospital, which has since moved to Huntington Avenue in Jamaica Plain. He points out where horses were tethered in the courtyard as they waited to be seen by a veterinarian. He indicates a barely visible tower protruding from the rear roof where dismannered dogs were once quarantined. “It was hard work,” he recalls, somewhat wistfully, of the internship and residency he served at Angell. “But it was rewarding. You might sit up all night with a sick dog or cat, trying to save its life.”

Today, Lage cannot devote as much time to saving animals' lives. Instead, as he says, he's helping save human lives through animal research, while ensuring that animals are used humanely. Embodied in his work are many of the contradictions that many of us feel when we consider the millions of animals—from mice to monkeys—that annually give their lives for human health. The use of animals in research will not end today, nor tomorrow, but opinions on the matter appear to be evolving, perhaps toward a better life for animals in the laboratory, and toward better science.


Geneticist Philip Leder's transgenic mice are used to test the safety and efficacy of new medicines.