

The Benefits and Ethics of Animal Research

Experiments on animals are a mainstay of modern medical and scientific research. But what are the costs and what are the returns?

by Andrew N. Rowan

For the past 20 years, we have witnessed an intense but largely unproductive debate over the propriety and value of using animals in medical and scientific research, testing and education. Emotionally evocative images and simple assertions of opinion and fact are the usual fare. But we do not have to accept such low standards of exchange. Sound bites and pithy rhetoric may have their place in the fight for the public's ear, but there is always room for dispassionate analysis and solid scholarship.

When it comes to animal research, there is plenty of reason for legitimate dispute. First, one has to determine what values are being brought to the table. If one believes animals should not be used simply as means to ends, that assumption greatly restricts what animal research one is willing to accept. Most people, though, believe some form of cost-benefit analysis should be performed to determine whether the use of animals is acceptable. The costs consist mainly of animal pain, distress and death, whereas the benefits include the acquisition of new knowledge and the development of new medical therapies for humans.

There is considerable disagreement among scientists in judging how much pain and suffering occur in the housing and use of research animals. More attention is at last being given to assessing these questions and to finding ways of minimizing

such discomfort. Developing techniques that explicitly address and eliminate animal suffering in laboratories will reduce both public and scientific uneasiness about the ways animals are used in science. At present, indications are that public attention to the animal research issue has declined somewhat; however, the level of concern among scientists, research institutions, animal-rights groups and those who regulate animal use remains high.

There is also much room to challenge the benefits of animal research and much room to defend such research. In the next few pages, you will find a debate between opponents and supporters of animal research. It is followed by an article that sets out the historical, philosophical and social context of the animal-research controversy. We leave it to you to judge the case.

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CHRISTOPHER BURME/JOE



Animal Research Is Wasteful and Misleading

by Neal D. Barnard and Stephen R. Kaufman

The use of animals for research and testing is only one of many investigative techniques available. We believe that although animal experiments are sometimes intellectually seductive, they are poorly suited to addressing the urgent health problems of our era, such as heart disease, cancer, stroke, AIDS and birth defects. Even worse, animal experiments can mislead researchers or even contribute to illnesses or deaths by failing to predict the toxic effects of drugs. Fortunately, other, more reliable methods that represent a far better investment of research funds can be employed.

The process of scientific discovery often begins with unexpected observations that force researchers to reconsider existing theories and to conceive hypotheses that better explain their findings. Many of the apparent anomalies seen in animal experiments, however, merely reflect the unique biology of the species being studied, the unnatural means by which the disease was induced or the stressful environment of the laboratory. Such irregularities are irrelevant to human pathology, and testing hypotheses derived from these observations wastes considerable time and money.

The majority of animals in laboratories are used as so-called animal models: through genetic manipulation, surgical intervention or injection of foreign substances, researchers produce ailments in these animals that “model” human conditions. This research paradigm is

fraught with difficulties, however. Evolutionary pressures have resulted in innumerable subtle, but significant, differences between species. Each species has multiple systems of organs—the cardiovascular and nervous systems, for example—that have complex interactions with one another. A stimulus applied to one particular organ system perturbs the animal’s overall physiological functioning in myriad ways that often cannot be predicted or fully understood. Such uncertainty severely undermines the extrapolation of animal data to other species, including humans.

Animal Tests Are Inapplicable

Important medical advances have been delayed because of misleading results derived from animal experiments. David Wiebers and his colleagues at the Mayo Clinic, writing in the journal *Stroke* in 1990, described a study showing that of the 25 compounds that reduced damage from ischemic stroke (caused by lack of blood flow to the brain) in rodents, cats and other animals, none proved efficacious in human trials. The researchers attributed the disappointing results to disparities between how strokes naturally occur in humans and how they were experimentally triggered in the animals. For instance, a healthy animal that experiences a sudden stroke does not undergo the slowly progressive arterial damage that usually plays a crucial role in human strokes.

During the 1920s and 1930s, studies on monkeys led to gross misconceptions that delayed the fight against poliomyelitis. These experiments indicated that the poliovirus infects mainly the nervous system; scientists later learned this was because the viral strains they had administered through the nose had artificially developed an affinity for brain tissue. The erroneous conclusion, which contradicted previous human studies demonstrating that the gastrointestinal system was the primary route of infection, resulted in misdirected preventive measures and delayed the development of a vaccine. Research with human cell cultures in 1949 first showed that the virus could be cultivated on nonneural tissues taken from the intestine and limbs. Yet in the early 1950s, cell cultures from monkeys rather than humans were used for vaccine production; as a result, millions of people were exposed to potentially harmful monkey viruses.

In a striking illustration of the inadequacy of animal research, scientists in the 1960s deduced from numerous animal experiments that inhaled tobacco smoke did not cause lung cancer (tar from the smoke painted on the skin of rodents did cause tumors to develop, but these results were deemed less relevant than the inhalation studies). For many years afterward, the tobacco lobby was able to use these studies to delay government warnings and to discourage physicians from intervening in their patients’ smoking habits.

Of course, human population studies provided inescapable evidence of the tobacco-cancer connection, and recent human DNA studies have identified tobacco’s “smoking gun,” showing how a derivative of the carcinogen benzo(a)pyrene targets human genes, causing cancer. (It turns out that cancer research is especially sensitive to differences in physiology between humans and other animals. Many animals, particularly rats

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and mice, synthesize within their bodies approximately 100 times the recommended daily allowance for humans of vitamin C, which is believed to help the body ward off cancer.)

The stress of handling, confinement and isolation alters an animal's physiology and introduces yet another experimental variable that makes extrapolating results to humans even more difficult. Stress on animals in laboratories can increase susceptibility to infectious disease and certain tumors as well as influence levels of hormones and antibodies, which in turn can alter the functioning of various organs.

In addition to medical research, animals are also used in the laboratory to test the safety of drugs and other chemicals; again, these studies are confounded by the fact that tests on different species often provide conflicting results. For instance, in 1988 Lester Lave of Carnegie Mellon University reported in the journal *Nature* that dual experiments to test the carcinogenicity of 214 compounds on both rats and mice agreed with each other only 70 percent of the time. The correlation between rodents and humans could only be lower. David Salsburg of Pfizer Central Research has noted that of 19 chemicals known to cause cancer in humans when ingested, only seven caused cancer in mice and rats using the standards set by the National Cancer Institute.

Indeed, many substances that appeared safe in animal studies and received approval from the U.S. Food and Drug Administration for use in humans later proved dangerous to people. The drug milrinone, which raises cardiac output, increased survival of rats with artificially induced heart failure; humans with severe chronic heart failure taking this drug had a 30 percent increase in mortality. The antiviral drug fialuridine seemed safe in animal trials yet caused liver failure in seven of 15

humans taking the drug (five of these patients died as a result of the medication, and the other two received liver transplants). The commonly used painkiller zomepirac sodium was popular in the early 1980s, but after it was implicated in 14 deaths and hundreds of life-threatening allergic reactions, it was withdrawn from the market. The antidepressant nomifensine, which had minimal toxicity in rats, rabbits, dogs and monkeys, caused liver toxicity and anemia in humans—rare yet severe, and sometimes fatal, effects that forced the manufacturer to withdraw the product a few months after its introduction in 1985.

These frightening mistakes are not mere anecdotes. The U.S. General Accounting Office reviewed 198 of the 209 new drugs marketed between 1976 and 1985 and found that 52 percent had “serious postapproval risks” not predicted by animal tests or limited human trials. These risks were defined as adverse reactions that could lead to hospitalization, disability or death. As a result, these drugs had to be relabeled with new warnings or withdrawn from the market. And of course, it is impossible to estimate how many potentially useful drugs may have been needlessly abandoned because animal tests falsely suggested inefficacy or toxicity.

Better Methods

Researchers have better methods at their disposal. These techniques include epidemiological studies, clinical intervention trials, astute clinical observation aided by laboratory testing, human tissue and cell cultures, autopsy studies, endoscopic examination and biopsy, as well as new imaging methods. And the emerging science of molecular epidemiology, which relates genetic, metabolic and biochemical factors with epidemiological data on disease incidence, offers significant promise for

identifying the causes of human disease.

Consider the success of research on atherosclerotic heart disease. Initial epidemiological investigations in humans— notably the Framingham Heart Study, started in 1948—revealed the risk factors for heart disease, including high cholesterol levels, smoking and high blood pressure. Researchers then altered these factors in controlled human trials, such as the multicenter Lipid Research Clinics Trial, carried out in the 1970s and 1980s. These studies illustrated, among many other things, that every 1 percent drop in serum cholesterol levels led to at least a 2 percent drop in risk for heart disease. Autopsy results and chemical studies added further links between risk factors and disease, indicating that people consuming high-fat diets acquire arterial changes early in life. And studies of heart disease patients indicated that eating a low-fat vegetarian diet, getting regular mild exercise, quitting smoking and managing stress can reverse atherosclerotic blockages.

Similarly, human population studies of HIV infection elucidated how the virus was transmitted and guided intervention programs. In vitro studies using human cells and serum allowed researchers to identify the AIDS virus and determine how it causes disease. Investigators also used in vitro studies to assess the efficacy and safety of important new AIDS drugs such as AZT, 3TC and protease inhibitors. New leads, such as possible genetic and environmental factors that contribute to the disease or provide resistance to it, are also emerging from human studies.

Many animals have certainly been used in AIDS research, but without much in the way of tangible results. For instance, the widely reported monkey studies using the simian immunodeficiency virus (SIV) under unnatural conditions suggested that oral sex presented a transmission risk. Yet this study

PETA (left); BRIAN GUNN (A-AP/PA) (center); CHRISTOPHER BURKE/ODS (right)



did not help elucidate whether oral sex transmitted HIV in humans or not. In other cases, data from animal studies have merely repeated information already established by other experiments. In 1993 and 1994 Gerard J. Nuovo and his colleagues at the State University of New York at Stony Brook determined the route of HIV into the female body (the virus passes through cells in the cervix and then to nearby lymph nodes) using studies of human cervical and lymph node samples. Later, experimenters at New York University placed SIV into the vaginas of rhesus monkeys, then killed the animals and dissected the organs; their paper, published in 1996, arrived at essentially the same conclusion about the virus's path as did the previous human studies.

Research into the causes of birth defects has relied heavily on animal experiments, but these have typically proved to be embarrassingly poor predictors of what can happen in humans. The rates for most birth defects are rising steadily. Epidemiological studies are needed to trace possible genetic and environmental factors associated with birth defects, just as population studies linked lung cancer to smoking and heart disease to cholesterol. Such surveys have already provided some vital information—the connection between neural tube defects and folate deficiency and the identification of fetal alcohol syndrome are notable findings—but much more human population research is needed.

Observations of humans have proved to be invaluable in cancer research as well. Several studies have shown that cancer patients who follow diets low in fat and rich in vegetables and fruit live longer and have a lower risk of recurrence. We now need intervention trials to test which specific diets help with various types of cancers.

The issue of what role, if any, animal experimentation played in past discov-

eries is not relevant to what is necessary now for research and safety testing. Before scientists developed the cell and tissue cultures common today, animals were routinely used to harbor infectious organisms. But there are few diseases for which this is still the case—modern methods for vaccine production are safer and more efficient. Animal toxicity tests to determine the potency of drugs such as digitalis and insulin have largely been replaced with sophisticated laboratory tests that do not involve animals.

A Rhetorical Device

Animal “models” are, at best, analogous to human conditions, but no theory can be proved or refuted by analogy. Thus, it makes no logical sense to test a theory about humans using animals. Nevertheless, when scientists debate the validity of competing theories in medicine and biology, they often cite animal studies as evidence. In this context, animal experiments serve primarily as rhetorical devices. And by using different kinds of animals in different protocols, experimenters can find evidence in support of virtually any theory. For instance, researchers have used animal experiments to show that cigarettes both do and do not cause cancer.

Harry Harlow's famous monkey experiments, conducted in the 1960s at the University of Wisconsin, involved separating infant monkeys from their mothers and keeping some of them in total isolation for a year. The experiments, which left the animals severely damaged emotionally, served primarily as graphic illustrations of the need for maternal contact—a fact already well established from observations of human infants.

Animal experimenters often defend their work with brief historical accounts of the supposedly pivotal role of animal data in past advances. Such interpreta-

tions are easily skewed. For example, proponents of animal use often point to the significance of animals to diabetes research. But human studies by Thomas Cawley, Richard Bright and Appollinaire Bouchardat in the 18th and 19th centuries first revealed the importance of pancreatic damage in diabetes. In addition, human studies by Paul Langerhans in 1869 led to the discovery of insulin-producing islet cells. And although cows and pigs were once the primary sources for insulin to treat diabetes, human insulin is now the standard therapy, revolutionizing how patients manage the disease.

Animal experimenters have also asserted that animal tests could have predicted the birth defects caused by the drug thalidomide. Yet most animal species used in laboratories do not develop the kind of limb defects seen in humans after thalidomide exposure; only rabbits and some primates do. In nearly all animal birth-defect tests, scientists are left scratching their heads as to whether humans are more like the animals who develop birth defects or like those who do not.

In this discussion, we have not broached the ethical objections to animal experimentation. These are critically important issues. In the past few decades, scientists have come to a new appreciation of the tremendous complexity of animals' lives, including their ability to communicate, their social structures and emotional repertoires. But pragmatic issues alone should encourage scientists and governments to put research money elsewhere. ■

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Researchers have better methods at their disposal.



Animal Research Is Vital to Medicine

by Jack H. Botting and Adrian R. Morrison

Experiments using animals have played a crucial role in the development of modern medical treatments, and they will continue to be necessary as researchers seek to alleviate existing ailments and respond to the emergence of new disease. As any medical scientist will readily state, research with animals is but one of several complementary approaches. Some questions, however, can be answered only by animal research. We intend to show exactly where we regard animal research to have been essential in the past and to point to where we think it will be vital in the future. To detail all the progress that relied on animal experimentation would require many times the amount of space allotted to us. Indeed, we cannot think of an area of medical research that does not owe many of its most important advances to animal experiments.

In the mid-19th century, most debilitating diseases resulted from bacterial or viral infections, but at the time, most physicians considered these ailments to be caused by internal derangements of the body. The proof that such diseases did in fact derive from external microorganisms originated with work done by the French chemist Louis Pasteur and his contemporaries, who studied infectious diseases in domestic animals. Because of his knowledge of how contaminants caused wine and beer to spoil, Pasteur became convinced that microorganisms were also responsible for diseases such as chicken cholera and anthrax.

To test his hypothesis, Pasteur examined the contents of the guts of chickens suffering from cholera; he isolated a possible causative microbe and then grew the organism in culture. Samples of the culture given to healthy chickens and rabbits produced cholera, thus proving that Pasteur had correctly identified the offending organism. By chance, he noticed that after a time, cultures of the microorganisms lost their ability to infect. But birds given the ineffective cultures became resistant to fresh batches that were otherwise lethal to untreated birds. Physicians had previously observed that among people who survived a severe attack of certain diseases, recurrence of the disease was rare; Pasteur had found a means of producing this resistance without risk of disease. This experience suggested to him that with the administration of a weakened culture of the disease-causing bacteria, doctors might be able to induce in their patients immunity to infectious diseases.

In similar studies on rabbits and guinea pigs, Pasteur isolated the microbe that causes anthrax and then developed a vaccine against the deadly disease. With the information from animal experiments—obviously of an extent that could never have been carried out on humans—he proved not only that infectious diseases could be produced by microorganisms but also that immunization could protect against these diseases.

Pasteur's findings had a widespread effect. For example, they influenced the

views of the prominent British surgeon Joseph Lister, who pioneered the use of carbolic acid to sterilize surgical instruments, sutures and wound dressings, thereby preventing infection of wounds. In 1875 Queen Victoria asked Lister to address the Royal Commission inquiry into vivisection—as the queen put it, “to make some statement in condemnation of these horrible practices.” As a Quaker, Lister had spoken publicly against many cruelties of Victorian society, but despite the request of his sovereign, he was unable to condemn vivisection. His testimony to the Royal Commission stated that animal experiments had been essential to his own work on asepsis and that to restrict research with animals would prevent discoveries that would benefit humankind.

Dozens of Vaccines and Antibiotics

Following the work of Pasteur and others, scientists have established causes of and vaccines for dozens of infectious diseases, including diphtheria, tetanus, rabies, whooping cough, tuberculosis, poliomyelitis, measles, mumps and rubella. The investigation of these ailments indisputably relied heavily on animal experimentation: in most cases, researchers identified candidate microorganisms and then administered the microbes to animals to see if they contracted the illness in question.

Similar work continues to this day. Just recently, scientists developed a vaccine against *Hemophilus influenzae* type B (Hib), a major cause of meningitis, which before 1993 resulted in death or severe brain damage in more than 800 children each year in the U.S. Early versions of a vaccine produced only poor, short-lived immunity. But a new vaccine, prepared and tested in rabbits and mice, proved to be powerfully immunogenic and is now in routine use. Within two months of the vaccine's in-

CHRISTOPHER BURKE/DB (left); CORBIS-BETTSMANN (center); GEOFF TOMPKINSON SPL/Photo Researchers, Inc. (right)

Experiments using animals have played a crucial role in the development of modern medical treatments, and they will continue to be necessary.



Some questions can be answered only by animal research.

roduction in the U.S. and the U.K., Hib infections fell by 70 percent.

Animal research not only produced new vaccines for the treatment of infectious disease, it also led to the development of antibacterial and antibiotic drugs. In 1935, despite aseptic precautions, trivial wounds could lead to serious infections that resulted in amputation or death. At the same time, in both Europe and the U.S., death from puerperal sepsis (a disease that mothers can contract after childbirth, usually as a result of infection by hemolytic streptococci) occurred in 200 of every 100,000 births. In addition, 60 of every 100,000 men aged 45 to 64 died from lobar pneumonia. When sulfonamide drugs became available, these figures fell dramatically: by 1960 only five out of every 100,000 mothers contracted puerperal sepsis, and only six of every 100,000 middle-aged men succumbed to lobar pneumonia. A range of other infections could also be treated with these drugs.

The story behind the introduction of sulfonamide drugs is instructive. The team investigating these compounds—Gerhard Domagk's group at Bayer Laboratories in Wuppertal-Elberfeld, Germany—insisted that all candidate compounds be screened in infected mice (using the so-called mouse protection test) rather than against bacteria grown on agar plates. Domagk's perspicacity was fortunate: the compound prontosil, for instance, proved to be extremely potent in mice, but it had no effect on bacteria in vitro—the active antibacterial substance, sulfanilamide, was formed from prontosil within the body. Scientists synthesized other, even more powerful sulfonamide drugs and used them successfully against many infections. For his work on antibacterial drugs, Domagk won the Nobel Prize in 1939.

A lack of proper animal experimentation unfortunately delayed for a decade the use of the remarkable antibiotic pen-

icillin: Alexander Fleming, working in 1929, did not use mice to examine the efficacy of his cultures containing crude penicillin (although he did show the cultures had no toxic effects on mice and rabbits). In 1940, however, Howard W. Florey, Ernst B. Chain and others at the University of Oxford finally showed penicillin to be dramatically effective as an antibiotic via the mouse protection test.

Despite the success of vaccines and antibacterial therapy, infectious disease remains the greatest threat to human life worldwide. There is no effective vaccine against malaria or AIDS; physicians increasingly face strains of bacteria resistant to current antibacterial drugs; new infectious diseases continue to emerge. It is hard to envisage how new and better vaccines and medicines against infectious disease can be developed without experiments involving animals.

Research on animals has been vital to numerous other areas in medicine. Open-heart surgery—which saves the lives of an estimated 440,000 people every year in the U.S. alone—is now routine, thanks to 20 years of animal research by scientists such as John Gibbon of Jefferson Medical College in Philadelphia. Replacement heart valves also emerged from years of animal experimentation.

The development of treatments for kidney failure has relied on step-by-step improvement of techniques through animal experiments. Today kidney dialysis and even kidney transplants can save the lives of patients suffering from renal failure as a result of a variety of ailments, including poisoning, severe hemorrhage, hypertension or diabetes. Roughly 200,000 people require dialysis every year in the U.S.; some 11,000 receive a new kidney. Notably, a drug essential for dialysis—heparin—must be extracted from animal tissues and tested for safety on anesthetized animals.

Transplantation of a kidney or any major organ presents a host of compli-

cations; animal research has been instrumental in generating solutions to these problems. Experiments on cats helped develop techniques for suturing blood vessels from the host to the donor organ so that the vessels would be strong enough to withstand arterial pressure. Investigators working with rabbits, rodents, dogs and monkeys have also determined ways to suppress the immune system to avoid rejection of the donor organ.

The list continues. Before the introduction of insulin, patients with diabetes typically died from the disease. For more than 50 years, the lifesaving hormone had to be extracted from the pancreas of cattle or pigs; these batches of insulin also had to be tested for safety and efficacy on rabbits or mice.

When we started our scientific careers, the diagnosis of malignant hypertension carried with it a prognosis of death within a year, often preceded by devastating headaches and blindness. Research on anesthetized cats in the 1950s heralded an array of progressively improved antihypertensive medicines, so that today treatment of hypertension is effective and relatively benign. Similarly, gastric ulcers often necessitated surgery with a marked risk of morbidity afterward. Now antiulcer drugs, developed from tests in rats and dogs, can control the condition and may effect a cure if administered with antibiotics to eliminate *Helicobacter pylori* infection.

Common Misconceptions

Much is made in animal-rights propaganda of alleged differences between species in their physiology or responses to drugs that supposedly render animal experiments redundant or misleading. These claims can usually be refuted by proper examination of the literature. For instance, opponents of animal research frequently cite the drug



LONNY SHAVELSON/Impact Visuals (left); UNIPHOTO (right)

thalidomide as an example of a medicine that was thoroughly tested on animals and showed its teratogenic effect only in humans. But this is not so. Scientists never tested thalidomide in pregnant animals until after fetal deformities were observed in humans. Once they ran these tests, researchers recognized that the drug did in fact cause fetal abnormalities in rabbits, mice, rats, hamsters and several species of monkey. Similarly, some people have claimed that penicillin would not have been used in patients had it first been administered to guinea pigs, because it is inordinately toxic to this species. Guinea pigs, however, respond to penicillin in exactly the same way as do the many patients who contract antibiotic-induced colitis when placed on long-term penicillin therapy. In both guinea pigs and humans, the cause of the colitis is infection with the bacterium *Clostridium difficile*.

In truth, there are no basic differences between the physiology of laboratory animals and humans. Both control their internal biochemistry by releasing endocrine hormones that are all essentially the same; both humans and laboratory animals send out similar chemical transmitters from nerve cells in the central and peripheral nervous systems, and both react in the same way to infection or tissue injury.

Animal models of disease are unjustly criticized by assertions that they are not identical to the conditions studied in humans. But they are not designed to be so; instead such models provide a means to study a particular procedure. Thus, cystic fibrosis in mice may not exactly mimic the human condition (which varies considerably among patients anyway), but it does provide a way to establish the optimal method of administering gene therapy to cure the disease. Opponents of animal experiments also allege that most illness can be avoided by a change of lifestyle; for example, adop-

tion of a vegan diet that avoids all animal products. Whereas we support the promulgation of healthy practices, we do not consider that our examples could be prevented by such measures.

A Black Hole

Our opponents in this debate claim that even if animal experiments have played a part in the development of medical advances, this does not mean that they were essential. Had such techniques been outlawed, the argument goes, researchers would have been forced to be more creative and thus would have invented superior technologies. Others have suggested that there would not be a gaping black hole in place of animal research but instead more careful and respected clinical and cellular research.

In fact, there was a gaping black hole. No outstanding progress in the treatment of disease occurred until biomedical science was placed on a sound, empirical basis through experiments on animals. Early researchers, such as Pasteur and the 17th-century scientist William Harvey, who studied blood circulation in animals, were not drawn to animal experiments as an easy option. Indeed, they drew on all the techniques available at the time to answer their questions: sometimes dissection of a cadaver, sometimes observations of a patient, sometimes examination of bacteria in culture. At other times, though, they considered experimentation on animals to be necessary.

We would like to suggest an interesting exercise for those who hold the view that animal experiments, because of their irrelevance, have retarded progress: take an example of an advance dependent on animal experiments and detail how an alternative procedure could have provided the same material benefit. A suitable example would be treatment of the cardiac condition known as mitral valve

insufficiency, caused by a defect in the heart's mitral valve. The production of prosthetic heart valves stemmed from years of development and testing for efficacy in dogs and calves. The artificial valve can be inserted only into a quiescent heart that has been bypassed by a heart-lung machine—an instrument that itself has been perfected after 20 years' experimentation in dogs. If, despite the benefit of 35 years of hindsight, critics of animal research cannot present a convincing scenario to show how effective treatment of mitral valve insufficiency could have developed any other way, their credibility is suspect.

Will animal experiments continue to be necessary to resolve extant medical problems? Transgenic animals with a single mutant gene have already provided a wealth of new information on the functions of proteins and their roles in disease; no doubt they will continue to do so. We also anticipate major progress in the treatment of traumatic injury to the central nervous system. The dogma that it is impossible to restore function to damaged nerve cells in the mammalian spinal cord has to be reassessed in the light of recent animal research indicating that nerve regeneration is indeed possible. It is only a matter of time before treatments begin to work. We find it difficult to envision how progress in this field—and so many others in biological and medical science—can be achieved in the future without animal experiments. SA

JACK H. BOTTING and ADRIAN R. MORRISON have been active in the defense of animal research since the 1980s. Botting, a retired university lecturer, is the former scientific adviser to the Research Defense Society in London. Morrison is director of the Laboratory for Study of the Brain in Sleep at the University of Pennsylvania School of Veterinary Medicine.

LLEWELLYN UNIPHOTO



Trends in Animal Research

Increased concern for animals, among scientists as well as the public, is changing the ways in which animals are used for research and safety testing

by Madhusree Mukerjee, *staff writer*

There is no question about it: the number of animals used in laboratory experiments is going down. In the U.K., the Netherlands, Germany and several other European countries, the total has fallen by half since the 1970s. In Canada, mammals have largely been replaced by fish. The figures for the U.S. are unclear. The U.S. uses between 18 and 22 million animals a year, but exact numbers are unknown for roughly 85 percent of these—rats, mice and birds. Primate use has stayed constant, whereas the use of dogs and cats is down by half since the 1970s.

No one reason accounts for the decline, but several factors are obvious. In 1975 the animal-rights movement exploded onto the scene with the publication of *Animal Liberation* by the Australian philosopher Peter Singer. The book's depiction of research, and a series of exposés by suddenly vigilant activists, threw a harsh spotlight on scientists. In the following years, public perceptions of animals became increasingly sympathetic. Dian Fossey, Jane Goodall and other ethologists related to an enthralled audience tales of love, sorrow,

jealousy and deceit among primates. Although not so popular with scientists, such anthropomorphic views of animals fueled the passage of laws regulating experimentation.

And the scientists have changed. Those entering the biomedical profession in recent decades have imbibed at least some of the concerns of the movement, if not its ideals; many are willing to acknowledge the moral dilemmas of their craft. Some experiments that were applauded in the 1950s would not be done today, because they would be deemed to cause too much suffering. Oftentimes biotechnology is allowing test tubes to be substituted for animals. And a few researchers, cognizant that only their expertise can help reduce the need for animals, are avidly seeking alternatives. All these efforts are bearing fruit.

The Philosophers

The underlying force behind these changes appears to be society's evolving views of animals. These perceptions owe a great deal to philosophy and to science—and very little to reli-

gion. The Bible is unequivocal about the position of animals in the natural order: God made man in his image and gave him dominion over all other creatures. And although Hinduism and Buddhism envisage a hierarchy of organisms rather than a sharp division, their influence on the animal-rights movement is limited to vague inspiration and vegetarian recipes. The real roots lie in secular philosophy. In 1780 the English barrister Jeremy Bentham asked what "insuperable line" prevented humans from extending moral regard to animals: "The question is not, Can they reason? nor, Can they talk? but, Can they suffer?"

The question became more poignant in 1859 with the advent of Charles Darwin's theory of evolution. The theory provided a scientific rationale for using animals to learn about humans, and Darwin endorsed such use. But he also believed in an emotional continuum between humans and animals and was troubled by the suffering that experimentation could cause. This dichotomy inspired clashes between animal lovers and experimenters in 19th-century England, culminating in the 1876 British

The Evolution of Animal Use in Research

1822 **British anticruelty act** introduced



ROYAL SOCIETY FOR THE PREVENTION OF CRUELTY TO ANIMALS

by Richard Martin (holding donkey). He later founded the RSPCA

1859

Charles Darwin publishes the theory of evolution

THE ORIGIN OF SPECIES

BY MEANS OF NATURAL SELECTION,

OR THE

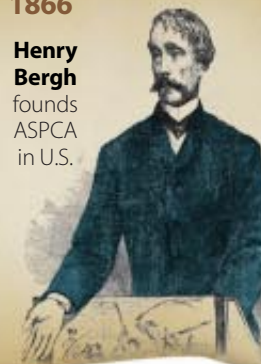
PRESERVATION OF FAVOURED RACES IN THE STRUGGLE FOR LIFE.

By CHARLES DARWIN, M.A.,

CORBIS-BETTMANN

1866

Henry Bergh founds ASPCA in U.S.



CORBIS-BETTMANN

Cruelty to Animals Act regulating animal experimentation. But the phenomenal success of medicine in the next century made the animal-protection movement recede into the background.

It rebounded in the 1970s, with Singer's attack. A philosopher in the utilitarian tradition of Bentham, Singer holds that in all decisions the total amount of good that results—human and animal—should be weighed against the suffering—human and animal—caused in the process. Not that to him the interests of humans and animals have equal weight: life is of far greater value to a human than, for example, to a creature with no self-awareness. But if there is something one would not do to, say, a severely incapacitated child, then neither should one do it to an animal that would suffer as much. Ignoring the interests of an animal just because it is not human is, to Singer, "speciesism," a sin akin to racism. Invoking the connections between humans and the great apes, Singer, Goodall and others have issued a call for these creatures, at least, to be freed from experimentation.

Although Singer started the modern animal-rights movement, it takes its name and its most uncompromising ideas from Tom Regan's *The Case for Animal Rights* (University of California Press, 1983). Regan believes that all humans and most animals have inherent rights, which he describes as invisible "no trespassing" signs hung around their necks. They state that our bodies may not be transgressed, no matter how much good might thereby result. Regan does not equate humans with animals—to save survivors in a lifeboat, a dog could be thrown overboard before a human would—yet he states that animals cannot be experimented on, because

they are not merely means to an end.

Many other philosophers have lent their voices to the animals, but few have come to the aid of researchers. One who did so, Michael A. Fox, author of *The Case for Animal Experimentation* (University of California Press, 1986), later declared himself convinced by his critics and became an advocate for animals. Attempts to refute Singer and Regan usually involve pointing to morally relevant criteria that separate humans from animals. Raymond G. Frey of Bowling Green State University has written that animals cannot have interests, because they cannot have desires, because they cannot have beliefs, because they do not have language. Regan counters that a dog may well believe "that bone is tasty" without being able to formulate the phrase and that a human infant would never learn to speak unless it could acquire preverbal concepts to which it could later assign words, such as "ball."

Another supporter of research, Carl Cohen of the University of Michigan, has argued that rights are not inherent: they arise from implicit contracts among members of society, and they imply duties. Because animals cannot reciprocate such duties, they cannot have rights. This argument meets with the retort that infants and the mentally ill cannot fulfill such obligations either but are not left out of the realm of rights: Why omit animals? (One response is that human rights are based on characteristics of "typical" humans, not on borderline cases, prompting animal advocates to ask what these special qualities are—and so on and on.)

Some research proponents also note that nature is cruel: lions kill zebras, cats play with mice. Evolution has placed humans on top, so it is only natural for us

to use other creatures. This argument, which some say elevates "survival of the fittest" to a moral philosophy, falls prey to a proposition called the naturalistic fallacy. To paraphrase the 18th-century philosopher David Hume, what "is" cannot dictate what "ought to be." So natural history may well illuminate why human morals evolved into their present form, but humans can transcend their nature. One animal advocate declares: "Killing and eating [meat] is an integral part of the evolution of human beings. Not killing and not eating [meat] is the next step in our evolution."

Many philosophers fall into the troubled middle, arguing for interests or rights to be ordered in a hierarchy that allows some uses of animals but bars others. Such distillations of animal-liberation ideas have been finding their way into legislation. The U.K., Australia, Germany and several other nations require a utilitarian cost-benefit analysis to be performed before an animal experiment can proceed. And in November 1996 the Netherlands passed into law the statement that animals have "intrinsic value": they are sentient beings, entitled to the moral concern of humans.

The Public

Not that, of course, all the Dutch are vegetarians. Rational argumentation may have influenced public opinion, but as Harold A. Herzog, Jr., a psychologist at Western Carolina University, remarks, the average person's stance on animal issues remains wildly inconsistent. In one survey, questions phrased in terms of rats yielded a far more pro- vivisection outcome than those mentioning dogs. Jesse L. Owens, a neuroscientist at the University of Alaska, protests

ILLUSTRATION OF SCROLL BY LAURIE GRACE

1876

British Cruelty to Animals Act regulates animal experimentation



1885

Louis Pasteur (at patient's right) develops rabies vaccine



1891

Diphtheria antitoxin produced (serum is being drawn from a horse)

Tetanus antitoxin found



SCIENTIFIC AMERICAN

SCIENTIFIC AMERICAN

OLIVER MECKES Photo Researchers, Inc.

that medical research is “the only use of animals that is essential” and like other researchers is bewildered by people who eat meat and in the same gulp condemn experimentation.

Not surprisingly, the animal-liberation movement has coincided with society’s becoming increasingly distant from farms—and shielded from the reality behind dinner. Those who grew up on farms often see animals as objects to be used, whereas those who had pets tend to express more sympathy. One line along which attitudes divide is gender. In all countries surveyed, women are more pro-animal and antivivisectionist than men, and three quarters of American animal-rights activists are women. Also noticeable is a generation gap. Surveys by Stephen R. Kellert of Yale University find that those who are older or less educated are more likely to see animals as resources, whereas those who are younger or more educated tend to view animals with compassion.

Public support of animal experimentation, though higher in the U.S. than in Europe, has been slowly declining. In 1985, 63 percent of American respondents agreed that “scientists should be allowed to do research that causes pain and injury to animals like dogs and chimpanzees *if* it produces new information about human health problems”; in 1995, 53 percent agreed. Even in disciplines that have traditionally used animals, the trend is unmistakable. A survey by Scott Plous of Wesleyan University finds that psychologists with Ph.D.’s earned in the 1990s are half as likely to express strong support for animal research as those with Ph.D.’s from before 1970. (Part of this result comes from the increased presence of women, but there is a significant drop among men as well.)

Opposition to animal experimentation is often said to derive from antisci-

ence sentiments, aggravated by poor public knowledge of science. But according to a 1994 survey led by Linda Pifer of the Chicago Academy of Sciences, negative attitudes toward animal experimentation in the U.S. correlate only weakly with lack of knowledge about science. And in Belgium, France and Italy, for instance, greater scientific literacy is connected with an increased rejection of animal experimentation.

Sociologists agree that opposition to vivisection derives primarily from sympathy for animals. Almost all animal rightists are vegetarians; many are “vegans,” eschewing milk, eggs, leather and other animal products. “My philosophy of living as softly on the earth as I can is my life,” one activist told Herzog. In striving to cause the least suffering possible, these individuals labor under a heavy moral burden that sits lightly on the rest of us. Some activists have indulged in threatening researchers, breaking into laboratories or even arson. But the number of such illegal acts, listed by the U.S. Department of Justice, dropped from about 50 a year in 1987 to 11 in 1992. (More recent figures are unavailable but are believed to be small.)

Many animal experimenters are also animal lovers. Surveys by Harold Takooshian, a sociologist at Fordham University, reveal that biomedical researchers have the same mixed feelings about animals and animal research as does the general public. (The groups that gave animals the lowest rating and vivisection the highest were farmers, hunters and the clergy.) Thomas M. Donnelly, a veterinarian at the Rockefeller University’s animal center, also runs a shelter to which he takes cats that are no longer needed for research. Almost all the toxicologists and pharmacologists at a 1996 meeting on alternatives to animal experimentation had experience with us-

ing animals and were moved enough by it to seek substitutes. Scientists choose to use animals because they feel it is the only way to help humans. Donald Silver, who did cancer studies on mice at Sloan-Kettering Hospital in the 1970s, recounts that whenever he had doubts about his work, he had only to think about the terminally ill patients in the children’s ward.

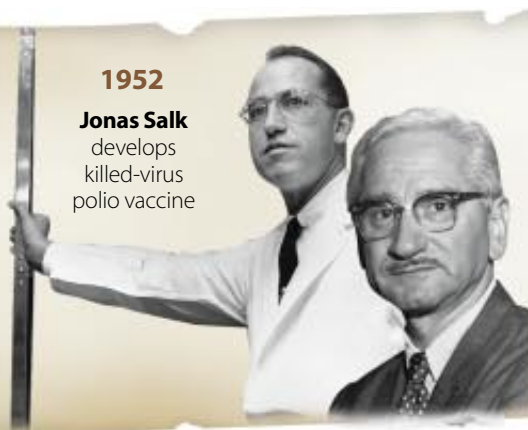
The Scientists

Of course, scientists’ perceptions of animals have evolved as well. In the early 20th century Darwinian worries about emotions were dispelled by the rise of behaviorism. Because thoughts cannot be measured, but behavior can, practitioners such as C. Lloyd Morgan and, later, B. F. Skinner sought to describe animals purely in terms of their responses to stimuli. Bernard Rollin, author of *The Unheeded Cry* (Oxford University Press, 1989), argues that at some point, the animal psyche went from being impossible to measure to being non-existent. The test of a good theory, “Morgan’s canon,” required all actions to be interpreted in terms of the lowest psychological faculties possible. In practice, this meant that a rat would not be feeling pain even if its “writhes per minute” were being used to test the efficacy of an analgesic. Its neurochemistry was merely inducing a physiological reflex.

“We were taught as undergraduates not to think of animals as other than stimulus-response bundles,” asserts Melanie Stiassney, an ichthyologist at the American Museum of Natural History. “The dogma is you can’t credit them with feelings.” In turn, it is often thought undesirable for a researcher to have feelings about the animal under study: emotions can impair professional judgment and also make it hard to perform cer-



1951
Christine Stevens
founds Animal Welfare Institute in U.S.



1952
Jonas Salk
develops killed-virus polio vaccine

1954
Humane Society of the U.S.
founded

1953
Albert Sabin
develops live, attenuated polio vaccine

UPI/CORBIS-BETTMANN

UPI/CORBIS-BETTMANN

tain procedures. Arnold Arluke, a sociologist at Northeastern University who studied animal laboratories from 1985 to 1993, reports that some technicians were deeply disturbed when a playful dog or a roomful of mice had to be put down. Such distress was officially discouraged and therefore kept secret. But after being “burned” by the death of a favorite animal, laboratory workers learned to avoid emotional connections with the creatures.

The resulting dissociation, which is often likened to that of a surgeon from a patient, allows a researcher to function with a minimum of stress. But given the emotional separation, a scientist may not realize when an animal is in pain—especially if the very existence of pain is in doubt. Nowadays, many researchers are aware of dissociation and seek objective ways to detect distress. And animal pain has come into its own. At a 1996 meeting on the *Guide to the Care and Use of Laboratory Animals*—a collection of guidelines that all researchers funded by the National Institutes of Health have to follow—veterinarian Gerald F. Gebhart of the University of Iowa stated that the pain-sensing apparatus is the same throughout the vertebrate kingdom and offered this rule of thumb: “If it hurts you, it probably hurts the animal.”

Increasingly, animal experimenters try to balance scientific imperatives with humaneness. Keith A. Reimann, a veterinarian at Harvard University’s animal facility, does AIDS-related research in monkeys. He insists that a macaque be euthanized as soon as it becomes sick, even if additional information might be gained by following the course of the illness. Franz P. Gruber of the University of Konstanz in Germany, who serves on a board overseeing animal experimentation, says his committee does not allow “death as an end point”—studies

in which the animal dies of the disease or procedure being studied. Instead the committee works with the researcher to define a stage at which the creature can be put out of its misery.

One area of concern to American veterinarians involves paralytic drugs. These agents immobilize an animal for surgery, for six or more hours at a time; anesthesia, however, may wear off in an hour or two. A few researchers are reportedly reluctant to administer additional anesthetics for fear that an overdose could kill the animal before the experiment is over, leading to a loss of data. But without such “topping up,” the animal may become conscious during the operation and not be able to convey, by twitch or cry, that it is in agony. And some scientists object to using painkillers because they do not want to introduce a new variable into the experiment.

Compassionate feelings for animals also influence studies, although researchers rarely admit to such unscientific, if creditable, motivations. When asked about their choice of species subjects, for example, three neuroscientists—working on monkeys, rats and frogs, respectively—replied unhesitatingly that it was determined by the scientific question at hand. But later in the conversation, the frog experimenter confided that he, personally, could not work on “a furry animal,” and the rat experimenter said he would not work with a cat or even with a rat in a more painful protocol.

The Three Rs

Scientists’ concern for animals first became visible professionally in the 1950s, when the behavioristic paradigm came under attack. British zoologist William M. S. Russell and microbiologist Rex L. Burch published *The Principles of Humane Experimental Technique*

(Methuen, London, 1959), in which they put forth the “three Rs.” This principle sets out three goals for the conscientious researcher: replacement of animals by in vitro, or test-tube, methods; reduction of their numbers by means of statistical techniques; and refinement of the experiment so as to cause less suffering. Although they took some decades to catch on, the three Rs define the modern search for alternatives.

Starting in the 1960s, humane organizations and governments began to fund studies in alternative methods. European governments, especially, have invested considerable resources. For the past 15 years, Germany has been giving out about \$6 million a year in research grants alone; the Netherlands spends \$2 million a year (including overheads for its alternatives center). The European Center for the Validation of Alternative Methods, a body set up in 1992 by the European Commission, requires another \$9 million annually. In the U.S., governmental interest has been comparatively low; the National Institute of Environmental Health Sciences (NIEHS) is now offering \$1.5 million worth of grants a year, for three years. And industry provides the \$1 million a year that the Center for Alternatives to Animal Testing (CAAT) at Johns Hopkins University disburses in grants. (Although 15 federal agencies have recently formed the Interagency Coordinating Committee for Validation of Alternative Methods, this venture is as yet unfunded.)

All this effort has yielded a variety of means for reducing animal use. Statistical sophistry, for example, is allowing the classical LD50 (or lethal dose 50 percent) test for acute toxicity to be eliminated. This test requires up to 200 rats, dogs or other animals to be force-fed different amounts of a substance, to determine the dose that will kill half a

1959

William M. S. Russell and Rex L. Burch state **three Rs** of animal experimentation

**REPLACE
REDUCE
REFINE**

1966

Animal Welfare Act
(AWA) passed
in the U.S.



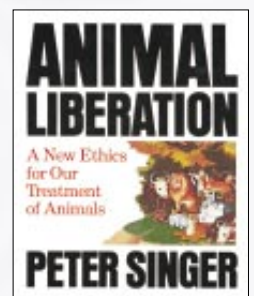
1969

Dorothy Hegarty founds Fund
for the Replacement of Animals in
Medical Experiments in U.K.

1970

**Amendments
to AWA**
cover warm-
blooded animals
and require
pain relief

1975



Peter Singer publishes
animal-liberation philosophy

COURTESY OF NEW YORK REVIEW OF BOOKS

group. Although in vitro alternatives are still far away—because the mechanisms underlying toxicity are poorly understood—protocols currently accepted worldwide call for a tenth the number of animals. The Organization for Economic Cooperation and Development, for example, asks for between three and 18 animals to be used: if the substance kills the first three, it need be tested no further.

Another unpleasant procedure is the LD80 test for vaccines. Experimental animals are vaccinated against a disease; they and a control group are then exposed to it. The vaccine passes only if at least 80 percent of the experimental group remains healthy and if 80 percent of the control group dies. Again using statistics, Coenraad Hendriksen of the National Institute of Public Health and the Environment in the Netherlands found a way of testing diphtheria and tetanus vaccines that requires simply checking the level of antibodies. Apart from greatly reducing the suffering, it uses half the number of animals.

“Data mining”—the sifting of mountains of information for relevant new findings—has also proved astonishingly helpful. Horst Spielmann of ZEBET, the German center for alternatives to animal testing, surveyed decades of industry data on pesticides and concluded that if mice and rats prove sensitive to a chemical, it does not have to be tested on dogs. Spielmann anticipates that 70 percent of the dog tests can be dispensed with. Klaus Cussler of the Paul Ehrlich Institute in Langen, Germany, reviewed data on the “abnormal safety test” for vaccines (called the “mouse and guinea pig safety test” in the U.S.), which involves vaccinating mice and guinea pigs and watching for untoward reactions. Their findings led to the test being dropped for vaccines checked in other

standard ways. “It was so senseless,” Cussler shakes his head.

In 1989, after observing that production of monoclonal antibodies in mice with tumors causes much suffering, ZEBET funded industry research into test-tube alternatives. Consequently, the antibodies, used in cancer therapy, are now rarely manufactured in mice in Europe (although mice remain the norm in the U.S.). Production of polio vaccines is another success story. In the 1970s the Netherlands used 5,000 monkeys a year; now kidney cell cultures from just 10 monkeys provide enough vaccine for everyone. Hormones or vaccines manufactured in cell cultures are also purer than those made in vivo (that is, in the animals themselves), so each batch need not be tested as before for safety and efficacy.

In 1993 the Department of Transportation became the first U.S. agency to accept in vitro tests, for skin corrosivity. The traditional test requires placing a substance on a rabbit’s shaved back to see how far it eats in. The test’s replacement uses reconstructed human skin or a biomembrane such as Corrositex—testimony to the role played by venture capital in finding alternatives. Several cosmetics manufacturers have entirely eliminated animal testing: they rely on in-house substitutes or use ingredients that have been tested in the past.

As yet, most researchers in the basic sciences see little hope of replacing animals. They stick to reduction or refinement, such as using an animal lower on the phylogenetic tree. The next spate of cuts in animal use, Spielmann predicts, will come in the field of medical education, for which alternative teaching tools have been devised. British surgeons, in fact, have not trained on animals since the 1876 act banned such use; instead they practice on human cadavers and

later assist experienced surgeons in actual operations. In the U.S., more than 40 of the 126 medical schools do not use animals in their regular curricula.

The most significant change has been in mind-set. Since 1985 in the Netherlands, every scientist starting research on animals has been required to take a three-week course. They learn hands-on procedures, proper anesthesia, specifications of inbred strains and so on—as well as the three Rs. First the students design an animal experiment; then they are asked to find ways of answering the same question without animals. The resulting discussion and hunt for information induces a new way of thinking. “It gives them time for reflection,” says Bert F. M. van Zutphen of Utrecht University, who pioneered the course. “It’s of utmost importance. To know how far I can go for my own conscience.”

The Laws

Another source of change in scientists’ attitudes has been legislation. In the U.S., laws tend to derive from isolated incidents. The Animal Welfare Act of 1966—the federal law regulating animal use—came into being because of Pepper, a Dalmatian believed by its owners to have been stolen and sold to a lab, and a *Life* magazine article depicting starving dogs in dealers’ pens. Perhaps the most significant change came in 1985, in the wake of two exposés involving primates. In Silver Spring, Md., macaques belonging to Edward Taub of the Institute for Behavioral Research were found to be chewing on their limbs, to which the nerves had been cut. And in 1984 videotapes from the University of Pennsylvania Medical Center displayed laboratory personnel mocking baboons whose heads had been smashed in dur-

1981



Center for Alternatives to Animal Testing founded in U.S.

JOHNS HOPKINS SCHOOL OF PUBLIC HEALTH

1985

Amendments to AWA

result from Silver Spring, Md., and Pennsylvania primate exposés



COURTESY OF NATIONAL PRESS BOOKS

1992

European Center for the Validation of Alternative Methods founded



1996

Second World Congress on Alternatives held in the Netherlands

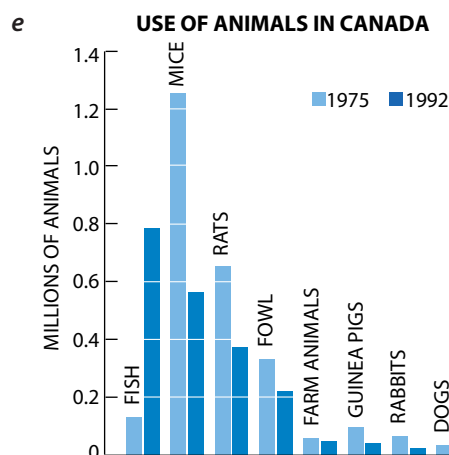
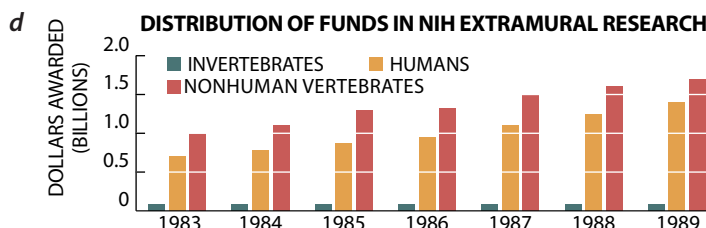
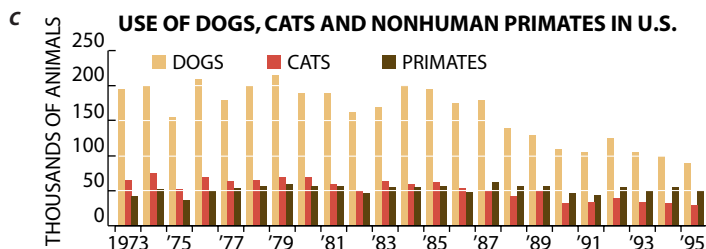
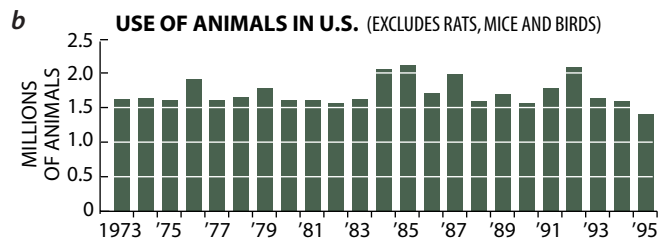
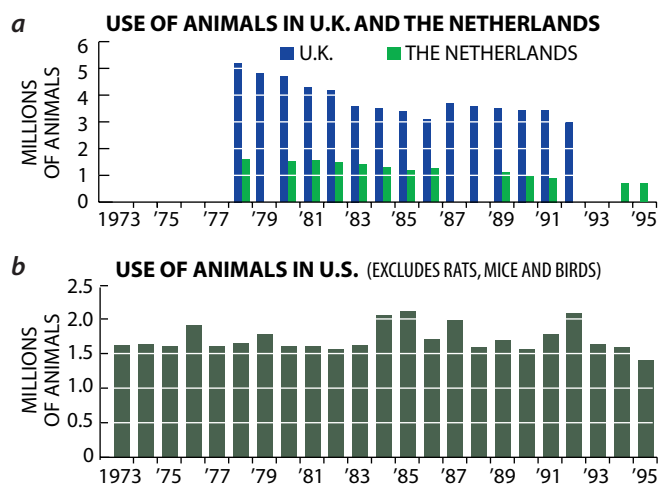
1993

First World Congress on Alternatives held in the U.S.

The Numbers of Research Animals

Use of animals in European laboratories has been slowly declining (*a*). In the U.S., the available statistics (*b*) include primates, dogs, cats, guinea pigs, rabbits, hamsters and others but exclude rats, mice and birds—an estimated 17 million additional animals per year. Primate use is roughly constant, although the numbers of cats and dogs (*c*) is declining. (In many instances, dogs are being replaced by pigs, calves and other farm animals. These have been counted since 1990 but are not included in the chart.) The National Institutes of Health supports research into invertebrate models (*d*); however, funding has been increasing more steeply for vertebrate (and human) studies. In Canada, animal numbers (*e*) have hovered at around two million a year, but fish have replaced mammals in many areas, especially toxicology.

BRYAN CHRISTIE; SOURCES: USDA (a-c); NATIONAL CENTER FOR RESEARCH RESOURCES, NIH (d); CANADIAN COUNCIL ON ANIMAL CARE (e)



ing experiments on head trauma. The outcry following these revelations allowed Senator Robert Dole of Kansas to bring an amendment to the act. It established institutional animal care and use committees (IACUCs) at each facility using regulated animals and required laboratories to exercise dogs and to ensure the psychological well-being of primates.

The “well-being” clause can be considered an instance of the public’s imposing a scientific paradigm on scientists. An inspector from the U.S. Department of Agriculture, which administers the Animal Welfare Act, sought expert advice at that time on primate psychology. There was no such thing, he was told. Now, just 10 years later, primates have emotions. At the 1996 NIH meeting, Gebhart listed fear, anxiety, boredom, separation and isolation as conditions to which experimenters should attend in their subjects. And a few labs are even trying to enrich the lives of their rabbits.

The laws have generally had the effect of driving up the costs of animal research. Animal protectionists complain, however, that the Animal Welfare Act and its amendments invariably get diluted at the implementation stage. The act, for instance, refers to warm-blooded animals, but the regulations written by the USDA exclude rats, mice and birds. The agency says it does not have funds for inspecting the laboratories that use these creatures, which is true; animal welfarists, however, say the omission originally came from lobbying by the biomedical community. In 1990 humane organizations sued to have these animals included. Although they initially won, the suit was thrown out on appeal, on the grounds that animal protectionists have no legal standing; only those who are injured—that is, the rats, mice and birds—can bring a civil suit. Dale Schwindaman of the USDA has promised, however, to include these animals within the next five years.

Another controversy has to do with so-called performance standards. When writing regulations for the 1985 amendments, the USDA refrained, for example, from stating how many times a week the dogs had to be walked. Such specifics are referred to as engineering standards. Instead the agency allowed each facility to come up with its own plans for dog and primate well-being, the “performance” of which was to be evaluated. (Because these plans are kept in-house, and not with the USDA, the public cannot obtain them through the Freedom of Information Act.)

Researchers are enthusiastic about the flexibility of performance standards, whereas Martin L. Stephens of the Humane Society of the U.S. calls them “euphemisms for no standards.” USDA inspectors are divided. Some argue that the standards are vague and unenforceable. Among others, Harvey McKelvey of the USDA’s northwestern region says they let him use his judgment: “If I see



ANTIVIVISECTION POSTER attacks the rationales behind animal research.

an animal is bored with its toy, I can write that it needs a new one. I couldn't do that with engineering standards." The new NIH guide also embraces performance standards.

The animal care committees have empowered those scientists who wish to cut down on wastage and improve conditions for animals. "If you have an institution with conscientious people, the IACUC system works fairly well," says Ralph A. Meyer of Carolinas Medical Center. Cathy Liss of the Animal Welfare Institute in Washington, D.C., agrees that some committees do far better than the law. But there is concern about the remainder. In 1992 an audit of the USDA's enforcement activities by the Office of the Inspector General revealed that out of 26 institutions selected at random, 12 "were not adequately fulfilling their responsibilities under the act." Everyone agrees that enforcement is inadequate: at present, there are only 69 inspectors, who may not be able to visit each of the 1,300 regulated laboratories (and also animal dealers, transporters and exhibitors) every year.

As a result, the inspectors rely on whistle-blowers. "We need eyes out there," McKelvey explains. It might be an animal-rights activist who has infiltrated a laboratory: groups such as People for the Ethical Treatment of Animals (PETA) prepare detailed case histories that they

present to the USDA or the NIH. Or it might be a researcher or technician.

Still, the USDA can offer few reassurances to informants. A former member of the animal care committee at New York University Medical Center claims to have been fired in August 1995 for protesting irregularities in N.Y.U.'s labs and cooperating with the USDA's investigations. The university states that his position became redundant. But the scientist, along with an administrator who was also dismissed, is suing N.Y.U., as well as the USDA—which, he says, failed to provide whistle-blower protection. (The agency did fine N.Y.U. \$450,000 for assorted violations of the Animal Welfare Act.) Several USDA inspectors express frustration with their agency's provisions on informants. "We can't protect a whistle-blower," McKelvey says. "The regulation is weak."

Unlike civil-discrimination suits, which require only a concatenation of circumstances, the USDA needs to prove that the person was fired because of having blown the whistle.

Also controversial are the statistics on pain and distress provided by the IACUCs to the USDA. They indicate that in 1995, 54 percent of the regulated animals had no pain or distress, 37 percent had distress alleviated by painkillers, and only 8.8 percent suffered unalleviated pain or distress. The data have been widely criticized for being unreliable, because the USDA does not specify how to classify pain. Andrew N. Rowan of the Tufts University Center for Animals and Public Policy has noted that some rather painful procedures, such as toxicity testing or antibody production, are commonly placed in the nonpainful category. Although the USDA proposed a pain scale in 1987, it was withdrawn after objections by researchers.

There are difficulties with assessing animal distress. Nevertheless, many European nations, as well as Canada, Australia and New Zealand, have developed pain scales in which each procedure is assigned a grade. As a result, their reports are more informative. The Netherlands listed in 1995 that 54 percent of animals had minor discomfort, 26 percent had moderate discomfort, and 20 percent suffered severe discomfort.

A pain scale would make it easier for IACUCs to rate the suffering involved in different schemes for doing an experiment. At present, the committees are required to certify that the animal researcher has looked for alternatives and that the number of animals used is reasonable. Alan M. Goldberg of CAAT wishes that they would also evaluate the experimental design. "Right now, using method A, they check: Is it the right number of animals? They don't look at method B or C"—which could involve *in vitro* techniques. Nor—unlike committees in Germany, Australia and elsewhere—are they required to weigh the benefits of research against the suffering or to include representatives of animal-welfare organizations in the review process. (The IACUCs do have to include someone unaffiliated with the institution, but who fills that position is again a source of controversy.)

The Propaganda

Change in the U.S. has been slow and painful. Notwithstanding some evolution of practices, the ferocity of the attacks by the most fervent animal rightsists has led to a sense of moral outrage and an unwillingness to compromise—on both sides. Almost all activists insist that animal research is unnecessary; to them, investigators using animals are cruel and corrupt, consumed by a desire for ever more papers and grants. One antivivisection tract is entitled *Slaughter of the Innocent*, and the cover of another features splashes of blood. To animal liberators, the killing of more than six billion animals a year, mostly for food, represents a holocaust, and Adolf Hitler's doctors are proof that experimenters can be inhumane.

Many animal researchers, in turn, think of animal rightists as being brainless "bunny huggers" at best and dangerous fanatics at worst. Leaflets published by the American Medical Association represent the animal-rights position as equating humans with animals; a quote from Ingrid Newkirk of PETA, "A rat is a pig is a dog is a boy," is offered as evidence. (Newkirk claims her statement was "When it comes to feeling pain, a rat is a pig is a dog is a boy.")

In an essay entitled "We Can't Sacrifice People for the Sake of Animal Life," Frederick K. Goodwin, former head of the National Institute of Mental Health, has argued that the issue of animal rights threatens public health. In this vein, re-

search advocates sometimes portray proposals to control animal research as being attacks on human life. For instance, one organization advises this response to a query about experimentation on pound animals: "How would you feel if the one research project that may save your child's life was priced out of existence because pound animals were banned?" Some writers invoke Hitler as proof that animal advocates are antihuman: he was an animal lover who passed anticruelty laws in 1930s Germany.

Finding itself under moral—and sometimes physical—siege, the research community has often retreated behind electronic surveillance systems—and an ethical code that frequently denounces internal dissent as treason, "giving ammunition to the enemy." One scientist interviewed for this article said that if his criticisms became known, he would be fired. In 1991 two animal researchers, John P. Gluck and Steven R. Kubacki of the University of New Mexico, wrote a treatise deploring the lack of ethical introspection in their field. Gluck testifies that the article quickly changed his status from an insider to a distrusted outsider. Arluke's studies revealed an absence of discussion about ethics: in 33 of 35 laboratories, moral positions were defined institutionally. Newcomers were given to understand that senior scientists had answered all the difficult questions, leaving them little to worry about.

The insulation has made it difficult for changes in other branches of the life sciences—or from across the Atlantic—to filter in. Primatologists, for instance, have been discussing complex emotions in their subjects for decades. But many American experimenters still refuse to use the word "suffering," because it suggests an animal has awareness. Even the word "alternatives" is suspect; instead the NIH describes these as "adjuncts" or "complements" to animal research. Some researchers seem to regard the three Rs as an animal-rights conspiracy. Robert Burke of the NIH has stated: "To argue that we must refine our methods suggests that they are currently inadequate or unethical.... In my view, it is intellectually dishonest and hypocritical to continue to advocate the original three Rs as a goal for science policy. It is also, without question, dangerous to give our enemies such useful tools with which to pervert the scientific enterprise."

Of the 17 institutes included in the NIH, only the NIEHS has been active in researching alternatives. Following a di-

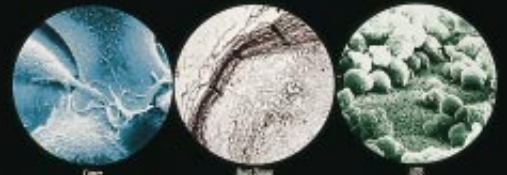
rective by Congress, the NIH awarded about \$2.5 million in earmarked grants between 1987 and 1989. But F. Barbara Orlans of the Kennedy Institute of Ethics at Georgetown University charges that the money did not constitute a special allocation for alternatives: 16 of the 17 grants went to studies that had traditionally been funded. (Like other public health agencies worldwide the NIH supports research into invertebrate, in vitro and computer models that are not billed as alternatives.)

In 1993 Congress directed the NIH to come up with a plan for implementing the three Rs. The resulting document, entitled "Plan for the Use of Animals in Research," is an overview of biomedical models, with some emphasis on nonmammalian systems. "The central message of the plan," explains Louis Sibal of the NIH, "is that scientists have to decide for themselves what the best method of solving their problem is." Whereas the European Union plans to cut animal use in half by the year 2000, a 1989 NIH report stated that animal use is not likely to decrease.

One arena in which the propaganda battles have been especially fierce is the classroom: both sides see dissection as the key to the next generation's sympathies. Animal advocates say dissection in schools is unnecessary and brutalizing and that the 5.7 million vertebrates (mostly wild frogs, but also cats, fetal pigs, pigeons and perch) used every year are procured in inhumane ways. Research advocates fear that without dissection, instruction will be inadequate, and fewer students will be attracted to or equipped for the life sciences.

In 1989, when the National Association of Biology Teachers (NABT) announced a new policy encouraging alternatives, it provoked a violent reaction. Barbara Bentley of the State University of New York at Stony Brook, for instance, denounced the monograph on implementing the policy as "an insidiously evil publication—evil because it is a barely disguised tract produced by animal rightists." An intense campaign followed, and in 1993 the NABT issued a new policy statement, warning teachers to "be aware of the limitations of alternatives." There is no high school dissection in most European countries.

If we stop animal research, who'll stop the real killers?



Without animal research we couldn't have put an end to polio, smallpox, rabies and diphtheria. Now, some would like to put an end to animal research. Obviously, they don't have cancer, heart disease or AIDS.

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MEDICAL NECESSITY of animal experiments is emphasized in a pro-research poster.

"It is possible to be both pro research and pro reform," Orlans says. She and others in the troubled middle have a simple message: the impasse must end. Animal liberators need to accept that animal research is beneficial to humans. And animal researchers need to admit that if animals are close enough to humans that their bodies, brains and even psyches are good models for the human condition, then ethical dilemmas surely arise in using them. But the moral burden is not for scientists alone to bear. All of us who use modern medicine and modern consumer products need to acknowledge the debt we owe to our fellow creatures and support science in its quest to do better by the animals. SA

Further Reading

- IN THE NAME OF SCIENCE: ISSUES IN RESPONSIBLE ANIMAL EXPERIMENTATION. F. Barbara Orlans. Oxford University Press, 1993.
- THE MONKEY WARS. Deborah Blum. Oxford University Press, 1994.
- THE ANIMAL RESEARCH CONTROVERSY: PROTEST, PROCESS AND PUBLIC POLICY. Andrew N. Rowan and Franklin M. Loew, with Joan C. Weer. Center for Animals and Public Policy, Tufts University School of Veterinary Medicine, 1995.
- More coverage of the animal-rights debate is available on-line at <http://www.sciam.com>