SCIENCE, MEDICINE, AND ANIMALS

National Academy of Sciences
Institute of Medicine

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Prepared for the Councils of the National Academy of Sciences and the Institute of Medicine

Committee on the Use of Animals in Research

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Photomicrographs of the drug AZT, which was tested and developed in animals for the treatment of AIDS in humans, taken at magnifications of 30x and 50x and illuminated with polarized and darkfield lighting techniques.
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Committee on the Use of Animals in Research

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Preface

If human beings had chosen a hundred years ago to stop using animals in scientific and medical research, the world would be a very different place today. Many of us are here because we did not die as children, or our parents did not die, from diseases that have been controlled through the knowledge gained from animal research. The biological information that has unlocked the secrets of genetics, shed light on the workings of the brain, and made it possible to understand new diseases like AIDS would not exist. Even the animals that we keep as pets and raise for food would live shorter and less healthy lives, because many of the vaccines and treatments that have become staples of veterinary medicine would never have been developed.

Scientists assume two major responsibilities when they study animals in research. The first is to ensure that the use of animals contributes to the advancement of knowledge. The second is to minimize any possible pain or distress that the animals may experience. Researchers take both of these obligations very seriously.

Scientists and nonscientists alike have been working for well over a century to promote and formalize these responsibilities. The first humane societies were established in the 19th century, first in England and then in the United States. Similarly, researchers have followed formal guidelines at least since the 1890s, when the Hygienic Laboratory, the forerunner of the National Institutes of Health, adopted a statement on humane animal care. To this day, researchers and animal welfare advocates have worked to establish standards that ensure the humane care and use of animals while permitting research to proceed, and the well-being of research animals has increased as a result.

We recognize that the use of animals in science may not always have been as well-justified or well-executed as today's sensibilities require. Yet such use today in the United States is as well-regulated and overseen as any in the world. In such a setting mistakes are rare, and the benefits to our society are actually and potentially very great.

In recent years, a new voice has increasingly made itself heard in discussions of animal research. Many of the proponents of this new viewpoint are motivated not by a desire to see that research animals are treated humanely but by a desire to eliminate all uses of animals, whether for research or food production. Some of these individuals deny, despite overwhelming evidence to the contrary, that animal research has improved human and animal health. Some accuse scientists of routinely mistreating animals and of conducting research that is unnecessary, although they are unable to provide evidence to support these accusations. The number of people who take this position is small, but they have had a considerable impact on the public and on the research community.

These individuals have adopted a new banner, that of "animal rights," to describe their movement, but actually they are an extension of an old tradition. In England, proponents of the idea to eliminate animal research totally have traditionally been known as anti-vivisectionists. At the end of the 19th century, the anti-vivisectionist movement was strong in England and the United States, before declining in the 20th century as biomedical advances dependent on animal research became increasingly obvious. Now the anti-vivisectionist movement has returned with a new name and an even broader agenda.

The sentiments may not be new, but the tactics being employed by animal rights advocates are thoroughly modern. They have skillfully used the media and the political process to advance their position. They have taken their message to the schools, presenting to children an inaccurate and emotionally distorted picture of animal research. Elements within the animal rights movement have even resorted to violence, breaking into laboratories, setting fires, destroying records, and harassing researchers.

The National Academy of Sciences and Institute of Medicine view these developments with growing alarm. Despite the remarkable progress that animal research has produced, many diseases and illnesses still remain largely untreatable, and significant progress toward prevention or treatment will not occur without further animal research. Furthermore, even though only a small percentage of the members of the National Academy of Sciences or Institute of Medicine use animals in their research, our institutions are concerned about the animal rights movement because of the broad antiscience message implicit in its position.

The Councils of the National Academy of Sciences and Institute of Medicine have prepared this position paper to present our view of animal research. We have sought to answer the most commonly asked questions about animal research and to depict some of the many ways in which animal research has benefited, and will continue to benefit, human and animal health and well-being and advance our knowledge of biological processes. We have used real people in the introduction to emphasize the fact that, behind the statistics of lives saved and illnesses reduced, lie real stories of human triumph and tragedy.

In writing this position paper, our intention has been not to end the debate on whether and how animals are used in research; rather, it has been to inform that debate. By describing the history, status, and potential of animal research, we hope to make it possible for people to judge for themselves the necessity and merit of continuing that research.

FRANK PRESS
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SCIENCE, MEDICINE, AND ANIMALS

S everal months before his thirtieth birthday, Greg Maas discovered a lump in his abdomen that would not go away.[1] He went to his doctor for tests, and then to a specialist for a biopsy, and 2 weeks before his birthday he was told that he had non-Hodgkin's lymphoma, a cancer of the lymph nodes that was once invariably fatal. An initial round of chemotherapy controlled the cancer for 3 years, during which time Maas and his wife had their second child. When the cancer reappeared, Maas underwent a more aggressive round of chemotherapy, followed by a bone marrow transplant to repair the damage done to his immune system by the chemotherapy. Today, several years after the treatment, the cancer appears to have been eliminated.

The drugs used to kill the cancer cells in Greg Maas's body have been screened and tested over the past several decades in inbred strains of mice susceptible to leukemia. These mice are genetically identical, making it possible to compare chemotherapeutic compounds and develop treatment regimes that minimize the compounds' side-effects. More recently, inbred mice have been developed that contract a disease virtually identical to non-Hodgkin's lymphoma, offering both the possibility of more specific chemotherapies and basic information about the biological causes of the disease.[2]

Mice and other laboratory animals have also been instrumental in the development of organ transplantation. By studying inbred mice with slightly different immune systems, researchers discovered that transplanted organs are rejected because of immunological reactions in the host. This work led to tissue typing techniques that make it possible to identify the best donor for an organ transplant. At the same time, studies of mice, rats, dogs, and other animals led to drugs that suppress the immune reaction to a transplanted organ, greatly increasing the transplant's survival. Today, many thousands of people are alive because of transplanted kidneys, hearts, lungs, livers, bone marrow, and other organs and tissues.[3]

In 1976, at the age of 52, Gloria Barry sank into a depression worse than any she had ever experienced. Her family doctor referred her to a psychiatrist, who at first treated her with standard antidepressants. But the antidepressants tended to make Barry slightly manic, leading her doctor to conclude that she actually suffered from manic-depressive illness, which affects as many as 1 in 200 adults. He therefore decided to treat her with lithium, a drug that had been used for several decades to treat manic-depression. The result was what Barry calls a "miracle": her depression quickly disappeared and in the years since then has never returned.

The psychiatric effects of lithium were discovered in 1949 by an Australian psychiatrist who was trying to find a toxic substance responsible for mania. In the course of his research, he observed that one compound—lithium urate—had a calming effect on guinea pigs. He then tested lithium in humans and obtained dramatic results: patients who had been manic for years showed greatly relieved symptoms. However, lithium was denied immediate acceptance, because in the 1940s it had been used in very high doses as a substitute for sodium in low-sodium diets, and severe intoxication and several deaths had resulted. It took another two decades of research with animals, and subsequently humans, before lithium gained acceptance as a safe and effective treatment for manic–depressive illness.[4]

When Charlotte Evert was 8 weeks old, she contracted pneumonia, which was successfully treated using antibiotics. During follow-up studies, she was found to have hypoplastic pulmonary artery syndrome, a potentially fatal narrowing of the arteries leading from the heart to the lungs. At 12 months, she became one of the 600,000 people to undergo open-heart surgery in the United States each year. However, by the age of 3, her heart was again failing because of the excessive pressures required to pump blood to her lungs. Doctors considered a heart–lung transplant, but such procedures are still experimental and are rarely used in children. So Charlotte instead underwent an experimental procedure known as balloon angioplasty to widen the arteries to her lungs and improve blood flow. The procedure was totally successful: it has given Charlotte a normal life, and it is unlikely that she will ever need a heart–lung transplant.

Balloon angioplasty for the treatment of cardiovascular disease was developed by a Swiss physician in the 1970s using dogs and cadavers. The technique involves passing a very narrow catheter through an artery to the blood vessels very near the heart. When the catheter encounters a narrowing of the arteries, whether congenital or caused by the buildup of cholesterol, a balloon surrounding the catheter is inflated, widening the vessel. Today, more than 200,000 people in the United States receive balloon angioplasty each year for the treatment of heart disease, and various catheterization techniques are saving the lives of an increasing number of children with congenital heart defects.

When Jaques Washington, show here with his daughter, was diagnosed as having osteogenic sarcoma in his upper left arm, surgeons performed a daring new procedure of implanting a metal rod in place of the cancerous bone. Because his muscle and tendon were saved, he is still able to use his left arm.

People who recover from previously incurable diseases are the most obvious beneficiaries of research involving animals. But in fact we all benefit from animal research. The vaccines against diphtheria, whooping cough, tetanus, and polio that we received as children were developed and are still tested in animals. New antibiotics used to treat everything from minor infections to severe illnesses are continually being discovered and then tested in animals to make sure that they do not cause unexpected side effects. We are much more confident about the safety of food, water, pharmaceuticals, and household products that we use than we would be without animal research.[5]

This white paper contains a number of examples, set off from the main text, of diseases that have been controlled through animal research and of diseases that will be cured only through continued animal research. These examples can be multiplied many times over. Nearly half of the biomedical investigations carried out in the United States would not have been possible without laboratory animals. More than two-thirds of the research projects that have led to the Nobel Prize in physiology or medicine directly involved animal experiments.[6] Laboratory animals are an indispensable part of biomedical research, and their contributions to health, well-being, and increased understanding are unassailable.

Research using laboratory animals has also had a less direct but ultimately even more important benefit. It has taught us more about the world we live in and about the living things that inhabit that world. This process of discovery is a profound intellectual adventure in its own right. But it is also true that without this fundamental knowledge, most of the clinical advances described in these pages would not have occurred. This connection between scientific understanding and clinical applications will become even stronger as biomedical research reveals more of the basic principles of biological systems.

Why Are Animals Used in Research?

Human beings use animals for a wide variety of purposes, including research. The approximately 260 million people in the United States keep about 110 million dogs and cats as pets. More than 5 billion animals are killed in the United States each year as a source of food. Animals are used for transportation, for sport, for recreation, and for companionship.[7]

Animals are also used to learn more about living things and about the illnesses that afflict human beings and other animals. By studying animals, it is possible to obtain information that cannot be learned in any other way. When a new drug or surgical technique is developed, society deems it unethical to use that drug or technique first in human beings because of the possibility that it would cause harm rather than good. Instead, the drug or technique is tested in animals to make sure that it is safe and effective.

Animals also offer experimental models that would be impossible to replicate using human subjects. Animals can be fed identical and closely monitored diets. As with inbred mice, members of some animal species are genetically identical, enabling researchers to compare different procedures on identical animals. Some animals have biological similarities to humans that make them particularly good models for specific diseases, such as rabbits for atherosclerosis or monkeys for polio. (The polio vaccine was developed, and its safety is still tested, in monkeys.) Animals are also indispensable to the rapidly growing field of biotechnology, where they are used to develop, test, and make new products such as monoclonal antibodies.

Researchers draw upon the full range of living things to study life, from bacteria to human beings.[8] Many basic biological processes are best studied in single cells, tissue cultures, or plants, because they are the easiest to grow or examine. But researchers also investigate a wide range of animal species, from insects and nematodes to dogs, cats, and monkeys. In particular, mammals are essential to researchers because they are the closest to us in evolutionary terms. For example, many diseases that affect human beings also affect other mammals, but they do not occur in insects, plants, or bacteria.

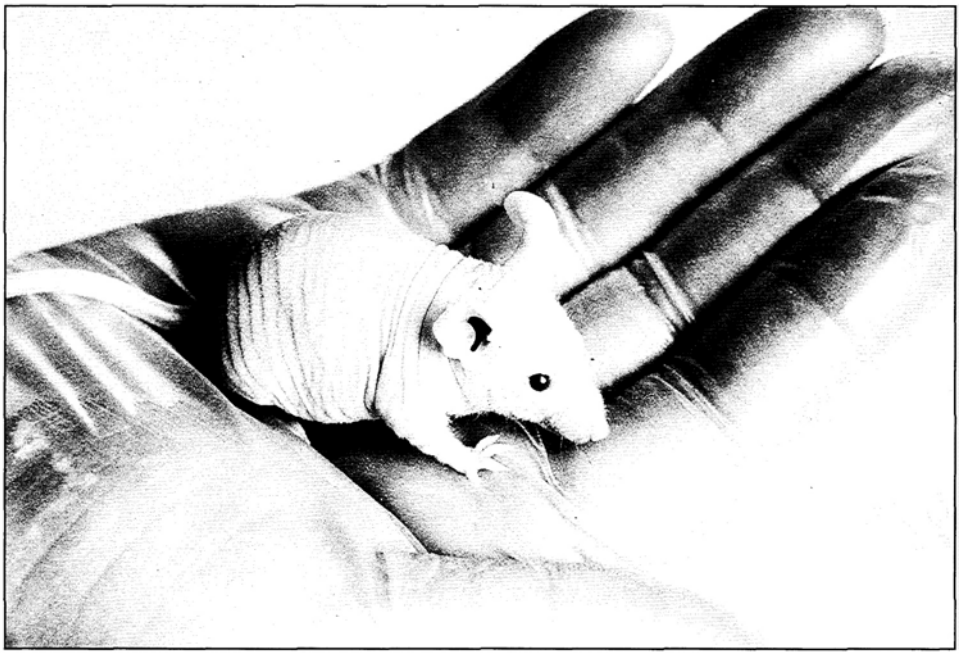
Far fewer animals are used in research than are used for other purposes. An estimated 17 to 22 million vertebrate animals are used each year in research, education, and testing—less than 1 percent of the number killed for food.[9] About 85 percent of these animals are rats and mice that have been bred for research. In fiscal year 1988, about 142,000 dogs and 52,000 cats were used in experimentation, with 40,000 to 50,000 of those dogs being bred specifically for research and the others being acquired from pounds.[10] Between 50,000 and 60,000 nonhuman primates, such as monkeys and chimpanzees, are studied each year, many of them coming from breeding colonies in the United States.[11]

How Have Animals Contributed to Improving Human Health?

A hundred years ago, good health was much rarer than it is today. In 1870, the leading cause of death in the United States was tuberculosis.[12] Of all the people born in developed countries like the United States, a quarter were dead by the age of 25, and about half had died by the age of 50. Those fortunate enough to have survived to old age had probably experienced several bouts with diseases like typhoid fever, dysentery, or scarlet fever.[13]

Today, the leading causes of death in the United States are heart disease and cancer—diseases of old age rather than infancy and childhood. Fully 97 percent of Americans live past their 25th birthday, and over 90 percent live to be more than 50.

Better nutrition and sanitation did much to reduce the toll from infectious diseases. But these diseases could not have been eliminated as significant causes of death and illness without animal research. Animal research has also made people healthier, since it has contributed to virtually eliminating many infectious diseases like polio or rheumatic fever that can be debilitating without causing death. Animal research has even contributed to better nutrition and sanitation, since it has helped to identify the agents that contribute to good or bad health.

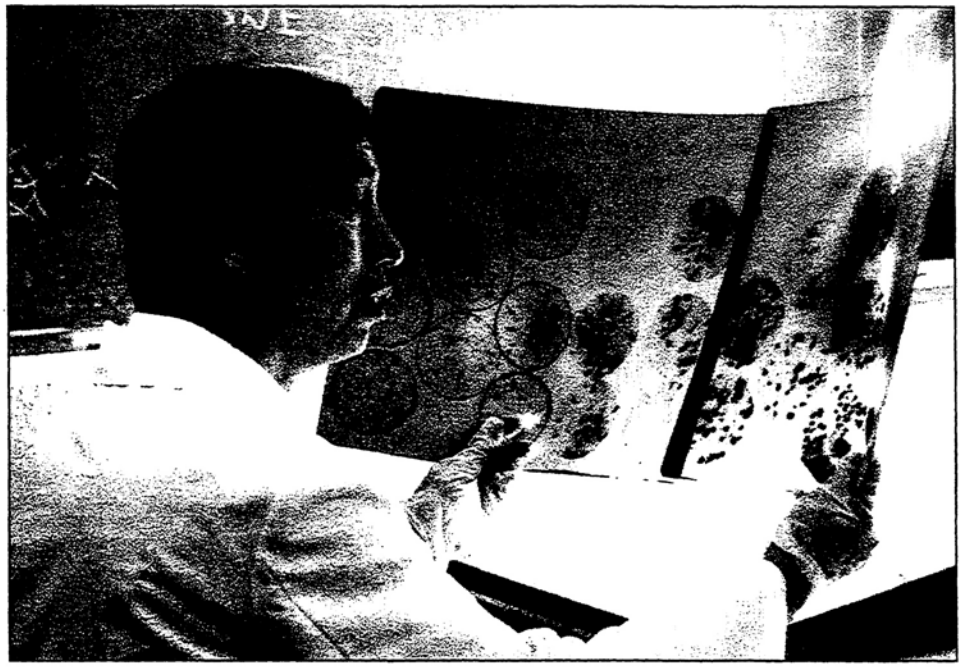


Because of a genetic defect, nude mice such as the one shown here have no thymus and cannot make certain cells essential for various immune responses. This characteristic makes them extremely helpful to scientists working in immunology research.

Methods to combat infectious diseases have not been the only dividends of animal research. Surgical procedures, pain relievers, psychoactive drugs, medications for blood pressure, insulin, pacemakers, nutrition supplements, organ transplants, treatments for shock trauma and blood diseases—all have been developed and tested in animals before being used in humans.[14] In fact, according to the American Medical Association, "Virtually every advance in medical science in the 20th century, from antibiotics and vaccines to antidepressant drugs and organ transplants, has been achieved either directly or indirectly through the use of animals in laboratory experiments."[15]

Animals will continue to be essential in combatting human illness. Though human health has improved greatly over the last 100 years, much remains to be done. Many of today's leading killers, such as cancer, atherosclerosis, diabetes, Alzheimer's disease, and AIDS, remain inadequately understood. Furthermore, debilitating conditions such as traumatic injury, strokes, arthritis, and a variety of mental disorders continue to exact a severe toll on human well-being.

Animal research will be no less important in the future than it has been in the past. Indeed, it may be even more important, because the questions remaining to be answered generally involve complex diseases and injuries that require whole organisms to be studied.



A scientist compares similarities in baboon virus and HIV-1. This is one of the studies being conducted to help discover the proper sequence of the AIDS virus.

HEART SURGERY

In the nineteenth century, physicians could do very little to treat heart disease, because there was no way to repair the heart in living patients. But around the turn of the century, pioneering surgeons began to operate on the hearts of dogs and other animals, experimenting with the procedures needed to work directly on the heart. They concentrated on repairing heart valves, since damaged valves were a common consequence of rheumatic fever and other illnesses. By 1923 the procedures had advanced to the point that they were successfully used on a 12-year-old comatose girl, who lived for another 4 years before succumbing to pneumonia.

Nevertheless, heart surgery remained very limited, because the heart could be stopped only for very short intervals if the patient were to survive. Some way had to be found of stopping the heart while continuing blood circulation so that more extensive repairs could be made. Consequently, researchers began working with animals in the 1930s to develop pumps that could circulate and aerate the blood. It was a complex task, requiring basic knowledge of such factors as blood clotting, transfusions, the constituents of the blood, and the effect of prolonged pumping on both the blood and the heart. But in 1953 the first operation using a heart–lung machine was performed on a human being, inaugurating the modern era of open-heart surgery.

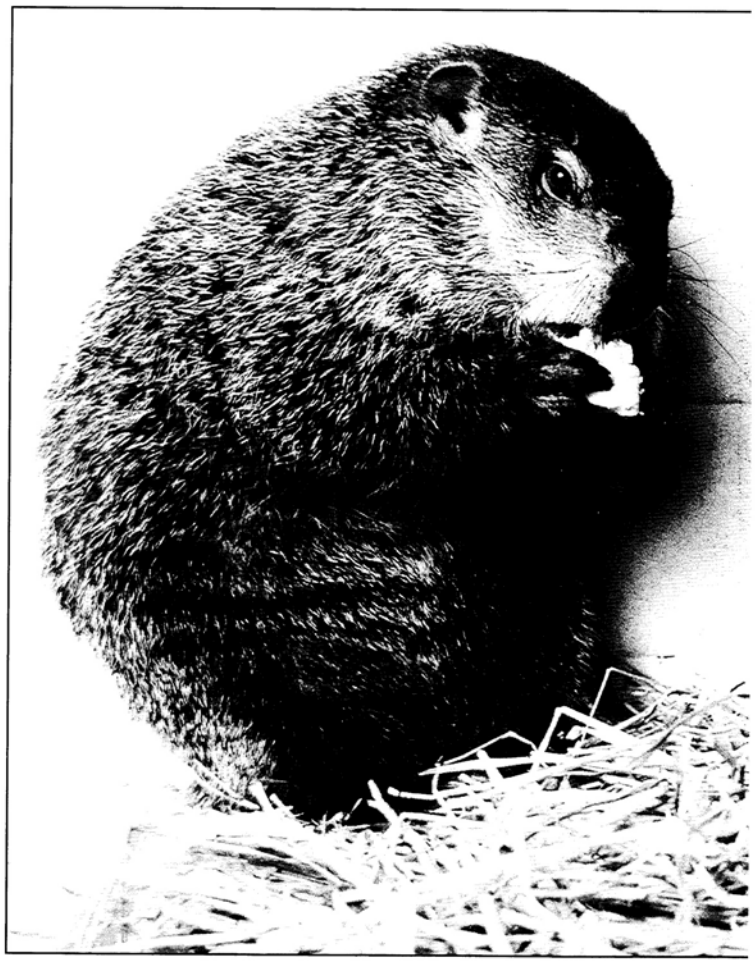
Today, heart surgery has extended and improved the lives of many people. More than 80 percent of the infants born with congenital heart defects can be treated surgically and lead normal lives. Some 3 million people undergo various kinds of cardiovascular operations and procedures in the United States each year. Without animal research, none of these techniques could have been developed.

How Has Science Advanced as a Result of Animal Experimentation?

Scientists use animals to do both basic and applied research. Applied research seeks to answer specific questions about a given disease or condition, usually in the context of a specific prevention therapy or treatment. Basic research seeks to build a base of knowledge about living organisms and how they function. Both forms of research are essential to continued medical progress.

Some people contend that scientists should use animals only for applied research, since that way the use of animals can be clearly associated with immediate benefits. But such a contention does not take into account the way scientific research works. Basic research provides the foundation on which applied research is built, and without the former the latter would cease.[16] For example, research that examines the nerve cells responsible for vocalization in rhesus monkeys may seem far removed from any practical applications. But over 6 million people in the United States suffer from some kind of speech impairment, and without this fundamental research into speech mechanisms the hope for new treatments is slim.

It is difficult to predict which basic research will lead to eventual applications. But much of it eventually does, sometimes in areas far removed from the original research. All living things share certain characteristics, and basic research on one organism often produces knowledge that applies to many other organisms.



Both basic and applied research using animals are subject to a number of safeguards that make it very unlikely that the research will be unnecessary or poorly done. Before an experiment using a vertebrate animal is carried out, the protocol for that experiment must be reviewed by an institutional committee that includes a veterinarian and a member of the public, and during the research the animal's health and care are monitored regularly. Researchers need healthy animals for study in science and medicine, because unhealthy animals could lead to erroneous results. This is a powerful incentive for scientists to make certain that any animals they use are healthy and well-nourished.[17] Furthermore, research involving animals is expensive, and because funding is limited in science, only high-quality research is able to compete effectively for support.

These two woodchucks carry a virus similar to hepatitis B in their blood and are being studied to understand the link of the virus to liver cancer.

MYASTHENIA GRAVIS

Myasthenia gravis is a disease that causes excessive fatigue and muscle weakness, in some cases leading to death. The history of how researchers have come to understand the disease, which afflicts about 150,000 people in the United States, illustrates how a number of seemingly unrelated strands of biological knowledge can merge to form a significant advance.

An important part of the story begins with curare, a poison derived from plants, insects, and snake toxins that the Indians of Central and South America used on the tips of their arrows to immobilize and kill prey and enemies, in the nineteenth century, French researchers showed in frogs and other animals that curare blocks the transmission of signals from the nervous system to muscles. However, the transmission process itself was not well understood until the 1930s, when English researchers demonstrated in animals that nerves communicate with muscles by releasing a chemical, acetylcholine, that activates receptor molecules on the muscles. Curare somehow blocked the action of acetylcholine, paralyzing the muscle.

Next, two chemists from Taiwan isolated a powerful toxin from snake venom that paralyzed animals by blocking the receptors for acetylcholine. Other investigators used this toxin to obtain large quantities of the receptor from electric eels, which have many receptors in their electricity-generating organs. When researchers injected this receptor into rabbits, the rabbits developed a syndrome virtually identical to myasthenia gravis. The rabbits were making antibodies to the injected receptors, and these antibodies were attacking the rabbits' own receptors, causing the muscle weakness characteristic of the disease.

In this way, scientists came to realize that myasthenia gravis was an autoimmune disease, in which a person's own immune system attacks acetylcholine receptors on muscles. Treatments have been available for some time to lessen the effects of the disease—by improving the transmission of signals, for instance, or by suppressing the effects of the immune system. Further research, again being conducted in animals, is seeking a permanent cure by focusing on what causes the immune system to attack the body's own acetylcholine receptors.

Why Are Animals Used to Study the Brain?

Just as animals are used as models to study the heart or lungs of human beings, so they are used as models to gain insight into the human brain and nervous system. But the brain is much more complex and subtle than any other organ. Not only does it control the functions of the rest of the body but it is responsible for movement, communication, memory, perception, emotion—all of the activities encompassed by the general term behavior.

It may seem paradoxical to use animals to study the one organ that most clearly distinguishes humans from animals. Animals, after all, are not capable of many of the more complex functions found in humans, such as advanced language, moral reasoning, or complex learning skills. But many of the basic structures and functions of the brain are common to all animals. Since complex human thoughts are built on a foundation of simpler mental processes that are evident in animals, animal studies can shed light on uniquely human behaviors.

Animal research involving the brain has already produced dramatic improvements in human health and well being, and it promises many more.[18] Drug therapies developed in part in animals have revolutionized the treatment of mental illness in the last generation. For example, chlorpromazine, which was developed in the 1950s using animals, and other antipsychotic drugs have eliminated the horrific conditions that used to exist in the wards of mental hospitals where the most severely disturbed patients were once kept. More generally, drugs have proven effective in treating the symptoms of schizophrenia, which affects millions of Americans. Anti-anxiety drugs that have proven of immense benefit in treating human anxiety are developed and tested with animals. Animal tranquilizers have also made it possible to examine and treat livestock, pets, or wildlife that are normally difficult to handle.

In addition, many purely behavioral treatments that do not rely on drugs have been developed through animal research. Behavior modification therapies are the most effective and widely applied techniques for treating alcoholism, drug abuse, obesity, neuroses, compulsions, and phobias. These therapies are partly the result of many years of basic animal research on the fundamental properties of learning and on the effects of reinforcement (either positive or negative) on behavior.

Animals are used in many other kinds of behavioral studies. Animal experiments have produced valuable information on the effects of visual stimulation on brain development, biofeedback techniques, memory loss, programmed instruction in education, aggression, stress, and recovery after strokes or brain injury. We would know much less about these aspects of human life without animal research, and continued animal research is essential if new ways are to be found to cope with behavioral problems. Nonhuman primates are particularly valuable in behavioral research, as they are in a wide range of biomedical research, because of their many similarities to humans.[19]

DRUG ADDICTION

Animals can become addicted to drugs and alcohol just as human beings can. In fact, the addictive quality of cocaine was first demonstrated in animals. When humans quit using cocaine, the withdrawal does not cause severe physical symptoms, which has been the traditional measure of addiction. But animal studies showed that if monkeys were given a choice of receiving cocaine or food, they would administer cocaine to themselves to the point of starvation. Clearly they were addicted to cocaine, but the addiction was behavioral, not physical.

Because animals can become addicted to drugs, they provide excellent models of the addiction process. For example, cocaine has been found to block the uptake of a chemical known as dopamine from nerve junctions in the brain. Animal researchers are now investigating several promising compounds that could reduce the craving for drugs or block the effects of drugs in the brain.

Animal studies have also been integral to many of the behavioral therapies that are currently the only proven long-term methods for dealing with drug addiction and other compulsive behaviors. Animals have been used to study the reinforcing mechanisms that promote or discourage certain behaviors. In addition, animal research has illuminated the complicated interactions between addictive behavior and the environment. One example involves an animal model of heroin overdose. If rats are given repeated injections of heroin (morphine) of increasing dosage in the same environment, they develop great tolerance just as humans do. They easily survive a dose that would have been lethal if given first. But if the same heroin dosage is administered to these tolerant rats in a new and novel environment, many of them die. Perhaps the effects of novel environments or new situations account for a portion of the deaths from heroin overdose in human addicts.

How Do Animals Benefit from Animal Research?

The same methods that have been developed to prevent and treat diseases in humans have improved the lives of countless animals.[20], [21] Vaccines, antibiotics, anesthetics, surgical procedures, and other approaches developed in animals for human use are now commonly employed throughout veterinary medicine. Pets, livestock, and animals in zoos live longer, more comfortable, and healthier lives as a result of animal research.

In many cases, treatments have been developed specifically for animals. Vaccines for rabies, canine parvovirus, distemper, and feline leukemia virus have kept many animals from contracting these fatal diseases. Treatments for heartworm infestation (a painful and ultimately fatal affliction in dogs), therapies for cholera in hogs, and diagnostic and preventive techniques for brucellosis and tuberculosis in cattle are all now available because of animal research.

Animal research has also been integral to the preservation of many endangered species. The ability to eliminate parasitism, treat illnesses, use anesthetic devices, and promote breeding has improved the health and survival of many species. Through techniques like artificial insemination and embryo transfer, species that are endangered or have disappeared in the wild can now be managed or maintained. Research on the sexual behavior of animals has made it possible to breed many species in captivity, enabling endangered species to be reintroduced to the wild.

Animal research has also greatly extended and improved the lives of many companion animals.

Are There Alternatives to the Use of Animals in Research?

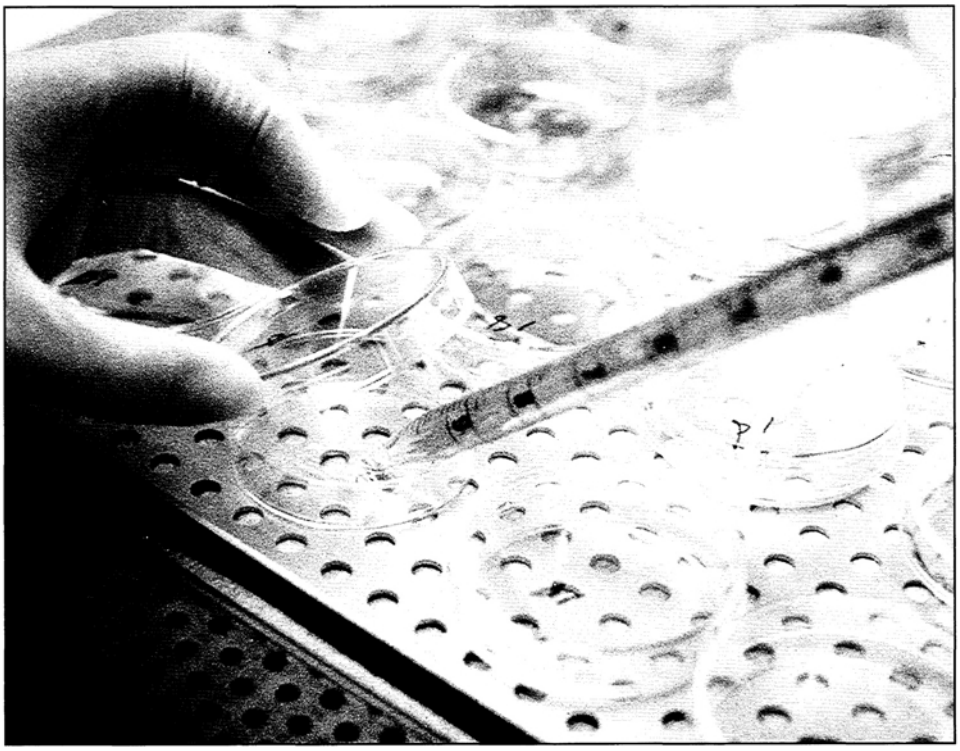
Some people contend that many animal experiments could be replaced by experiments that yield the same information without the use of animals. In fact, the present ability to replace animal experiments with alternatives such as tissue cultures, microorganisms, or computer models is very limited.[22] Researchers have developed replacements for some animal experiments, and the search for alternatives is continuing. But if scientists could replace a large number of animal experiments with experiments that do not use animals, they would, because animals are expensive and difficult to use, and because scientists do not want to experiment on animals unnecessarily. Researchers who use animals do so because that is the best way to get the appropriate information.

Progress is being made in reducing the number of animals used in testing. Testing involves the use of animals, primarily rats and mice, to assess the safety or effectiveness of consumer products such as drugs, chemicals, and cosmetics. Many researchers are now searching for ways to further reduce the use of animals in testing, and these efforts could reduce the need for animals in research as well.

The term “alternatives” encompasses a range of options. In the research community, an alternative has been defined to mean reducing the number of animals used, refining experimental designs to lessen any pain or distress in animals, or replacing animals with other organisms or techniques.[23] An alternative may therefore still involve the use of animals, but it might mean using fewer animals or using them in different ways.

Most researchers generally hold that nonanimal experiments are adjuncts rather than alternatives to animal experiments. Studies that do not use animals can produce much valuable information, but they cannot completely replace the information gained from animal experiments. Only animals can demonstrate the effects of a disease, injury, treatment, or preventive measure on a complex organism. For example, some aspects of the causation, treatment, or prevention of blindness cannot be studied in bacteria because they do not have eyes; some aspects of high blood pressure cannot be studied in protozoa because they do not have hearts or blood vessels; some aspects of arthritis cannot be studied in tissue culture cells without bones or joints.

New experimental procedures can sometimes reduce the numbers of animals used, particularly in the testing of new compounds for toxicity. For instance, new chemical compounds are now routinely screened in cell cultures, and if they are found to be toxic they are not given to animals. But cell cultures cannot replace animals. If a compound proves innocuous in a cell culture, it must still be tested in an animal to gauge its effects in a complex organism. Similarly, computer models and other nonanimal alternatives can at most supplement, rather than replace, animal experimentation.



A technician pipets into a culture dish used to test the effects of chemicals on cultured hamster embryo cells.

What Are the Issues Surrounding "Animal Rights"?

Much of the current opposition to animal research is being fueled by a philosophical position known as "animal rights." According to this viewpoint, animals have inherent legal and moral rights, just as humans do. This implies that it is unethical to use animals as pets or for any other purpose, whether for food, clothing, recreation, or research.[24]

Whether or not animals have "rights" depends on how the term is defined. If living things are ascribed a "right" to remain living, then animals would have rights. But most ethicists do not use the term so broadly. They generally ascribe rights only to members of societies that are capable of applying mutually accepted ethical principles to specific situations.[25]Animals are not capable of forming or belonging to such societies. In this light, they cannot be ascribed rights.

The animal rights viewpoint also leads to some philosophically untenable conclusions. For instance, in its strongest form it implies that the lives of all animals, including humans, are equal. But the death of a human being is not equivalent to the death of a mouse. We do not commit an act equivalent to the murder of a human every time we eat meat. We do not think it is immoral to attempt to control the rodent populations in sewers or the roach population in homes. Nor do we believe that keeping animals as pets is the moral equivalent of slavery.

There are many groups in the United States that are concerned with the use of animals in research. These groups have a wide variety of positions, and it is an oversimplification to speak of the "animal rights movement." But a fundamental distinction can be made between those who believe that animal research should continue, albeit with various modifications or restrictions, and those who believe that it should simply stop. These latter individuals, comprising a highly vocal minority in society, are the ones included under the term "animal rights movement."

They have worked assiduously and skillfully in legislatures, schools, and the media to pursue their cause, and in many cases their actions have met with a great deal of success. Animal research has become more costly and difficult, in part because of self-regulation by scientists but also because of externally imposed regulations. Some animal researchers have left the field, and young researchers have chosen not to enter it. Many members of the general public have the impression, based not on facts but on repeated allegation, that too much animal research is done.

Some members of the animal rights movement pursue more extreme tactics, often with the implicit backing of more moderate elements.[26] Since 1980, more than 30 break-ins, thefts, and acts of vandalism against research facilities have caused millions of dollars in damage.[27] Records representing years of work have been destroyed. Researchers and their families have been harassed and threatened.

The scientific community can find no moral justification for these acts, although they are excused and even supported by leaders and leading organizations in the animal rights movement. Vandalism and harassment have slowed medical research that is dedicated to improving human well-being. Individuals who vandalize laboratories and harass researchers are not only breaking the law; they are also materially harming the people who would eventually benefit from the research being done and are denying hope to those with presently incurable diseases.

What Is the Difference Between Animal Rights and Welfare?

The assertion that animals do not have rights does not mean that researchers are free to use them without appropriate concern. Animals are living things; they have evolved with us on this planet; they can feel pain and distress—and because of our kinship with living things, animals have a value above and beyond anything that is not living. This value finds concrete expression in the concern scientists feel for the animals they use and in the laws and regulations that govern that use.

Researchers who study animals have a number of obligations toward those animals and toward society. They have an obligation to minimize the pain and distress of laboratory animals. They have an obligation to see that animals are used for productive and meaningful goals. And they have an obligation to provide society with an accounting of how they use animals.

A number of groups have been working for many years to safeguard and promote these obligations. These groups are committed to the welfare of animals, as distinct from the concept of animal rights, and they have made a significant contribution to the well-being of research animals. They agree that animal research has benefited and will continue to benefit human and animal health; they want to ensure that research animals are treated as humanely as possible and are used only for important studies.

This position is one with which animal researchers not only agree but actively promote. It is also, according to polls, the position held by a large majority of the American public.[28]

HYPERCHOLESTEROLEMIA

Scientists have known since early in this century that rabbits and other research animals fed cholesterol-rich diets develop atherosclerosis—a buildup of cholesterol and other substances that narrows the arteries and can lead to chest pain, heart attacks, or strokes. Further animal research, confirmed by human experience, has shown that low-cholesterol diets and exercise can partially reverse this buildup, while stress and high-blood pressure can contribute to the disease.

These animal experiments laid the groundwork for a brilliant series of investigations into the molecular mechanisms of the disease. Researchers began by concentrating on a genetic defect that causes a disease known as familial hypercholesterolemia. About one in 500 people around the world has a single copy of a defective gene that causes their cholesterol levels to be above normal; many of these individuals suffer heart attacks in their thirties and forties. About one in a million people has two copies of the defective gene, leading to extremely high cholesterol levels; these individuals usually suffer from heart disease while they are still children.

Experiments in animals and tissue cultures showed that the genetic defect is related to a receptor molecule on the surfaces of cells. This receptor binds cholesterol in the bloodstream so that it can be absorbed into the cell and metabolized. People with single copies of the defective gene have reduced numbers of functioning receptors, so that their cholesterol rises to dangerous levels. People with two copies of the defective gene have no functioning receptors at all.

Knowledge of this receptor mechanism has led to experimental work with compounds that boost the numbers of receptors on cells. Research is also being conducted on transgenic mice—mice into which foreign genes have been inserted—to understand the kinds of genetic defects that lead to defective receptors. It may well be that genetic factors influence the effectiveness of the receptors at clearing cholesterol from the blood and therefore influence a person's chance of suffering from heart disease.

How Do Laws and Regulations Govern the Use and Care of Animals?

Animal experiments are subject to a wide variety of overlapping laws, regulations, and guidelines. At the federal level, the Animal Welfare Act was passed in 1966 and has been amended several times since then. It sets standards for handling, housing, transportation, feeding, veterinary care, and use of pain-relieving drugs in dogs, cats, nonhuman primates, rabbits, hamsters, guinea pigs, marine mammals, and horses and other farm animals used in nonagricultural research. Originally designed to prevent the theft of dogs and cats, its focus has shifted progressively toward safeguarding the welfare of laboratory animals. For instance, it requires that investigators consider alternative methods that do not involve animals and that investigators first consult with a veterinarian experienced in laboratory animal care before beginning any experiment that might cause pain. Unannounced inspections are made by federal employees to ensure compliance with the Act.

The other major federal law governing animal research is the Health Research Extension Act of 1985, which transformed into law many of the provisions contained in the Public Health Service Policy on Humane Care and Use of Laboratory Animals. This policy requires compliance with a number of other laws, regulations, and guidelines, including the Animal Welfare Act, and establishes procedures that researchers must follow to assure the government that they are in compliance. It applies to investigators funded by the Public Health Service, which includes the National Institutes of Health, the Food and Drug Administration, the

A surgeon and a pathologist use a double-headed microscope to check for the presence of cancer cells in biopsy tissue.

Centers for Disease Control, and the Alcohol, Drug Abuse, and Mental Health Administration. These investigators account for about half of the biomedical research done in the United States.

Through the combination of the Animal Welfare Act and the Health Research Extension Act, virtually all animal researchers are now under the oversight of a local review committee known as an Institutional Animal Care and Use Committee. These committees always include a veterinarian experienced in laboratory animal care and at least one person not affiliated with the institution to represent the interests of the community. The committees inspect animal research areas at least twice each year, make sure that the various sets of guidelines and regulations are followed, and review the design of proposed experiments to ensure that any animals will be used humanely.

Within the scientific community, professional societies and scientific organizations have for many decades prepared various sets of guidelines that govern the use of animals. The one most widely used now is the National Research Council's *Guide to the Care and Use of Laboratory Animals,* which was first released in 1963.[29] The *Guide* deals with the logistics of animal experimentation, such as cage size, the use of anesthetics, and the review of proposed experiments, and with the institutional monitoring of animal use and care.

Facilities that use animals in research or testing can also be accredited by the American Association for the Accreditation of Laboratory Animal Care (AAALAC). Using the Animal Welfare Act, the Guide, and other statements of principles, AAALAC requires adherence to high standards of animal care and use before granting accreditation. All research institutions funded by the Public Health Service must file a letter of assurance that all animal care and use standards are being met and maintained.

A number of other entities have also established laws, regulations, and guidelines that animal researchers must follow. Every state and many localities have laws about animal cruelty. Professional societies have set up guidelines to be followed by their members. And many scientific journals require compliance with sets of principles as a prerequisite for publication.

The many laws, regulations, and guidelines that govern animal care and use serve a valuable purpose by setting standards about the use of animals and by providing public accountability. But some laws and regulations have served more to impede animal research than to improve the well-being of laboratory animals. By making animal research more costly and difficult, these rules lessen the amount of productive work that can be done.

How Much Pain Do Animals Experience in Animal Research?

Most animals experience only minimal pain or brief discomfort when they are used in research. According to the 1988 Animal Welfare Enforcement Report by the Department of Agriculture, about 94 percent of all laboratory animals reported are not exposed to painful procedures or are given drugs to relieve any pain caused by a procedure.[30] The remaining 6 percent of animals are exposed to painful procedures because to relieve them of the pain would defeat the purpose of the experiment. Even in these cases, however, the pain is usually neither severe nor long-lasting.

A small fraction of animals do experience acute or prolonged pain during experiments. But the researchers who conduct these experiments and the institutional committees that oversee them believe that this pain is justified by the magnitude of the problem the experiments are designed to solve. An estimated 85 million Americans suffer from chronic pain caused by arthritis, back disorders, injuries, cancer, headaches, or other conditions. The annual economic costs in terms of work days lost and health care expenditures from chronic pain run into the tens of billions of dollars.[31] Without research on a relatively small number of laboratory animals, there is little hope that continued progress can be made in alleviating this widespread human suffering.

The statistics concerning pain in laboratory animals confirm a general conviction of the research community. Animal activists are wrong when they accuse researchers of inflicting needless pain on experimental animals. Researchers strive to cause animals either no pain or no more pain than is absolutely necessary. When a rare instance of abuse does arise, researchers are condemned by their colleagues, are subject to sanctions by the research community, and generally lose their support for further research.

AIDS

The sudden appearance of acquired immune deficiency syndrome (AIDS) in the early 1980s demonstrates both the unpredictability of future health needs and the essential role of animals in responding to those needs. Within a few years of its appearance, researchers knew that AIDS was caused by a virus, now known as the human immunodeficiency virus (HIV), and tests had been devised to detect antibodies to the virus in the blood. Progress would not have been nearly as rapid without the previous two decades of animal research, in which naturally-occurring viruses similar to HIV were studied in a variety of laboratory, pet, and farm animals. Chimpanzees are the only species besides humans that can be infected with HIV, but infected chimps do not develop symptoms of AIDS. However, rhesus monkeys do get a disease very similar to AIDS that is caused by a similar virus, known as simian immunodeficiency virus (SIV). Thus, rhesus monkeys provide a model in which to study the prevention and treatment of AIDS in humans.

Researchers have already developed a vaccine that protects monkeys from given strains of SIV, opening up the possibility that similar vaccines can be developed for humans. In addition, potential vaccines and treatments for AIDS are tested in monkeys and other animals to ensure their efficacy and safety for human use. This was the process, for example, that led to the use of AZT to treat AIDS.

Should Pound Animals Be Used in Research?

About two-thirds of the dogs and most of the cats used in research come from animal shelters and pounds. However, for every dog or cat released for research, pounds and shelters have to kill about 100 animals—at least 10 million dogs and cats every year—that do not find a home.[32]

Some groups have played on public sentiments by implying that people's pets will be used in experiments unless laws restricting the use of pound animals in research are passed. But animals are not released for research until enough time has passed to let owners redeem lost pets. Furthermore, people who take animals to pounds usually do not object to the possible use of those animals in research. As with the donation of human organs for transplantation, the general feeling is that using pound animals in research is a way to bring some benefit from an otherwise unfortunate situation.

Nevertheless, several states and communities have restricted the use of animals from pounds, either by requiring that such animals be imported from other states or, in the case of Massachusetts, by forbidding the use of pound animals in any research. If dogs and cats are to be used in research in Massachusetts, they have to be raised by breeders specifically for research. Yet the logic seems perverse: animals will continue to be killed in pounds, and even more animals will be raised for research. As a result of this law, more animals are killed rather than fewer.

What these laws actually do is make animal research more expensive and difficult. Animals raised by breeders cost several hundred dollars apiece, whereas pound animals, about to be put to death, can be obtained for a nominal cost. If all of the animals now obtained from pounds were instead acquired from breeders, the additional cost would be tens of millions of dollars. Without additional funding, this expense would inevitably curtail valuable research.

What Is the Cost to Society of the Animal Rights Movement?

The animal rights movement imposes costs on society in both the short term and the long term. In the short term, the animal rights movement has driven up the costs of research, with a corresponding decrease in how much research can be done. Money has to be spent on the tighter security in response to the threat of break-ins, and facilities must be repaired and work redone after a break-in or vandalism.

These are substantial costs, but even more significant are the long-term costs. If research is slowed, human health will suffer—maybe not immediately, but at some point in the future. New treatments for cancer, Alzheimer's disease, AIDS, and heart disease, new antibiotics and vaccines, ways to regenerate damaged nerve and brain cells, treatments for mental disorders, and a host of other therapies and advances will be delayed or may not occur at all if animal research is curtailed. These are the very real costs that must be taken into account in considering animal research.

A nurse reads to a child in a laminar airflow unit used to protect people with suppressed immune systems. In this germ-free environment, air flows out one way and germs cannot reenter the system.

Conclusion

People clearly want the benefits that derive from animal research. They also want animals to be well-treated and to undergo a minimum of pain and distress. These desires result from our values, from the importance we ascribe to both human and animal life.

But decisions about the use of animals should be based both on reason and values. It makes no sense to sacrifice future human health and well being by not using animals in research today. In fact, it would be immoral and selfish not to use animals in research today, given the harm that could accrue to future generations if such research were halted.

The promise that animal research holds for generations of humans remains undiminished

The majority of Americans agree that animal research must continue. But legislators rarely hear from this majority, whereas they are bombarded by appeals from the small minority who wish to stop or severely curtail such research. Many scientific, medical, and patient groups have come out strongly in favor of humanely conducted animal research. The National Academy of Sciences and Institute of Medicine would like to add their voices to the chorus of support for animal research.

We owe our good health to past investigators and the animals they studied. As we decide on the future of animal research, we should keep in mind the future generations who will look back at us and ask if we acted wisely.

Notes

1. Real names have been used with the permission of the individuals involved.

2. Jonas, A. M. “The Mouse in Biomedical Research.” In *Health Benefits of Animal Research,* William Gay, ed. Washington, D.C.: Foundation for Biomedical Research, no date.

3. Committee on Use of Laboratory Animals in Biomedical and Behavioral Research, National Research Council and Institute of Medicine. *Use of Laboratory Animals in Biomedical and Behavioral Research.* Washington, D.C.: National Academy Press, 1988.

4. Department of Health, Education, and Welfare. Public Health Service. *Lithium in the Treatment of Mood Disorders.* Washington, D.C.: U.S. Government Printing Office, 1970.

5. U.S. Department of Health and Human Services, National Institute of Environmental Health Sciences. *With Respect to Life: Protecting Human Health and the Environment through Laboratory Animal Research.* Research Triangle Park, North Carolina: National Institute of Environmental Health Sciences, 1989.

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7. Committee on Use of Laboratory Animals in Biomedical and Behavioral Research, National Research Council and Institute of Medicine. *Use of Laboratory Animals in Biomedical and Behavioral Research.* Washington, D. C.: National Academy Press, 1988.

8. Committee on Models for Biomedical Research, National Research Council. *Models for Biomedical Research: A New Perspective.* Washington, D.C.: National Academy Press, 1985.

9. U. S. Congress, Office of Technology Assessment. *Alternatives to Animal Use in Research, Testing, and Education.* Washington, D.C.: U.S. Government Printing Office, 1986.

10. U.S. Department of Agriculture. *Animal Welfare Enforcement Report—Fiscal Year 1988.* Washington, D.C.: U.S. Department of Agriculture, 1989.

11. Most research animals are humanely killed at some point during the course of the research, but nonhuman primates, because of their expense and special value in animal research, are often used in experiments, such as behavioral experiments, that do not require that they be killed. Only about half of the primates used in research each year are killed.

12. Shorter, E. *The Health Century.* New York: Doubleday, 1987.

13. Riley, J. C. *Sickness, Recovery, and Death.* Iowa City, Iowa: University of Iowa Press, 1989.

14. A number of organizations have compiled summaries of biomedical advances achieved through animal research. See, for example, "Animals in Research" by the Council of Scientific Affairs, American Medical Society, pp. 3602-3606 in *Journal of the American Medical Association,* Vol. 261 (June 23/30, 1989), and *The Use of Animals in Biomedical Research and Testing* by the Foundation for Biomedical Research (Washington, D.C.: Foundation for Biomedical Research, 1988). The California Biomedical Research Association in Berkeley, California, has also published a series of brochures on specific diseases being studied in laboratory animals.

15. American Medical Association. *Use of Animals in Biomedical Research: The Challenge and Response.* Chicago: American Medical Association, 1989.

16. In their study "Scientific Basis for the Support of Biomedical Science" (pp. 105-111 in *Science,* Vol. 192 [April 9, 1976]), Julius H. Comroe, Jr., and Robert D. Dripps found that of the articles judged essential for 10 major advances in cardiovascular and pulmonary medicine, 62 percent focused on basic research. The authors conclude that "planning for future clinical advances must include generous support for innovative and imaginative research that bears no discernible relation to a clinical problem."

17. Foundation for Biomedical Research. *The Biomedical Investigator's Handbook.* Washington, D.C.: Foundation for Biomedical Research, 1987.

18. Miller, N. E. "The Value of Behavioral Research on Animals." In *American Psychologist,* Vol. 40 (1985), pp. 423–440.

19. King, F. A., et al. "Primates." *Science,* Vol. 240 (June 10, 1988), pp. 1475–1482.

20. Ewald, B. E., and D. A. Gregg. "Animal Research for Animals." Pp. 48–58 in *The Role of Animals in Biomedical Research.* J. A. Sechzer, ed. New York: New York Academy of Sciences, 1983.

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23. Russell, W. M. S., and R. L. Burch. *Principles of Humane Experimentation Techniques.* Springfield, Illinois: Charles C Thomas, 1959.

24. Two of the seminal works of the animal rights movement are: Singer, P. *Animal Liberation.* New York: Avon Books, 1977 (paperback edition). Regan, T. *The Case for Animal Rights.* Berkeley, California: University of California Press, 1983.

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29. Committee on Care and Use of Laboratory Animals, National Research Council. *A Guide for the Care and Use of Laboratory Animals.* Washington, D.C.: U.S. Department of Health and Human Services, 1985.

30. U.S. Department of Agriculture. *Animal Welfare Enforcement Report—Fiscal Year 1988.* Washington, D.C.: U.S. Department of Agriculture, 1989.

31. Dubner, R. “Pain Research in Animals.” Pp. 277–282 in *National Symposium on Imperatives in Research Animal Use: Scientific Needs and Animal Welfare.* Bethesda, Md.: National Institutes of Health, 1984.

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