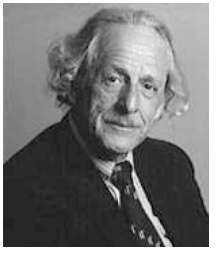

Current Comments®

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NAS and Institute of Medicine, Alarmed by Animal Rights Activists, Highlight Medical Advances Based on Animal Research

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The National Academy of Sciences (NAS) and the Institute of Medicine (IOM) have joined recently in adding "their voices to the chorus of support for animal research."[1] Certainly, the animal-rights controversy is not new to *Current Contents* ® (*CC* ®).[2,3]

With this in mind, we have adapted a NAS/IOM report published earlier this year by its Committee on the Use of Animals in Research. *Science, Medicine, and Animals* follows this introduction.

In the preface to this report, Frank Press, president of the NAS, and Samuel O. Thier, former president of the IOM, state that the purpose of the document is to "depict some of the many ways in which animal research has benefited, and will continue to benefit, human and animal health." They acknowledge that "the use of animals in science may not always have been as well-justified or well-executed as today's sensibilities require." But they contend the use of animals in research is now well-regulated, with abuses rare and the benefits to society enormous.

Press and Thier, who stepped down this summer to become president of Brandeis University, Waltham, Massachusetts, view the "animal rights" movement with alarm. They charge some radical factions with distortion, violence, breaking into labs, setting fires, destroying records, and harassing researchers. Indeed, some of these acts were chronicled in our *CC* essay last year on this subject[3] and in *The Scientist*.[4] The new acting president of the IOM is Stewart Bonderant.

In our view, the NAS/IOM "position paper" gives a good overview of the history, status, and potential of animal research. As the preface authors state, the intent of the report is not "to end the debate on whether and how animals are used in research; rather, it...[is] to inform that debate."

Interestingly, the report, citing a study by Robert W. Leader and Dennis Stark of the American Association for Laboratory Animal Science, points out that more than two-thirds of the research projects that have led to the Nobel Prize in physiology or medicine have involved animal experiments.[5] So it is not surprising to learn that nearly half of the biomedical investigations carried out in the US involve some form of animal research.[1]

Let me quote just one of several examples edited from the report because of space constraints. It vividly describes the human benefits from animal research:

> Several months before his thirtieth birthday, Greg Maas discovered a lump in his abdomen that would not go away. He went to his doctor for tests, and then to a specialist for a biopsy. Two 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 report points out that the drugs used to kill the cancer cells in Maas's body were

Frank Press

Samuel O. Thier

tested during the last several decades on inbred strains of mice susceptible to leukemia. And that research on not only mice, but rats, dogs, and other animals, has led to drugs that suppress the immune reaction to a transplanted organ. Thus, thousands of people are alive today because of these animal studies. And this is but one example.

Surely, our responsibility to the future of society dictates continued but controlled experimentation with animals to combat disease and improve the quality of not only our lives, but those of animals as well.[6]

Fanatics would have the public believe that scientists do not love animals because we use them in research. But we, too, have pets, like my Boston terrier "Brian." He brings my family constant pleasure and companionship. Ironically, we can continue to enjoy his company because research veterinarians at the University of Pennsylvania were able to overcome a breathing defect at birth.

As the following report states, far fewer animals are used in research than for the myriad of other purposes they serve.

The Committee on the Use of Animals in Research that produced the following "position paper" consisted of Kurt J. Isselbacher, chairman, Massachusetts General Hospital Cancer Center, Charlestown; A. Clifford Barger, Department of Physiology, Harvard Medical School; Pedro Cuatrecasas, Warner-Lambert Pharmaceutical Research, Ann Arbor; Franklin M. Loew, School of Veterinary Medicine, Tufts University, North Grafton, Massachusetts; Dominick P. Purpura, Albert Einstein College of Medicine, Bronx, New York; and Richard F. Thompson, Department of Psychology, University of Southern California, Los Angeles. The staff consisted of John E. Burris, the study director, and Steve Olson, writer and editor.

The full version of the document is available for $5 for those living in the US, Canada, and Mexico, plus $3 shipping and handling. Send payment to: National Academy Press, 2101 Constitution Avenue, NW, P.O. Box 285, Washington, DC 20055. There are special rates for bulk orders.

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My thanks to Paul R. Ryan for his help in the preparation of this introduction and in the condensation of the following paper.

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Back to Introduction

Science, Medicine, and Animals

The following is a condensed and edited version of the animal research position paper published this year by the National Academy of Sciences and the Institute of Medicine. It contains descriptions of a small number of the many medical advances that have been made largely because of animal research. The examples could be multiplied many times over—Editor.

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.[1]

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.[2] 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.[3] 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.[4] 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.[5]

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.[6] 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.[7]

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.

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.[8] 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.[9] [The following are a number of medical advances that owe a large debt to animal research:]

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.

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.

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.

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.

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.

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.[10]

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.[11] 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.[12] Since 1980, more than 30 break-ins, thefts, and acts of vandalism against research facilities have caused millions of dollars in damage.[13] 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.

Laws and Regulations

Animal experiments are subject to a wide variety of overlapping laws, regulations, and guidelines. At the federal level, the An-

imal 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.

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 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.[14] 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.

Pain and 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.[15] 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.[16] 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.

Pound Animals and 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.[17]

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.

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 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.

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Editorial Schedule Change

With the first issue of 1991, ISI ® implemented a schedule change in the front matter for *Current Contents.* ® *Citation Classics* ® and the *ISI* ® *Press Digest*, including *Hot Topics*, now appear every other week. They alternate with either an essay by Eugene Garfield, a reprint with an appropriate introduction, or an essay by an invited guest.