A CRITICAL LOOK AT ANIMAL EXPERIMENTATION
Increasing numbers of scientists and clinicians are challenging animal experimentation on medical and scientific grounds.\textsuperscript{1-3} Considerable evidence demonstrates that animal experimentation is inefficient and unreliable, while newly developed methodologies are more valid and less expensive than animal studies.

**Historical Impact of Animal Experimentation**

Proponents of vivisection (tests, experiments, and "educational" exercises involving harm to animals) claim that it has played a crucial role in virtually all medical advances.\textsuperscript{4,5} However, several medical historians argue that key discoveries in such areas as heart disease, cancer, immunology, anesthesia, and psychiatry were in fact achieved through clinical research, observation of patients, and human autopsy.\textsuperscript{6-14} Human data have historically been interpreted in light of laboratory data derived from nonhuman animals. This has resulted in unfortunate medical consequences. For instance, by 1963 prospective and retrospective studies of human patients had already shown a strong correlation between cigarette smoking and lung cancer.\textsuperscript{15,16} In contrast, almost all experimental efforts to produce lung cancer in animals had failed. As a result, Clarence Little, a leading cancer animal researcher, wrote, "The failure of many investigators to induce experimental cancers, except in a handful of cases, during fifty years of trying, casts serious doubt on the validity of the cigarette-lung cancer theory."\textsuperscript{17} Because the human and animal data failed to agree, this researcher and others distrusted the more reliable human data. As a result, health warnings were delayed for years, while thousands of people died of lung cancer.

By the early 1940s, human clinical investigation strongly indicated that asbestos caused cancer. However, animal studies repeatedly failed to demonstrate this, and proper workplace precautions were not instituted in the U.S. until decades later.\textsuperscript{18} Similarly, human population studies have shown a clear risk from exposure to low-level ionizing radiation from diagnostic X-rays and nuclear wastes,\textsuperscript{19-22} but contradictory animal studies have stalled proper warnings and regulations.\textsuperscript{23} Likewise, while the connec-
Studies on monkeys falsely indicated that poliovirus infects only the nervous system. This erroneous assumption resulted in misdirected preventive measures and delayed the development of tissue culture methodologies critical to the discovery of a vaccine. While monkey cell cultures were later used for vaccine production, it was research with human cell cultures which first showed that poliovirus could be cultivated on non-neural tissue. Similarly, development of surgery to replace clogged arteries with the patient's own veins was impeded by dog experiments which falsely indicated that veins could not be used. Likewise, kidney transplants, quickly rejected in healthy dogs, were accepted for a much longer time in human patients. We now know that kidney failure suppresses the immune system, which increases tolerance of foreign tissues.

Nevertheless, the public continues to endorse vivisection, primarily because many people believe that animal experimentation has been vital for most medical advances. However, few question whether such research has been necessary or even, on balance, helpful in medical progress.

Contemporary Animal Experimentation

A. Selective Diseases

1. Cancer

In 1971 the National Cancer Act initiated a "War on Cancer" that many sponsors predicted would cure cancer by 1976. Instead, this multibillion dollar research program has proven to be a failure. The age-adjusted total cancer mortality rate climbed steadily for decades until the early 1990s, when this rate started to fall slowly, due largely to reduced smoking.

In order to encourage continued support for cancer research—now exceeding two billion dollars annually—researchers and administrators have "artificially inflate the amount of 'true' progress," concluding that even simple five-year survival statistics were misused. For one thing, the NCI termed five-year survival a "cure" even if the patient died of the cancer after the five-year period. Also, by ignoring well known statistical biases, the NCI falsely suggested advances had been made in the therapy of certain cancers. Commenting on the research program's discouraging results, epidemiologist John Bailar III has stated, "The more promising areas are in cancer prevention."

Why hasn’t progress against cancer been commensurate with the effort (and money) invested? One explanation is the unwarranted preoccupation with animal research. Crucial genetic, molecular, immunologic, and cellular differences between humans and other animals have prevented animal models from serving as effective means by which to seek a cancer cure. Cancer researcher Jerome Leavitt has explained that human cancer "may have critical mechanical differences which may in turn require different, uniquely human approaches to cancer eradication."

2. AIDS

Despite extensive use, animal models have not contributed significantly to AIDS research. While monkeys, rabbits, and mice born with severe combined immunodeficiency can be infected with...
monkeys from their mothers at birth and rear ing them in total isolation or with "surrogate" mothers made of wire and cloth. Their terror and subsequent psychopathology, Harlow claimed, demonstrated the importance of maternal contact. However, this had been shown conclusively in human studies.

Despite its conceptual shallowness, numerous maternal deprivation studies continue, claiming relevance to human developmental psychology, psychopathology, and even immune and hormone function.

Animal models of alcohol and other drug addiction are similarly ill-conceived, failing to reflect crucial social, hereditary and spiritual factors. Pharmacologist Vincent Dole has acknowledged, "Some 60 years of offering alcohol to animals has produced no fundamental insights into the causes of this self-destructive behavior or even a convincing analogue of pathological drinking."

"Experimental psychology" continues to rely on painful research on animals, despite clinical psychologists' disregard for the animal research literature. A review of two clinical psychology journals revealed that only 33 of 4,425 citations (0.75%) referred to animal-research studies.

4. Genetic Diseases

Scientists have located the genetic defects of many inherited diseases, including cystic fibrosis and familial breast cancer. Trying to "model" these diseases in animals, researchers widely use animals--mostly mice--with spontaneous or laboratory-induced genetic defects. However, genetic diseases reflect interactions between

HIV, none develops the human AIDS syndrome. Of over 100 chimpanzees infected with HIV over a ten year period, only a few have become sick. Even AIDS researchers acknowledge that chimpanzees, as members of an endangered species who rarely develop an AIDS-like syndrome, are unlikely to prove useful as animal models for understanding the mechanism of infection or means of treatment. Other virus-induced immunodeficiency syndromes in non-human animals have been touted as valuable models of AIDS, but they differ markedly from AIDS in viral structure, disease symptoms, and disease progression. Animal researcher Michael Wyand, discussing anti-AIDS therapy, has acknowledged:

"Candidate antivirals have been screened using in vitro systems and those with acceptable safety profiles have gone directly into humans with little supportive efficacy data in any in vivo [animal] system. The reasons for this are complex but certainly include . . . the persistent view held by many that there is no predictive animal model for HIV infection in humans."

AIDS researcher Margaret Johnston has concurred, "HIV/AIDS [animal] models have not yielded a clear correlate of immunity nor given consistent results on the potential efficacy of various vaccine approaches."

Human clinical investigation has isolated the AIDS virus (HIV), defined the disease's natural course, and identified risk factors. In vitro (cell and tissue culture) research using human white blood cells has identified both the efficacy and toxicity of anti-AIDS medicines, including AZT, 3TC, and protease inhibitors. Federal law, however, still mandates unnecessary animal toxicity testing.

3. Psychology and Substance Abuse

Animal "models" of psychology, traditionally employing painful stimuli to study behavior, have been strongly criticized in part because human psychological problems reflect familial, social, and cultural factors that cannot be modeled in nonhumans. Indeed, most psychologists disapprove of psychological vivisection that causes animal suffering.

Harry Harlow's "maternal deprivation" experiments involved separating infant monkeys from their mothers at birth and rearing them in total isolation or with "surrogate" mothers made of wire and cloth. Their terror and subsequent psychopathology, Harlow claimed, demonstrated the importance of maternal contact for babies.

Maternal deprivation experiments, in which infant rhesus monkeys were raised in isolation or with "surrogate mothers" of cloth and wire, followed human studies demonstrating the importance of maternal contact for babies.
B. Toxicity Testing

Numerous standard animal toxicity tests have been widely criticized by clinicians and toxicologists. The lethal dose 50 (LD50), which determines how much of a drug, chemical, or household product is needed to kill 50 percent of a group of test animals, requires 60 to 100 animals (usually rats and mice), most of whom endure great suffering. Because of difficulties extrapolating the results to humans, the test is highly unreliable.64 Also, since such variables as an animal’s age, sex, weight, and strain can have a substantial effect on the results, laboratories often obtain widely disparate data with the same test substances.65,66 In vitro tests could potentially completely replace the LD50.66-68

The Draize eye irritancy test, in which unanesthetized rabbits have irritant substances applied to their eyes, yields results that are inherently unreliable in predicting human toxicity.69 Humans and rabbits differ in the structure of their eyelids and corneas as well as their abilities to produce tears. Indeed, when comparing rabbit to human data on duration of eye inflammation after exposure to 14 household products, they differed by a factor of 18 to 250.70 A battery of in vitro tests would be less expensive and likely more accurate than the Draize test.68,71

Animal tests for cancer-causing substances, generally involving rodents, are also notoriously unreliable. Science editor Philip Abelson has asked, “Are humans to be regarded as behaving biochemically like huge, obese, inbred, cancer-prone rodents?”72 Of course, humans are not. Of 19 known human oral carcinogens, only 7 caused cancer in nonhuman animals using the standard NCI protocol.73 Even different rodent species produce conflicting results. When Lester Lave et al. compared rat and mouse carcinogenicity for 214 chemicals, they found a correlation of only 70 percent.74 (Chance alone would yield a 50 percent correlation.) A combination of in vitro tests provides data that compare favorably with existing carcinogenicity databases and costs far less than animal tests.75

C. Educational Exercises

Animal laboratories are not necessary for teaching biological and medical material, and studies have repeatedly demonstrated their lack of educational superiority.76,77 Diagrams, pictures, computer simulations, and interactive videos can replace animal exercises to supplement lectures and reading material. During surgical training, medical students and residents properly begin to learn procedures by observing human operations because of the human’s unique anatomical features. To perfect manual skills—such as cutting and suturing—surgical training has traditionally relied on carefully monitored work with human patients. When this is not practical, creative use of human tissues can be an alternative. For example, students can practice microsurgery with human placental tissue.78 Similarly, surgeons can learn new procedures with virtual reality computer systems, and medical students can study physiology and pharmacology on life-sized patient simulators.79

Scientific Limitations of Animal Models

Animal studies can neither confirm nor refute hypotheses about human physiology or pathology; human clinical investigation is the only way such hypotheses can be tested. At best, animal experiments can suggest new hypotheses that might be relevant to...
creased survival of rats with artificially induced heart failure, but humans taking this drug experienced a 30% increase in mortality. Fialuridine appeared safe in animal tests, but it caused liver failure in 7 of 15 human taking the drug, five of whom died and two required liver transplantation. Animal studies failed to predict dangerous heart valve abnormalities in humans induced by the diet drugs fenfluramine and dexfenfluramine. Similarly, tests in monkeys failed to predict side-effects (jaundice, blood-clotting disorder, kidney failure, and lung failure) that killed an 18-year-old gene therapy patient in September 1999.

The General Accounting Office reviewed 198 of 209 drugs marketed from 1976 to 1985 and found that 52% had "serious postapproval risks" not predicted by animal tests. Of 548 drugs (10%) approved between 1975 and 1999 were removed from the market or needed one or more special warnings for possible serious or life-threatening side-effects. Subsequently, agents showing efficacy in animals have been unhelpful or even hazardous for human patients.

Animal tests frequently mislead. Milrinone increased survival of rats with artificially induced heart failure, but humans taking this drug experienced a 30% increase in mortality. Fialuridine appeared safe in animal tests, but it caused liver failure in 7 of 15 human taking the drug, five of whom died and two required liver transplantation. Animal studies failed to predict dangerous heart valve abnormalities in humans induced by the diet drugs fenfluramine and dexfenfluramine. Similarly, tests in monkeys failed to predict side-effects (jaundice, blood-clotting disorder, kidney failure, and lung failure) that killed an 18-year-old gene therapy patient in September 1999.

In contrast to human clinical investigation, vivisection involves manipulations of artificially induced conditions. Furthermore, the highly unnatural laboratory environment invariably stresses the animals, and stress affects the entire organism by altering pulse, blood pressure, hormone levels, immunological activities, and myriad other functions. Indeed, many laboratory "discoveries" reflect mere laboratory artifact. For example, artifact from unnaturally induced strokes in animals has repeatedly misled researchers. In the 1980s researchers reported 25 compounds that reduce ischemic-stroke damage in nonhuman animals, but none proved effective in humans. Subsequently, agents showing efficacy in animals have been unhelpful or even hazardous for human patients.

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Scientists recognize that, just within humans, gender, ethnicity, age, and health can profoundly influence drug effects. Obviously, extrapolating data between species is much more hazardous than within species. Consequently, animal studies are reliable at only the crudest levels—such as the ability of strong acids to damage eyes. However, such
effects can be assessed easily with in vitro systems. For more subtle effects, animal models are unreliable.\footnote{113}

**Animal Research Risks**

In addition to squandering scarce resources and providing misleading results, vivisection poses real risks to humans. The mindset that scientific knowledge justifies (and may require) harming innocent individuals endangers all who are vulnerable. Even after Nazi and Japanese experiments on prisoners horrified the world, American researchers denied African-American men syphilis treatment in order to assess the disease's natural progression,\footnote{114,120} injected cancer cells into nursing home patients,\footnote{114} subjected unwitting patients to dangerous radiation experiments,\footnote{115} and, despite no chance of success, transplanted nonhuman primate and porcine organs into children, chronically ill, and impoverished people.\footnote{116} Psychiatrist Robert Jay Lifton argues that this "science at any cost" mentality may have provided medical justification for the Holocaust.\footnote{117}

Furthermore, through animal research, humans have been exposed to a wide variety of deadly nonhuman primate viruses. About 16 laboratory workers have been killed by the Marburg virus and other monkey viruses, and there have been two outbreaks of Ebola in American monkey colonies.\footnote{118,120} Polio vaccines grown on monkey kidney cells exposed millions of Americans to simian virus 40, which causes human cells to undergo malignant transformation in vitro and has been found in several human cancers.\footnote{121} Ignoring the obvious public health hazards, researchers transplanted baboon bone marrow cells into an AIDS patient. The experiment was unsuccessful;\footnote{122} moreover, a large number of baboon viruses, which the patient could spread to other people, may have accompanied the bone marrow. Indeed, vivisection may have started the AIDS epidemic. HIV-1, the principal AIDS virus, differs markedly from any virus found in nature, and there is evidence that it originated either through polio vaccine production using monkey tissues\footnote{123,124} or through manufacture in American laboratories, where HIV-like viruses were being produced by cancer and biological weapons researchers in the early 1970s.\footnote{125}

**The Importance of Clinical Research**

Typically, medical discovery begins with a clinical observation,\footnote{8,9} which animal researchers then try to mimic with artificially induced animal conditions.\footnote{6} These researchers tend to highlight animal data that accord with the previous clinical finding, while discounting or ignoring conflicting animal data (which are usually voluminous). Although animal research advocates routinely take credit for discoveries that actually occurred in a clinical context,\footnote{6} many clinicians have recognized the primary role of human-based clinical research. Reviewing the history of hepatitis, physician Paul Beeson concluded:

> Failing to learn from the AIDS epidemic, many policy makers and industrial interests support animal-to-human organ transplants (from pigs and primates) known as xenotransplants. These have failed in the past, and are likely to continue to fail, because of tissue rejection, the impossibility of testing animal tissues for unknown pathogens, and the prohibitive expense.\footnote{126-128}

Relatively, the growing field of genetic engineering includes adding genetic material to animals’ cells to change the animals’ growth patterns or induce the animals to produce human proteins in their milk, meat or urine. This poses serious human risks, such as exposure to pathogens (viruses, prions, and other microorganisms)\footnote{129,130} or development of malignancies,\footnote{131,132} allergic reactions,\footnote{133} or antibiotic resistance.\footnote{134} These concerns contributed to the European Union’s ban on rBGH, a genetically engineered bovine growth hormone that increases cows’ milk production.\footnote{135}
“Progress in the understanding and management of human disease must begin, and end, with studies of man... Hepatitis, although an almost ‘pure’ example of progress by the study of man, is by no means unusual; in fact, it is more nearly the rule. To cite other examples: appendicitis, rheumatic fever, typhoid fever, ulcerative colitis and hyper-parathyroidism.”

Similarly, key discoveries in immunology, anesthesiology, first aid, alcoholism and psychopharmacology were based primarily on human clinical research and investigation. Furthermore, clinical research is the only means by which effective public health education and prevention programs can be developed and evaluated.

Non-Animal Methodologies

In science, there are always many ways to address a given question. Vivisection is generally less efficient and reliable than many non-animal methods, which include:

1. Epidemiology (Population Studies)

Medical research has always sought to identify the underlying causes of human disease in order to develop effective preventive and therapeutic measures. In contrast to artificial animal model conditions that generally differ in causes and mechanisms from human conditions, human population studies have been very fruitful. For example, the identification of risk factors for heart disease, so important for prevention techniques, derives from epidemiological studies. Similarly, population studies have shown that passive smoking doubles the risk of developing lung cancer.

Epidemiology’s potential is illustrated by the growing field of molecular epidemiology. Researchers can analyze cellular and molecular characteristics of those suffering from cancer or birth defects, thereby elucidating the mechanisms and causes of DNA damage and yielding effective prevention and treatment approaches.

2. Patient Studies

The main source of medical knowledge has always been the direct study of human disease by closely monitoring human patients. For example, cardiologist Dean Ornish has demonstrated that a low-fat vegetarian diet, regular exercise, smoking cessation, and stress management can reverse heart disease. Similarly, Caldwell Esselstyn has shown that lowering cholesterol levels with plant-based diets and medicines as needed arrests and often reverses heart disease.

Human cancer syndromes have played important roles in understanding more common forms of cancer. Henry Heimlich has relied exclusively on human clinical investigation to develop techniques and operations that have saved thousands of lives, including the Heimlich Maneuver for choking and drowning victims, the Heimlich operation to replace the esophagus (throat tube), and the Heimlich Chest Drainage Valve.

Modern non-invasive imaging devices such as CAT, MRI, PET, and SPECT scans have revolutionized clinical investigation. These devices permit the ongoing evaluation of human disease in living human patients, and have contributed greatly to medical knowledge.

3. Autopsies and Biopsies

The autopsy rate in the United States has been falling steadily, much to the dismay of clinical investigators who recognize the value of this traditional research tool. Autopsies have been crucial to our current understanding of many diseases, such as heart disease, appendicitis, diabetes and Alzheimer’s disease.

Although the usefulness of autopsies is generally limited to the disease’s lethal stage, biopsies can provide information into other disease stages. Diagnostic needle and endoscopic biopsies often permit safe procurement of human tissues from living patients. For example, endoscopic biopsies have demonstrated that colon cancers derive from benign tumors called adenomas. In contrast,
Antibodies have broad research and clinical applications. Researchers use millions of animals to produce antibodies by techniques that cause great suffering. Despite the ready availability of inexpensive in vitro methods, many researchers (who claim to use animals "only when necessary") don’t bother to use the humane alternative.

Mathematical models using human clinical data are another source of information that is more reliable than data derived from animal studies. Mathematical models use human clinical and epidemiological data to generate hypotheses about complex disease processes. For example, a mathematical model has indicated that there are two distinct types of breast cancer—one very malignant, the other much less so—that look alike under the microscope. This model suggests that the more malignant form requires early diagnosis and aggressive treatment, while excision is likely to be curative in the less malignant form.

Why Vivisection Persists

If animal experimentation is so flawed, why does it persist? There are several likely explanations.
Vivisection appears more "scientific" than clinical research. Researchers often assert that laboratory experiments are "controlled," because they can change one variable at a time. The control, however, is illusory. Any animal model differs in myriad ways from human physiology and pathology. In addition, the laboratory setting itself creates confounding variables—for example, stress and undesired or unrecognized pathology in the animals. Such variables can have system-wide effects, skew experimental results, and undermine extrapolation of findings to humans.

Vivisection is lucrative. Its traditionally respected place in modern medicine results in secure financial support, which is often an integral component of a university’s budget. Many medical centers receive tens of millions of dollars annually in direct grants for animal research, and tens of millions more for overhead costs that are supposedly related to that research. Since these medical centers depend on this overhead for much of their administrative costs, construction, and building maintenance, they perpetuate vivisection by praising it in the media and to legislators.

Vivisection's morality is rarely questioned by researchers, who generally choose to dogmatically defend the practice rather than confront the obvious moral issues it raises. Animal researchers' language betrays their efforts to avoid morality. For example, they "sacrifice" animals rather than kill them, and they may note animal "distress," but they rarely acknowledge pain or other suffering. Young scientists quickly learn to adopt such a mindset from their superiors, as sociologist Arnold Arluke explains:

"One message—almost a warning—that newcomers got was that it was controversial or risky to admit to having ethical concerns, because to do so was tantamount to admitting that there really was something morally wrong with animal experimentation, thereby giving 'ammunition to the enemy.'"

Animal researchers' ethical defense of the practice has been superficial and self-serving. Usually, they simply point to supposed human benefits and argue that the ends justify the means. Often, they add that nonhuman animals are "inferior," lacking certain attributes compared to humans, such as intelligence, family structure, social bonding, communication skills, and altruism. However, numerous nonhuman animals—among them rats, pigs, dogs, monkeys, and great apes—reason and/or display altruism. There is accumulating evidence that many animals experience the same range of emotions as humans. Chimpanzees and gorillas can be taught human sign language, and sign with one another even without humans present.

Furthermore, evidence indicates that many animal researchers fail to acknowledge—or even perceive—animal pain and suffering. For example, sociologist Mary Phillips observed animal researchers kill rats in acute toxicity tests, induce cancer in rodents, subject animals to major surgery with no post-

Many nonhuman animals demonstrate that their emotions and thoughts closely resemble those of humans.
operative analgesia, and perform numerous other painful procedures without administering anesthesia or analgesia to the animals. Nevertheless, in their annual reports to the USDA, none of the researchers acknowledged that any animals had experienced unrelieved pain or distress. Phillips reported, "Over and over, researchers assured me that in their laboratories, animals were never hurt. . . "Pain" meant the acute pain of surgery on conscious animals, and almost nothing else. . . [When I asked] about psychological or emotional suffering, many researchers were at a loss to answer."  

The tens of millions of animals used and killed each year in American laboratories generally suffer enormously, often from fear and physical pain, nearly always from the deprivation inflicted by their confinement, which denies their most basic psychological and physical needs.

**Conclusion**

The value of animal experimentation has been grossly exaggerated by those with a vested economic interest in its preservation. Because animal experimentation focuses on artificially created pathology, involves confounding variables, and is undermined by differences in human and nonhuman anatomy, physiology, and pathology, it is an inherently unsound method to investigate human disease processes. The billions of dollars invested annually in animal research would be put to much more efficient, effective, and humane use if redirected to clinical and epidemiological research and public health programs.

**References and Notes**

1. The Physicians Committee for Responsible Medicine and the Medical Research Modernization Committee combined have over 4500 scientist and physician members, most of whom are highly critical of vivisection.


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