Discussion

Educators can have a profound effect on the replacement, reduction, and refinement of educational uses of animals. In order to develop and implement alternatives, educators need the proper motivation, the support of their colleagues, and financial and academic incentives. Scientists recognize the importance of academic incentives in developing educational alternatives, as this observation on development of computer-based simulators indicates:

In the long run, the most serious problem to developing these simulators may well be the lack of professional academic rewards for faculty members working in this area. Promotion, tenure, and salary increments are awarded predominantly for productivity in the research laboratory, not for efforts to develop innovative teaching techniques and materials. With essentially no external grant support for computer-based education activities and with few refereed high-quality journals in which to publish, two of the measures by which rewards are apportioned are not available to developers of novel educational software. This is a particular problem for junior faculty members, who often must devote their major efforts to climbing the academic ladder. Computer-based education seemingly fails to meet the perception of an academically valid and credible enterprise.

Although lack of funding may impede the development of alternatives in some cases, it may actually dictate the adoption of non-animal methods in others. For example, the expense of procuring and housing dogs in medical schools may force these schools to implement computer programs instead.

Money, therefore, is not all that's needed to foster widespread application of the alternatives approach in education. Concerned instructors, educational administrators, funding agencies, students, and parents must be involved as well.

But no amount of effort will succeed unless the existing alternatives have merits in their own right. Does each alternative get the job done as well as or better than its animal-related counterpart? If not, is each alternative still adequate? Educators should clearly spell out the goals of their animal projects and determine whether or not alternatives meet those goals.

PROGRESS IN IMPLEMENTING the alternatives approach has been encouraging, especially in light of the modest investment of money and effort. In toxicity testing, the first generation of alternative screening tests is being developed, validated, and implemented. In biomedical research, investigators are applying alternative techniques to answer questions in diverse fields. In education, technological innovation is yielding new alternatives, such as robot-like mannequins and computer simulators.

Much of this progress has occurred within the last ten years, as the animal-rights movement has infused the search for alternatives with an ethical imperative. Prior to this, alternatives were pursued primarily for economic, public health, and scientific reasons but rarely as a reflection of a sense of moral duty or compassion. Even today, when specific alternatives are introduced to the scientific community in research reports, concern for animals is not necessarily cited as a reason for their development or possible implementation. Nevertheless, the introduction of new alternatives, for whatever reason, is still good news.

The most exciting alternatives in the areas of research and testing are based on the development of techniques such as tissue culture and computer modeling. Such breakthroughs in technique have been extremely important in the history of science, as Rowan has emphasized. Technical innovations are used to answer old questions and address new ones. A historical example is the application of tissue culture to the prevention of polio. The development of a polio vaccine required that large amounts of polio virus be readily available. This was impractical using mice and monkeys, which were used extensively in polio research. Enders and coworkers discovered that the virus could be cultivated in vitro. This paved the way for Salk, Sabin, and others to develop effective vaccines. A testament to the importance of the tissue-culture work in combating polio is that Enders and coworkers, not Salk or Sabin, were awarded the Nobel Prize for their polio research.

Some new techniques are not alternatives in themselves but can, nonetheless, decrease reliance on laboratory animals by creating new possibilities for studying humans without recourse to questionable animal models. An example is positron emission tomography, discussed earlier in relation to human studies of Parkinson's disease.

Techniques such as positron emission tomography, which decrease reliance on
animal models by facilitating the direct study of humans, are sorely needed in biomedical research. Consider the remarks of Stephen Suomi, himself an advocate of animal models:

The primary problem in conducting research on humans is avoiding undue risk or harm to the subjects. Consequently, new, powerful techniques that are relatively harmless should be eagerly embraced by animal modelers.

Biomedical research is not the only area of laboratory animal use that has benefited from the application of new techniques. Alternative techniques, especially tissue-culture and computer modeling, are transforming toxicology from an empirical exercise into a predictive science. Tissue-culture techniques can not only determine whether or not chemicals are toxic but also uncover how toxic chemicals exert their effects. Modeling can help identify the structural features of chemicals that are likely to cause toxicity. Current methods treat each new chemical as a complete unknown and use whole animals to determine whether or not a substance is toxic.

The need for a transformation in toxicology was forcefully underscored by Nobel Laureate Joshua Lederberg, president of Rockefeller University:

I think the testing of substances could be greatly improved above all by better understanding of the mechanisms by which these substances work. The one or two or three hundred millions of dollars a year that we're now spending on routine animal tests are almost all worthless from the point of view of standard-setting. It is simply not possible with all the animals in the world to go through new chemicals in the blind way that we have at the present time, and reach credible conclusions about the hazards to human health.4

To a substantial degree, our continued need for animals in testing is a function of our ignorance rather than our knowledge. In 1972, Nobel Laureate Sir Peter Medawar predicted that the use of laboratory animals on its then-current scale would decrease as biomedical knowledge increased. This should hold especially for toxicity testing, given that its goals and methods are much more limited than those pertaining to research.

Toxicity testing does comprise a diverse array of tests. The replacement of all of these tests with alternative techniques will take a long time. In the meantime, toxicologists should exploit existing alternatives to the fullest extent. For example, if a comprehensive evaluation of a new chemical requires both alternative tests and traditional tests, the former should be conducted first; in this manner, chemicals that "fail" the alternatives tests need not be tested further on animals.

Another way of reducing animal use in toxicity testing is to make results of these tests public. Many manufacturers of drugs, cosmetics, pesticides, and other compounds make extensive use of animals not only in toxicity testing but also in product development. The results of these investigations are sometimes regarded as trade secrets; thus, competing companies may be inadvertently investigating the same compounds, resulting in a waste of animals. Although competition among companies requires that these investigations be kept confidential to some degree, such secrecy exacts a toll in animal life and suffering. A compromise solution would be to require companies to divulge the results of their investigations after a specified time.5

Some companies are taking steps to avoid unintentional repetition of toxicity tests. The Chemical Industry Institute of Toxicology, for example, earmarks contributions from member companies for toxicological testing and distributes the

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results widely.6 We have seen that poor and inhumane animal tests persist despite their faults. As Sharpe noted, "we cannot delegate our responsibilities onto other animals, who only reward us with illusions of safety." The remedy for this sorry state of affairs in toxicity testing is not only better tests, especially alternative tests, but also the realization that the proper measure of man is man. The United States should consider adopting a post-marketing surveillance scheme patterned after the one used in Britain. Early detection of problems with new products in actual use should be an essential component of safety programs. This was recommended by a 1977 European convention on drug monitoring. The scientists in attendance concluded, in part:

Only by the careful study of medicines in everyday use can greatest benefits be obtained from their administration, the untoward rare potential disaster recognised at the earliest possible moment, and the ill effects minimised. Absolute safety is unattainable and its pursuit, regardless of other considerations, is achieving more harm than good [emphasis added].8

Future progress on alternatives will depend, in part, on the extent to which the alternatives approach is embraced by biomedical scientists. While a few of these scientists view the approach favorably, the response of others has been lukewarm.9 Researchers seldom target their work toward alternatives as ends in themselves. Some dismiss the approach altogether.10,11 Recent progress on alternatives suggests that these naysayers are fighting a losing battle.

Several factors probably contribute to the scientific community's resistance to the alternatives approach. First, alternatives tend to be viewed in the narrow sense of replacements. Because replacements for some types of laboratory animal procedures will take many years to develop, this narrow view of alternatives engenders unnecessary pessimism. Adoption of the broader definition of alternatives as reductions and refinements as well as replacements should make the alternatives approach seem less quixotic.

A second reason for scientists' resistance to alternatives may be that alternatives are promoted by (among others) the opponents of animal research, namely, anti-vivisectionists. Animal researchers may not want to be seen as giving in to their opponents or they may view anti-vivisectionists as zealously promoting alternatives that are ineffective in order to save animals.

A third and related reason is that advocates for alternatives may be viewed as irrational and anti-research. However, the target of these advocates is not research in general, but animal research. Given the extent to which groups advocating alternatives are funding research on alternatives, the anti-research charge seems to be a smoke screen.

Fourth, researchers who were trained to use animals may be hesitant to learn new techniques. Perhaps the most cynical suggestion for the resistance to alternatives is that alternatives pose a threat to the multi-billion-dollar industry of animal research. Thousands of people make a living from animal research. Scientists do so by conducting and reporting research; veterinarians by administering to research animals; dealers by selling animals; and manufacturers by supplying cages, food, antibiotics, etc. Research institutions also profit by receiving a hefty percentage of the money awarded to their individual researchers. Some of these people or institutions undoubtedly would rather maintain the status quo than make the adjustment to an alternatives-based research industry.

Some money is given specifically for alternatives research. Though the amount is small compared to funding for animal research, it may lure some animal researchers into alternatives. T.D. Overcast and B.D. Sales claim that some animal researchers are pursuing alternatives for another reason, namely, to protect themselves from the impact of future regulations on animal research.12 However, this claim may have
been made more for its alarmist effect on regulators and its portrayal of animal researchers as beleaguered than for its reflection of a realistic trend. Of course, it would be foolish to suggest that all biomedical scientists oppose the alternatives approach and all have questionable motives, even those who pursue alternatives.

Whatever the motivations and beliefs of researchers, the case for alternatives must ultimately be judged on its own merits. There is a surprising amount of historical information on which to base this judgment. In the following analysis, consider alternatives in the narrow sense of techniques that avoid the use of intact animals altogether. Actually, this is too narrow a definition because we want to include the use of "less sentient organisms" (invertebrates, microorganisms, plants, and vertebrate embryos) as an alternative technique. And, of course, we are also including human and in vitro studies, mathematical modeling, and physical-chemical techniques.

Most of these techniques have existed for decades, although they have not been discussed much in the context of alternatives until the last ten years or so. Some alternatives techniques were used in projects that could have been conducted on intact vertebrate animals; today, we'd categorize these as alternative projects. In other instances, "alternative" techniques were used in projects that were beyond the capabilities of vertebrate studies.

Nobel Prize awards in medicine or physiology can be used as an index of the importance of alternative techniques in the history of biomedical research. These awards are generally believed to recognize research "of the highest caliber, the most enduring influence, and the most importance to biomedical science" according to the National Academy of Sciences (NAS).

Awards that were made for research whose success depended wholly or primarily on alternative techniques were identified. The remaining awards were for projects that were successful owing primarily to in vivo studies of vertebrates, labeled non-alternative techniques. Sufficient information was available to classify all but two awards. Although most of the other seventy-four awards were readily classified, some proved difficult. These were generally assigned to the non-alternative category. When the same award was divided among two or more projects, the award was classified in the alternative category as long as at least one project depended wholly or primarily on alternative techniques.

About fifty (or two-thirds) of the Nobel Prizes were awarded to projects using alternative techniques (see Appendix A). This finding clearly documents the importance of these techniques in the history of biomedical research. The techniques advocated in this report have been used to conduct in-vivo biomedical research and continue to do so.

Those projects that used alternative techniques were further classified as to whether the projects themselves can be considered alternatives to research on whole vertebrates or whether the projects investigated topics that could not have been investigated using whole vertebrates. Although there were several equivocal cases, the fifty awards for projects using alternative techniques fell about equally in both categories (twenty-four and twenty-six, respectively). The techniques advocated in this report have been the cornerstone of some of the twentieth century's most significant biomedical research. In some cases, they have substituted for the use of vertebrates; in other cases, they have added to our biomedical knowledge in ways that were not feasible using vertebrates.

Two considerations are important in interpreting the results of the Nobel analysis. One is that most of the award-winning projects were conducted before the alternatives approach was first articulated (1959). This increases expectations of what can be achieved if biomedical researchers actively pursue alternatives as ends in themselves.

The second consideration is that more awards would have gone to projects that used alternative techniques if not for the traditional emphasis on in vivo vertebrate studies in biomedical research. For example, many animal researchers were skeptical of tissue-culture systems in the early days of this technique's existence. According to NAS, if not for this skepticism, tissue culture "might have been used to discover many of the vitamins, amino acids, and hormones." Tissue culture could have been used to discover the hormone insulin, for instance. Even human studies could have yielded this discovery. Yet the researchers who discovered insulin used traditional in vivo methods, with dogs. They were awarded the Nobel Prize in 1923. This by-product of tradition is often regarded as a triumph of animal research, yet other techniques could have done the job.

Twentieth century Nobel Prizes in medicine or physiology were analyzed from a somewhat different perspective by NAS, which focused on the types of organisms used in the award-winning research, instead of on techniques. The results were compared to funding patterns of NIH to assess whether funds were allocated among types of organisms according to their representation in award-winning research (which presumably is some indication of the relative value of these organisms in biomedicine).

NAS concluded that research on mammals was being overfunded in relation to its representation in the Nobel awards and in other outstanding research:

Considering the great strides in our understanding of biology and medicine that have resulted from the study of microorganisms, invertebrates, and lower vertebrates, the proportion of NIH resources that supports research in this area may be small in comparison to the resources dedicated to research with mammals.

This suggested misapplication of funds may result from what was described earlier as the high fidelity fallacy—that mammals are of exceptionally high fidelity as models of humans and therefore should be used as often as possible; NAS recommended resisting this perspective.

Proposals for the study of invertebrates, lower vertebrates, microorganisms, cell- and tissue-culture systems, or mathematical approaches should be regarded as having the same potential relevance to biomedical research as proposals for work on systems that are phylogenetically more closely related to humans. Support should be given to good research without taxonomic or phylogenetic bias on the part of the sponsor and should include comparative and phylogenetic studies.

NAS's recommendation is directed at NIH funding patterns such as the one depicted in Figure 1. The figure displays information for 1983, the most recent year for which information is available. Information from previous years (1980-1982) shows similar trends. Note that research on vertebrate animals, especially mammals, was the highest funded category. It exceeded the combined funding for research using in vitro techniques, mathematical modeling, and less sentient organisms (invertebrates, microorganisms, and plants). Funding for research on nonhuman mammals alone exceeded funding for human research, despite the fact that the mission of NIH is to protect human health.

Funding decisions are influenced to a certain extent by the interests and perspectives of the scientific community. Hence, alternatives research undoubtedly would be a higher priority if scientists supported the alternatives approach. In issues that involve the use of animals in research, such as alternatives, scientists are often portrayed as being engaged in polarized battles with anti-vivisectionists. In a sense, we are all anti-vivisectionists because none of us wants animals to have to suffer or die in laboratories. The alternatives approach can provide a common ground for both researchers and animal advocates to demonstrate their humane concern. This view is reflected in the policy of The Humane Society of the United States on the use of...
FIGURE 1
NIH Funding, 1983

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humans</td>
<td>24%</td>
</tr>
<tr>
<td>Nonhuman Vertebrates</td>
<td>34%</td>
</tr>
<tr>
<td>Mammals</td>
<td>30%</td>
</tr>
<tr>
<td>Nonmammals</td>
<td>2%</td>
</tr>
<tr>
<td>Both</td>
<td>2%</td>
</tr>
<tr>
<td>Invertebrates</td>
<td>3%</td>
</tr>
<tr>
<td>Microorganisms</td>
<td>2%</td>
</tr>
<tr>
<td>Math. Models</td>
<td>2%</td>
</tr>
<tr>
<td>Plants</td>
<td>25%</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>2%</td>
</tr>
</tbody>
</table>

TOTAL: $3,234,737,694

1. Distribution of support from the National Institutes of Health (NIH) for research on various organisms during 1983. Figures are for extramural research (i.e., research not conducted at NIH) only. "Miscellaneous" includes projects on invertebrates in combination with various other organisms.


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Laboratory animals (see Appendix B).

Enthusiastic support for the alternatives approach, not only by researchers and animal-rights advocates but also by funding agencies, regulatory agencies, educators, and the general public, will hasten the day when laboratory animals are spared from their regrettable plight.

The alternatives approach is part of a more inclusive approach toward animal research that is characterized by concern for animals. This humane concern can be expressed in various ways in addition to seeking replacement, reduction, and refinement. For example, researchers contemplating the use of animals should determine, first, whether their topic is worth investigating and, second, whether their research would involve unnecessary duplication. Such duplication can be reduced by searching through computerized bibliographies of published research reports and by determining whether relevant research published in foreign languages has been translated. The John Crerar Library at the University of Chicago is a clearinghouse for such translations. Third, researchers should determine whether the chosen animal species is the best (or at least an adequate) subject of study. Research conducted on poor or invalid "animal models" is a waste of animals and effort.

Albert Schweitzer was a prominent exponent of this perspective. He wrote:

Those who carry out scientific experiments with animals, in order to apply the knowledge gained to the alleviation of human ills, should never reassure themselves with the generality that their cruel acts serve a useful purpose.

In each individual case they must ask themselves whether there is a real necessity for imposing such a sacrifice upon a living creature. They must try to reduce suffering insofar as they are able.

A humane approach to research goes beyond asking questions about specific projects. It calls for a reappraisal of the entire biomedical research paradigm, which emphasizes the development of treatments for people who are already sick. The application of this paradigm has exacted a heavy toll in animal suffering and death. Many people have cogently argued that this paradigm is misguided even from the point of view of human health. Human health would be better served if prevention were emphasized over treatment. A biomedical research program that emphasized prevention would shift research away from animal studies and direct it more toward screening programs and alternative techniques, especially epidemiological and clinical studies on humans.

The case for prevention over treatment was recently made by John Cairns of Harvard University's School of Public Health in a discussion of cancer research. About one hundred different kinds of human cancer are recognized. Because these cancers have their own characteristics, each should be considered as if it were a separate disease. Unfortunately, fewer than fifty percent of cancer patients can be cured by surgery. Supplementary treatments involve administration of hormones, radiation, and chemotherapy. The success rate of these supplementary treatments has been disappointing; they aver only about two to three percent of the 400,000 deaths from cancer each year in the U.S., and they can have serious, sometimes lethal, side effects. Cancer specialist Dr. H. Bush notes that some treatments are so physically and psychologically degrading that some patients wonder whether the treatment is more disabling than the disease. Although some cancers can be effectively treated, these are not the major forms of cancer.

Cairns contrasted the disappointments with our national cancer policy, which emphasizes treatment, with a potential policy that emphasizes screening and prevention. He wrote:

Thanks to the cigarette, the U.S. now suffers a completely unnecessary
additonal 100,000 deaths per year from lung cancer. These numbers dwarf the 3,000 to 10,000 lives that are being saved by chemotherapy. Some countries have banned all tobacco advertising, and this has had an almost instant effect on tobacco sales. The failure of the U.S. Government to take such a step far outweighs all the advances made in the treatment of cancer since the advent of modern surgery.

Cairns also turned to the history of modern medicine to support his case for a prevention–based cancer policy:

None of the important causes of death has been primarily controlled by treatment. The death rates from malaria, cholera, typhus, tuberculosis, scurvy, pellagra, and the other scourges of the past have dwindled in the U.S. mainly because humankind has learned how to prevent these diseases, not simply because they can be cured. There are many grounds for believing that when any major disease is tackled on a national scale, the chief effort should be to prevent its occurrence. To put most of the effort into treatment is to deny all precedent.

The so-called war on cancer is just one example of limited gains resulting from animal research. Millions of dollars have been spent searching for elusive cures to various other diseases, while support for diagnostic programs and preventive measures pales in comparison. Humans as well as animals are the losers.

While defenders of animal research are quick to point out the successes of animal research, they fail to add that the advancement of medicine and human health has been hindered by an overemphasis on this form of research. In addition to cancer research, examples include research on cocaine abuse, depression, and cardiovascular diseases.

Our inflated hopes for animal–based treatments are undoubtedly fueled by researchers’ self-aggrandizing pronouncements and the resulting media hype. As physician Bush noted with respect to cancer research, “Cures seem to happen more in press releases than in patients.” Dr. P. Goldhaber, the dean at Harvard’s School of Dental Medicine, argued that researchers are “boasting prematurely about the advances and triumphs” of their work and are “extrapolating prematurely from…animal studies to humans.” He cited the fields of dentistry, cancer, and tuberculosis research to support his conclusion.

An emphasis on cure detracts not only from prevention but also from the physical and psychological care of the sick. Bush wrote:

As many cancer clinicians have found, a diagnosis of cancer can so demoralize a patient that the debilitating effects are far worse than the early physical effects of the disease.

It is time that more of the research dollars now devoted to cures be diverted to finding new and more humane ways of caring that will make a cancer patient’s remaining years happier, more comfortable, and more productive. My experience suggests that in the patient’s eyes good care aimed at improving the quality of life may be just as important as cure.

There are signs that our national cancer policy is beginning to reflect the importance of prevention. The National Cancer Institute is financing the establishment of “cancer prevention research units” around the country to discover cancer–preventing strategies, including dietary changes. Instead of using laboratory animals, this research will test “likely cancer preventives in the most persuasive way possible—in the real world, over periods of years, on thousands of healthy human beings.”

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A reorientation of research toward prevention need not entail a total abandonment of research aimed at treatment. However, treatment–based research should take advantage of new applications of alternative techniques in a wide variety of areas, including cancer and AIDS.

The paradigm shift from treatment to prevention can be translated into our everyday lives. On the basis of numerous human studies, physician J. Schaffenberg concluded that personal health and salvation from disease are largely a matter of personal choice. He described a life-style that promotes health and dramatically reduces the risk of disease. It includes, among other things:

- a good diet of fruits, whole grains, nuts, and vegetables while avoiding the meat and high animal fat products and eggs, adequate sleep, good exercise in the open air, abstinence from harmful things such as tobacco, alcohol, coffee, tea, and other drugs, drinking plenty of water, moderation in all things including the amount of food eaten.

Taking greater personal responsibility for our own health would lessen our reliance on animal–based treatments. In the event that we become sick, we should think twice before taking drugs that were developed or tested on animals. Are treatments available that are not animal–based? Will rest and relaxation be sufficient for recovery?

In a similar vein, we should keep laboratory animals in mind when shopping. First, we should buy products whose development and testing did not involve animals. A list of companies that sell “cruelty–free” cosmetics and toiletries is available from The Humane Society of the United States. Second, we should avoid buying household products that are “new and improved,” as these modifications probably necessitated further animal testing.