BRUTE SCIENCE

"This is as important a book in applied ethics as one can hope to find. It mounts an impressive scientific and moral case against the current practice of animal experimentation, demanding that we either provide an adequate defense of that practice or radically change it."

James P. Sterba (Philosophy), University of Notre Dame

"Brute Science provides a careful, historical and interdisciplinary analysis of scientific experimentation using non-human animals. Everyone seriously interested in biomedical experimentation – those who use animals and those who use the results of experimentation – should read this book."

Marc Bekoff (Biology), University of Colorado

"One need not accept all of the authors' arguments and conclusions to benefit from their clear and perspective analysis of the scientific and philosophical issues involved . . . Their policy recommendations deserve serious consideration from both scientists and animal rights advocates."

John Parascandola, medical historian

Are humans morally justified in conducting sometimes painful experiments on animals in their search for a cure for cancer, heart disease, and AIDS? Apologists for animal experimentation claim for practice is morally justified, because humans are more valuable than animals, and scientifically justified, because the data derived from these experiments profoundly benefits humans. *Brute Science* investigates this standard defense of animal experimentation.

Hugh LaFollette and Niall Shanks show, on methodological and empirical grounds, that defenders of animal experimentation seriously exaggerate its benefits. The authors' analysis reveals that, although these experiments may be a rich source of hypotheses about human biomedical phenomena, they can never prove or establish anything about these phenomena. Consequently, we need to reassess, scientifically and morally, our use of animals in biomedical experimentation.

Brute Science is a ground-breaking analysis that should be read by philosophers, public policy analysts, animal rights activists, medical students, and anyone involved in research using animals.

Hugh LaFollette is Professor of Philosophy at East Tennessee State University; he is the author of *Personal Relationships: Love, Identity, and Morality* (1995) and editor of *Ethics in Practice: An Anthology* (1996). **Niall Shanks** is Associate Professor of Philosophy and Adjunct Professor of Biological Sciences at East Tennessee State University.

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BRUTE SCIENCE

Dilemmas of Animal Experimentation

Hugh LaFollette and Niall Shanks

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CONTENTS

PREFACE

> Vivisection is a very old procedure. It has been practiced since the beginning of scientific medicine, in ancient Greece and Rome. Through the seventeenth and eighteenth centuries it even acquired a certain degree of popularity. Doubt about vivisection, however, whether of a medical or moral kind, has been virtually coeval with the existence of the practice. But this doubt did not develop into a major public controversy until the second half of the nineteenth century. By then, experimentation on living animals had become a quintessential part of physiology as an institutionalized profession (Rupke 1990: 1–2).

The American Medical Association (AMA) estimates that biomedical researchers in the US use between 17–22 million animals each year (1992: 15); others estimate the number is higher. Although we can finally judge the scientific and moral legitimacy of the practice only if we determine more precisely the number of animals used in research, on all available estimates, the numbers are sufficiently high to demand that we evaluate the practice.

Most debates about the practice of animal experimentation are moral debates. Although parties to these debates disagree about the moral appropriateness of animal research, they often agree that the research is scientifically legitimate. Of course, some opponents of animal experimentation challenge the scientific validity of certain types of research. However, many of these objections, although perhaps suggestive, are inadequately developed and scientifically uninformed.

Nevertheless, there are scientific questions about the validity of

animal experimentation that both sides of this debate should consider seriously. A careful scientific and methodological assessment of the practice reveals that claims about the enormous benefits of animal research – claims made in both public policy statements designed for public consumption and in scientific texts – are exaggerated. More generally, we have reason to question whether the legitimacy of straightforwardly extrapolating the results of animal experimentation to humans.

Doubts about the grand claims made for animal experimentation emerge from a careful examination of evolutionary biology. Evolutionary theory is no mere adjunct to contemporary biology; rather, it is at its center. It is intricately connected to genetics, population biology, systematics, and ecology; evolutionary biology is the theoretical glue that holds these disparate fields together. Especially important to the current inquiry, evolutionary theory helps us understand the biological significance of speciation. Modern physiology and biomedicine assume we can legitimately extrapolate laboratory findings from one species to another. That is why a proper understanding of the nature of species and species differences will be central to a scientific evaluation of these practices.

In the popular debate about animal experimentation, these deeper scientific questions are seldom discussed, and when they are discussed they are discussed in ways that often distort rather than clarify the issues. Neither the critics nor the defenders of these practices have adequately explored the implications of evolutionary theory. We wish to remedy this deficiency. We will carefully analyze the scientific, methodological, and epistemological merits of the practice of animal experimentation. There are, contrary to some apologists, legitimate criticisms of the practice of animal experimentation. And, contrary to some critics, there are scientifically legitimate reasons for conducting research using animals. A proper understanding of the scientific issues will illuminate the ethical and public policy debates about animal experimentation. By some estimates the National Institute of Health currently allocates about 40 percent of its resources for animal research, 30 percent for human studies, and 30 percent for alternative research methodologies. Whether this is the best allocation of scarce research resources depends partly on the scientific and moral legitimacy of biomedical experimentation using animals.

THE STRUCTURE OF THE ARGUMENT

In Part I we set out the background information essential for a proper scientific evaluation of biomedical experimentation. We present prima facie cases for and against animal experimentation. These reveal the typical argumentative strategies employed by each side of this debate. Although both cases are plausible, neither plumb the deeper epistemological and methodological questions we think are so important. Both sides rely heavily on examples to defend their respective cases. Although this is an understandable strategy, it is not especially productive. Among other things, it overlooks the centrality of animal experimentation to the current biomedical paradigm, and how that central role affects our interpretation of these examples.

We first explore the roots of this paradigm in the work of the nineteenth-century French physiologist, Claude Bernard. Then we set out the contours of the current paradigm. We specifically explore the role of the *Intact Systems Argument*, the use of scaling principles, and the paradigm's commitment to biological reductionism. We end this section by introducing contemporary evolutionary theory. We focus on those elements of the theory especially relevant to a critical assessment of the current biomedical paradigm.

In Part II we explain how a proper understanding of the theory of evolution, in tandem with laboratory findings, undermines the claim that, since animal models are strongly analogous to the human conditions they model, we can straightforwardly extrapolate findings in laboratory animals to humans. We then explore other defenses of animal experimentation, including the claim that animal models, although not strongly analogous, are still useful. We show how the study of complex systems theory exposes weaknesses in the standard defenses of the practice. Then we discuss researchers' attempts to evade and avoid the consequences of causal disanalogy. Finally, we discuss basic research. Throughout the book, and in this section particularly, we quote extensively from evolutionary biologists and biomedical researchers. Although these citations may seem excessive, they provide the necessary background for evaluating animal experimentation.

Although the arguments in this book will expose the weakness of animal experiments whose results are to be directly extrapolated or applied to humans, the relevance of these arguments to other uses of animals is unclear. Animal experimentation is not all of a

piece. There are different scientific uses of animals, and these must be evaluated differently. Some specialized uses of animals will not be touched by the methodological arguments raised in this section (though perhaps some moral arguments developed in Part III will be relevant to their assessment). Some of these are: (a) using animals as hosts for viruses (e.g., the early use of rhesus monkeys to preserve strains of polio virus), (b) using animals as "bio-reactors" to produce biologically active compounds, or (c) epidemiologists' and pathologists' experiments on wild animals to uncover the natural hosts of human viruses, for example the Ebola virus.

For still other uses of animals our arguments may have some application, although not as direct as for applied research. For instance, our methodological arguments do not have direct bearing on the use of animals in education. Perhaps what is more important, these methodological arguments have less direct bearing on *basic research*, be it anatomical, physiological, toxicological, virological, and so on.

In Part III we build on the analysis from the previous chapters to evaluate animal experimentation morally. We first set the moral debate in historical context, showing how the moral understanding of non-human animals has evolved over time – especially after the advent of evolutionary theory. We argue that, although some arguments that humans have strong moral obligations to animals are plausible, any widely accepted evaluation of experimentation must be based on weaker moral assumptions. The assumption that non-human animals have some moral worth is sufficiently weak to be acceptable to most people, while also being sufficiently powerful to generate potent questions about the morality of the practice.

We first discuss speciesism, and, more generally, deontological defenses of animal experimentation. Then we consider the utilitarian defense of the practice, which claims the practice is justified because of its enormous benefits to human health. We conclude that the practice of using animals in medical research is morally questionable, partly because we cannot straightforwardly apply findings in animals to humans. However, as we noted earlier, the evaluation of basic research, will, by its nature, be somewhat different.

We end the book with some public policy recommendations about the continued use of non-human animals in biomedical experiments.

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Part I

UNDERSTANDING THE DEBATE

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1

A FIRST LOOK

The prima-facie cases

Why investigate the scientific and moral value of animal experimentation? We know that it increases our knowledge of the animal species under study. Don't we also know that it has promoted human health and well-being? Isn't the very act of questioning the scientific, epistemological, and moral status of animal research either misplaced, silly, or simply misanthropic?

Certainly there is a prima-facie case to be made for animal experimentation. Any adequate assessment of the scientific, epistemological, and moral appropriateness of animal experimentation cannot ignore this case. Although branding researchers and their public policy advocates as barefaced liars may be rhetorically effective, it is intellectually indefensible. Doubtless advocates on all sides of this debate have exaggerated their respective cases. However, this does not license the inference that researchers (or their opponents, for that matter) have nothing important to say, or that all or most of their claims are false.

Indeed, the public debate over animal experimentation has been unproductive largely because both sides have been reluctant to seriously consider their opponent's claims and to critically examine their own presuppositions. Were both sides to scrutinize the arguments, they would discover that the "opposition," even if mistaken, is neither crazy nor wholly off the mark. So we begin by setting out the prima-facie cases for and against biomedical research using animals, snapshots of the cases made by opposing sides in this debate. These prima-facie cases are not irrefutable. They do, however, offer evidence that suggests that there is a case to be considered – much as a preliminary hearing in a court of law does not establish guilt or innocence, but rather determines whether there is a case to be heard.

THE PRIMA-FACIE CASE IN FAVOR OF ANIMAL EXPERIMENTATION

What, precisely, is the case for animal experimentation? We begin by summarizing the arguments of the research community and their policy advocates. Then we shall briefly outline the principal philosophical defense of the practice. Finally, we will discuss some arguments offered by individual researchers and biologists.

Sigma Xi

Sigma Xi, the scientific research society, defends the use of non-human animals in biomedical research by citing what they take to be the enormous benefits of that research:

> Results from work with animals have led to understanding mechanisms of bodily function in humans, with substantial and tangible applications to medicine and surgery (e.g., antibiotics, imaging technologies, coronary bypass surgery, anti-cancer therapies), public health (e.g., nutrition, agriculture, immunization, toxicology and product safety) ... As the Surgeon General has stated, research with animals has made possible most of the advances in medicine that we today take for granted. An end to animal research would mean an end to our best hope for finding treatments that still elude us (1992: 74).

In their view animal experimentation is not a scientific technique that has outlived its usefulness. Biomedical inquiry would be seriously hampered were scientists unable to continue their reliance on animal experimentation:

> Research with animals has been remarkably successful in generating both basic and applied knowledge. Without such research, many of us would not have survived diseases that were once common. Without further research with animals, there will be no vaccine for AIDS and dramatically fewer advances for treating and preventing heart disease, cancer, and other serious health problems (1992: 74).

Doubtless, the development of alternatives to animal research (e.g., computer simulations, cell and tissue cultures) may reduce the numbers of animals used for certain purposes:

> However, these developments will not entirely replace the use of animals. Indeed, the number of animals used in research may actually increase, for several reasons: First, virtually all of these alternative methods are now adjuncts to the use of animal subjects in research, not replacements for such subjects. Second, because of complex interactions between organ systems, some physiological processes cannot be studied in isolation, but require entire animals. Third, new lines of animal research (e.g., transgenic animals) will be needed to reap the benefits of recent progress in fields such as molecular biology and genetics. Finally, results of computer simulations may raise research questions that can be addressed only by the use of animal subjects (1992: 75).

This Sigma Xi statement encapsulates the central features of the argument for animal experimentation, namely that (a) no matter how useful non-animal research methodologies are, they are mere adjuncts to animal research; (b) most significant research must be performed on whole, intact, animal systems; (c) research using whole animals has been the primary engine of biomedical advance.

The American Medical Association

The AMA White Paper, *Use of Animals in Biomedical Research*, echoes the Sigma Xi Statement's triumvirate of claims in support of research using animals. Such research, the authors claim, "is essential to improving the health and well-being of the American people, and the AMA actively opposes any legislation, regulation, or social action that inappropriately limits such research."

Why are they so concerned to maintain animal research? Because, they say,

> 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. The result of these experiments has been the elimination or control of many infectious diseases – smallpox, poliomyelitis, measles – and the development of numerous life-saving techniques – blood transfusions, burn therapy, open-heart and brain surgery. This has meant a longer, healthier, better

> life with much less pain and suffering. For many, it has meant life itself (1992: 11).

The White Paper not only argues for the value of animal experimentation, it responds to some claims of critics. For instance, some animal activists claim that increased longevity and well-being are due to public health measures. However, the White Paper avers that these activists are mistaken.

> [F]or most infectious diseases, improved public health and nutrition have played only a minor role. This is clear when one considers the marked reduction in the incidence of infectious diseases such as whooping cough, rubella, measles and poliomyelitis. Despite advances in public health and nutrition, eradication or control of these and most other infectious diseases was not achieved until the development of vaccines and drugs through research using animals (1992: 11–12).

In short, according to the AMA, the bulk of the improvement of longevity and well-being in the twentieth century is a consequence, directly or indirectly, of biomedical research using animals. Animal experiments are the core of current biomedical research.

Carl Cohen

In 1986, the *New England Journal of Medicine* published an article by philosopher Carl Cohen defending the use of animals in biomedical research (Cohen 1986). Cohen builds on the claims of researchers about the enormous benefits of animal experimentation to mount a utilitarian argument in favor of research:

> When balancing the pleasures and pains resulting from the use of animals in research, we must not fail to place on the scales the terrible pains that would have resulted, would be suffered now, and would long continue had animals not been used. Every disease eliminated, every vaccine developed, every method of pain relief devised, every surgical procedure invented, every prosthetic device implanted – indeed, virtually every modern therapy is due, in part or in whole, to experimentation using animals (1986: 868).

For Cohen, the moral to be drawn is clear. Had opponents of

animal experimentation been heeded, "Untold numbers of human beings – real persons, although not now identifiable – would suffer grievously as a consequence of this well-meaning but shortsighted tenderness" (Ibid.).

Like the scientific defenders of the practice, Cohen is pessimistic about the possibility of replacing animal-based research with non-animal research methodologies:

> No other methods now on the horizon – or perhaps ever to be available – can fully replace the testing of a drug, a procedure, or a vaccine, in live organisms. The flood of new medical possibilities being opened by the successes of re-combinant DNA technology will turn to a trickle if testing on live animals is forbidden (1986: 868).

In fact, Cohen thinks it would be a mistake to maintain, let alone reduce, the current level of animal experimentation: "Should we not at least reduce the use of animals in biomedical research? No, we should increase it, to avoid when feasible the use of humans as experimental subjects" (Ibid.).

Cohen's argument is considered by many scientists to be the definitive moral defense of animal research. The cogency of that defense, however, rests entirely on claims about the profound benefits of animal experimentation for humans' health. To this extent the moral defense of the practice rests upon scientific claims about its enormous benefits.

The perspective of bench scientists

The prima-facie case for animal research, however, does not rest solely on public policy statements or the writings of philosophers. Most theoretically sophisticated scientists assert that animal research has played a pivotal role in human biomedical research. For example:

> There is no question that most medical progress – perhaps all, in fact – has been attained through knowledge derived initially from experiments in various animal species. There is practically no way of replacing animals in these investigations and so-called "alternative methods" are in reality merely complementary. Tissue cultures, cell, microorganisms, enzymes, membranes, mathematical models – all are useful for

> preliminary screening tests and for testing hypotheses, but the complexity of a living organism is such that *in vivo* studies are essential before any test can responsibly be made in man (Garattini and van Bekkum 1990: vii).

However, it is not merely that animals have been useful historically. Rather, knowing how to continue research without using them is difficult if not impossible:

> Historically, models of human diseases reproduced in animals have long been a requisite for discovering new therapies. It is in fact difficult to imagine how to set up *in vitro* techniques for diseases which are expressed under the influence of complex systems such as blood circulation, nervous system regulation, neuroendocrine secretion, immune defenses (Garattini 1990: 1).

Doubtless clinical investigation has prompted some great medical advances. However, according to Sir Peter Medawar, were it not for animal experimentation we could not have made most of these advances (e.g., vaccination against smallpox). Thus, animal experimentation is "unconditionally necessary":

> It is better that laboratory animals should be used than that tests should be made directly upon human beings. So far as insulin is concerned, it was only by experimentation on dogs that it came to be learnt that removal of something manufactured by the pancreas caused diabetes . . . In the continuing debate between experimentalists and champions of the rights of animals, the discovery of insulin remains a shining example of the benefactions experimental animals have conferred upon man (1991a: 113).

A vast majority of researchers agree: they think experiments on non-human animals play a vital role in biomedicine. If two objects are relevantly similar, we naturally assume that the results of experiments on one will, under appropriate conditions, be legitimately extrapolated to the other. Since, researchers argue, we know humans and non-human animals are similar, then results of tests on animals can be applied to humans. Moreover, we know humans and non-human animals are similar in many significant respects. Schmidt-Nielsen identifies four common features of all organisms:

> (1) It was realized early in the last century that all animals and

> plants are made up of cells ... (2) In this century it has become clear that the energy metabolism of animals, the use of fuel, the metabolic enzymes and pathways, etc. universally are based on the same general principles. (3) More recently, revolutionary progress has been made with the revelation of striking similarities in the transmission of genetic information at the molecular level. (4) Another area in which general biological similarity has been established is concerned with cell membranes, membrane potentials, action potentials, and the very active field of membrane transport processes. These areas ... are all examples of striking, unifying principles of biological similarity of the greatest importance (1975: 287).

The claim that there are pervasive biological similarities between non-human animals and human beings is often linked to the further claim that many biomedical phenomena can be studied only in intact animal systems. Studies on isolated (non-intact) animal systems (like cell and tissue cultures) may uncover some simple, isolable biological facts. However, since such systems lack the organizational complexity which exemplifies intact systems, then these isolated systems cannot accurately model most significant biomedical phenomena. When discussing carcinogenicity and risk assessment, Chouroulinkov states this explicitly:

> Thus, the epigenetic systems and control mechanisms in a complex organism cannot be entirely elucidated using cellular models in culture, which have only to do with cellular biology. The *in vivo* reference is absolutely indispensable for investigation of these mechanisms and for assessment of cancer risks. There remains the decision concerning choice of species – human or rodent. Personally I recommend the rodent (1990: 208).

Of course animal researchers are not silly: they recognize biomedical similarities between organisms are not biomedical identities. That is, researchers realize there is no panacea species – no species that, while sufficiently different from humans in morally relevant respects to permit experimentation on them, is nonetheless sufficiently similar in relevant biomedical respects so that we can learn important biomedical information about humans by experimenting on this non-human species. Nonetheless, researchers do think that, under the appropriate conditions, we can legitimately extrapolate findings in laboratory animals to humans.

A brief summary

In short, the prima-facie case for animal experimentation asserts that:

- most medical advances in the twentieth century have resulted, directly or indirectly, from biomedical research using animals;
- halting such research would have serious consequences for human health and well-being;
- there are currently no alternatives to animal experimentation. Cell and tissue cultures, and computer simulations are at best adjuncts to animal experimentation;
- animal experimentation is scientifically justified because of the pervasive biological similarities between humans and non-human animals.

THE PRIMA-FACIE CASE AGAINST ANIMAL EXPERIMENTATION

Exaggerated contributions of medicine

Medicine has benefited humans. Nevertheless, opponents argue that its role in extending human life and in controlling human disease is much less than medical scientists have led us to believe. Consider, for example, the AMA's claim that the dramatic increase in lifespan is directly attributable to medical interventions based on animal research. Many medical historians disagree. Death rates attributable to tuberculosis, pneumonia, influenza, scarlet fever, measles, whooping cough, diphtheria and typhoid fever had dropped dramatically before the advent of vaccinations and chemotherapeutic treatments for these diseases. For instance, approximately 90 percent of the total decline in mortality rates from the most common childhood killers – scarlet fever, whooping cough, measles and diphtheria – occurred before the advent of the treatments and vaccinations for these diseases (McKeown 1976: chapter 5).

Other historians deny that interventionistic medicine has singlehandedly led to the elimination of smallpox, often cited as a triumph of interventionist medicine:

> The history of smallpox of the later years of the nineteenth century does not support the contention that vaccination was fully or finally responsible for the eventual disappearance of

> the disease in Britain. It was in those years, in fact, that there was developed the system for control of the disease that became the basis for the successful modern campaign for its eradication (Hardey 1983: 126).

More generally, many of these critics claim that much, if not most, of the decrease in mortality is traceable not to medical intervention but to preventive measures, especially improvements in diet and sanitation. As *Lancet* explains it in discussing risk assessment: "public health legislation and related measures have probably done more than all the advances of scientific medicine to promote the well-being of the community in Britain and in most other countries" (1978: 356–7). As McKinlay and McKinlay state it:

> In general medical measures (both chemotherapeutic and prophylactic) appear to have contributed little to the overall decline in mortality in the United States since 1900 – having in many instances been introduced several decades after a marked decline has already set in and having no detectable influence in most instances . . . More specifically, with reference to these five conditions (influenza, pneumonia, diphtheria, whooping cough and poliomyelitis) for which the decline in mortality appears substantially after the point of intervention – and on the unlikely assumption that all this decline is due to intervention – it is estimated that at most 3.5 per cent of the total decline in mortality since 1900 could be ascribed to medical measures introduced for the diseases mentioned here (1977: 425).

The limitations of interventionistic medicine are manifest in its inability to control some diseases like cancer. Forni *et al.*, note that

> [T]he overall incidence of tumors is rising but gains in survival time of cancer patients and reductions of cancer death rates are marginal. Of those diagnosed with cancer, only half will be alive in five years time. Surgery, radiotherapy and chemotherapy are improving continuously, but there seems little to support the hope of major breakthroughs (1990: 128).

These limitations of curative medicine are not really surprising. After all, cancer and most serious human diseases are caused, in no small measure, by environmental factors.

> Rates of heart disease . . . have changed much faster over recent decades than can be explained by genetic changes, implicating dietary and environmental causes. And the fact that no single cancer affects every population at the same rate suggests that factors external to the human body cause 70% to 90% of all cancers . . . Only a few of these environmental factors are known – cigarette smoke for lung cancer, or sunlight for skin cancer – and epidemiology seems to provide the best shot at identifying the others (Taubes 1995: 165).

For diseases caused by environmental conditions, it is more prudent to eliminate the conditions which cause the disease than to try to cure the disease once it has occurred. That is why some prominent epidemiologists and physicians, like the former director of the US's "War on Cancer," advocate policies that emphasize prevention:

> Research opportunities in other areas of cancer prevention may well merit sharp increases in support, even if this requires that current treatment-related research must be substantially curtailed. Certainly, the background of past disappointments must be dealt with in an objective, straightforward and comprehensive manner before we go much further in pursuit of a cure that always seems just out of reach (Bailar and Smith 1986: 731).

Exaggerated role of animal research in medical advances

Many opponents of experimentation argue that not only is modern medicine not the sole cause for the decline in mortality, many medical advances that did contribute to human health were not the result of animal experimentation. Defenders of research have claimed that since there is a strong correlation between the practice of animal experimentation and medical advancement, the former caused the later.

Opponents of research reject this inference. After all, we have independent reasons to expect these phenomena to be correlated. Since the law (at least in the US) prescribes that all new drugs, prosthetic devices, and surgical techniques be tried on animals before they are used in humans, we will subsequently find that all (recent) medical advances are correlated with prior experimenta-

tion on animals. Consequently, the correlation between animal experimentation and medical discovery is the result of legal necessity, not evidence that animal experimentation led to medical advances.

Moreover, several prominent physicians have offered historical evidence that animal experimentation has not been *as* responsible for biomedical discovery as advocates suggest. They claim that clinical discoveries played a more substantial role than animal researchers have led us to believe. As Paul Beeson explains in the *American Journal of Medicine*:

> 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 hyperthyroidism (1979: 368).

Apparently, the diseases and conditions cited by Beeson are not unique. "Similarly, key discoveries in immunology, anesthesia, and the treatment of depression were based on human clinical research and investigation" (MRMC 1990: 3).

Additionally, according to the former director of the Sloan Kettering Cancer Institute, the discoveries of insulin and of the mechanisms necessary for heart transplants were primarily the result of clinical investigation. In his Presidential Address before the American Society for Clinical Investigation, Robert Good challenged the claim that animal experimentation has been single-handedly responsible for medical advances:

> Recently a leading basic physiologist (cited) . . . a number of examples . . . in which basic contributions had paved the way for heart and organ transplantation. Included were such major advances as development of the science of circulatory physiology, control of infection, development of anesthesiology, pharmacological support of cardiovascular function, technological progress permitting secure diagnosis, control of the immune rejection, and others.
>
> From my somewhat prejudicial position, I seemed to hear a dramatic recitation of example after example in which investigation (of human patients) had led the way, asked the

> critical questions, established the incisive view . . . Certainly the control of infection is in great measure attributable to leadership of clinical investigators . . .
>
> The discovery and application of anesthesiology, to me, also derives from interpretation of several natural experiments and conduct of critical clinical investigations. The professional physiologists have contributed much to the understanding and control of the circulation, but was not the discovery of the circulation of the blood primarily an interpretation of a clinical experiment of nature? I think so . . . (1968: 1466).

Of course we should note that these physicians are not critics of animal research. Nevertheless, if these investigators are correct, then animal experiments have not played as central a role as the public has been led to believe. Substantial credit must go to the clinical sciences.

Places where animal experiments have misled us

A more serious criticism is that animal experimentation has sometimes resulted in measurable harm to humans. Opponents argue that the case of thalidomide, a "miracle" drug introduced in Britain in 1957, is instructive. Although at the time researchers did not test prospective drugs for teratogenic effects (birth defects), the drug did successfully negotiate the then current battery of animal tests. Researchers discovered that animals could tolerate massive doses of the drug without any ill-effects; they inferred the drug was safe for humans. Unfortunately they were mistaken: more than 8,000 children were born crippled or deformed.

As noted above, no animal tests had been done on pregnant animals. This leads defenders of research to argue that the thalidomide disaster in no way shows that animal research is flawed (Willis and Hulsey 1994: 213). As it turns out, that fact is of little solace to experimenters since what researchers would have learned from such tests had they been conducted before the appearance of human epidemiological data is not at all obvious. After all, the drug has since been shown not to produce detrimental effects in several strains of pregnant rats, mice, and other mammals:

> In approximately 10 strains of rats, 15 strains of mice, eleven breeds of rabbits, two breeds of dogs, three strains of ham-

> sters, eight species of primates and in other varied species as cats, armadillos, guinea pigs, swine, and ferrets in which thalidomide has been tested teratogenic effects have been induced only occasionally (Schardein 1976: 5).

Hindsight is 20–20. Although animals have since been found which produce teratogenic effects when exposed to thalidomide, these animals may not have been the experimental test subjects.

Opponents of animal research point out that the thalidomide case is not unique. For example, when Lilly introduced Opren (called Oraflex in the US) as a potential treatment for arthritis. It passed all animal tests, yet there were more than 3,500 documented cases of severe reaction and sixty-one deaths in Britain alone (*British Journal of Medicine* 1982: 459–60). More recently, FIAU, a drug to treat hepatitis B, passed all animal trials, yet had disastrous results in humans: it killed five of the fifteen human subjects who were given the drug in clinical trials. Even after the disaster, officials determined that increased or altered animal tests would not have avoided the problem.

> A retrospective evaluation of the material available in 1993 still supports [the original decision] . . . There was nothing in the preclinical toxicity studies that was suggestive of the tragic episode that transpired in the PPPC clinical trial. Furthermore, unfortunately, there is nothing to indicate that other laboratory animal studies would have been more appropriate or capable of better prediction of the fatal outcome (IOM 1995: 250).

Toxicologists openly acknowledge that different species often react differently to xenobiotics. Many researchers contend, however, that these differences disappear when doses are adjusted for differences in size, weight, and metabolism. We cannot make these adjustments until we know how humans respond to the xenobiotic – and that would undermine the predictive value of animal tests. Furthermore, it appears this assumption is false since, even when we do have data from both humans and non-humans, there is no straightforward way to correlate it. As Klaassen and Eaton note of cancer-causing agents: "All known chemical carcinogens in man, with the possible exception of arsenic, are carcinogenic in some species but not in all laboratory animals" (1993: 31).

Finally, some opponents of research question a basic assumption of toxicology. Toxicologists assume they can administer large doses

of test substances to laboratory animals (who have short lifespans) and then extrapolate findings to humans. However, this testing procedure is flawed. For example, large doses of insulin produce deformities in the offspring of laboratory animals (Friedman 1969: 499). However, we have no reason to think insulin is teratogenic to humans when administrated in standardly prescribed doses.

Moral concerns

Some philosophers, like Carl Cohen, support animal research; others morally oppose it. Peter Singer is probably the best known moral critic of our treatment of animals, including the use of animals in research laboratories. He writes:

> If a being suffers, there can be no moral justification for refusing to take that suffering into consideration. No matter what the nature of the being, the principle of equality requires that its suffering be counted equally with the like suffering . . . of any other being (1990: 8).

Singer sees speciesism – a bias in favor of members of one's own species – as morally odious, on a par with such evils as sexism and racism. He comments:

> The experimenter, then, shows a bias in favor of his own species whenever he carries out an experiment on a non-human for a purpose that he would not think justified him in using a human being at an equal or lower level of sentience, awareness . . . No one familiar with the kind of results yielded by most experiments on animals can have the slightest doubt that if this bias were eliminated the number of experiments performed would be a minute fraction of the number performed today (1989: 80).

These moral concerns go beyond the scientific concerns mentioned earlier. That is, some people, like Singer, claim that even if research is highly valuable we should not do it – at least not unless we are willing to do the same research on some humans. That is, most people consider non-consensual human experimentation morally odious; Singer and some critics of animal experimentation also see the practice of vivisection as morally odious for the same reason. Others may not go quite as far. They may claim that research can be morally justified if the benefits are sufficiently

substantial. What most critics would contend is that animal research cannot simply be evaluated on scientific grounds; it must be evaluated morally as well.

A brief review of the prima-facie case against animal experimentation

The prima-facie case against animal experimentation, as stated, is far from a knock-down refutation of the claims made by researchers. Rather, it is based on a series of examples intended to *deflate* researchers' claims:

- the contribution of interventionist medicine to the observable decline in mortality has been exaggerated;
- the contribution of animal research to interventionistic medicine has been exaggerated;
- the results of animal experimentation have occasionally been highly misleading;
- despite its scientific fecundity, the practice of animal experimentation is morally odious.

In short, even if animal research has played some role in prolonging life and improving health, its role has been less than defenders of research have claimed.

WHY AN ASSESSMENT OF THE SCIENTIFIC MERITS OF EXPERIMENTATION IS IMPORTANT

During the past twenty years, philosophers and others have written a great deal about the moral acceptability of using animals in research. Their arguments have doubtless raised people's moral sensitivities and prompted adoption of laws and policies that eliminated the most blatant cruelty to laboratory animals. Nonetheless, animals continue to be used extensively in research, both in the United States, the United Kingdom, and elsewhere in the world. Apparently the public does not find the moral arguments sufficiently persuasive, they think that the benefits to humans outweigh the suffering of animals, or they just don't care about moral issues.

Each of these responses reflects the public's firm belief that medical research pays enormous dividends for human health. Seeing why is not difficult: the research community has effectively

presented their prima-facie case for animal experimentation. As we stated earlier, ignoring this case would be silly, and dismissing all animal experiments as scientific fraud – as some critics (Reusch 1978) are wont to do – would be rash. Humans have benefited from some forms of animal research, and doubtless some beneficial medical research will cease if we abandon the use of animals. However, as we also argued, there is much room for disagreement about the extent of benefits (and loss of benefits, were the practice to cease). There are grounds for skepticism about the grand claims made for such experimentation.

In summary, although fanatical advocates and opponents of animal research think the opposition does not have even a prima-facie case, we think both sides offer arguments worthy of consideration. Yet often each side dismisses the other as misinformed, silly, or even malevolent. We hope the arguments in this book make each side less willing to reject opposing arguments out of hand. Only then are we likely to come closer to understanding the scientific merits of animal experimentation; only then are we likely to find a solution which most people will find reasonable. For, although both prima-facie cases are plausible; neither case, as it stands, is convincing. We must delve deeper to determine the scientific and methodological merits of animal experimentation. Only after we have done so will we be able to morally evaluate the practice.

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