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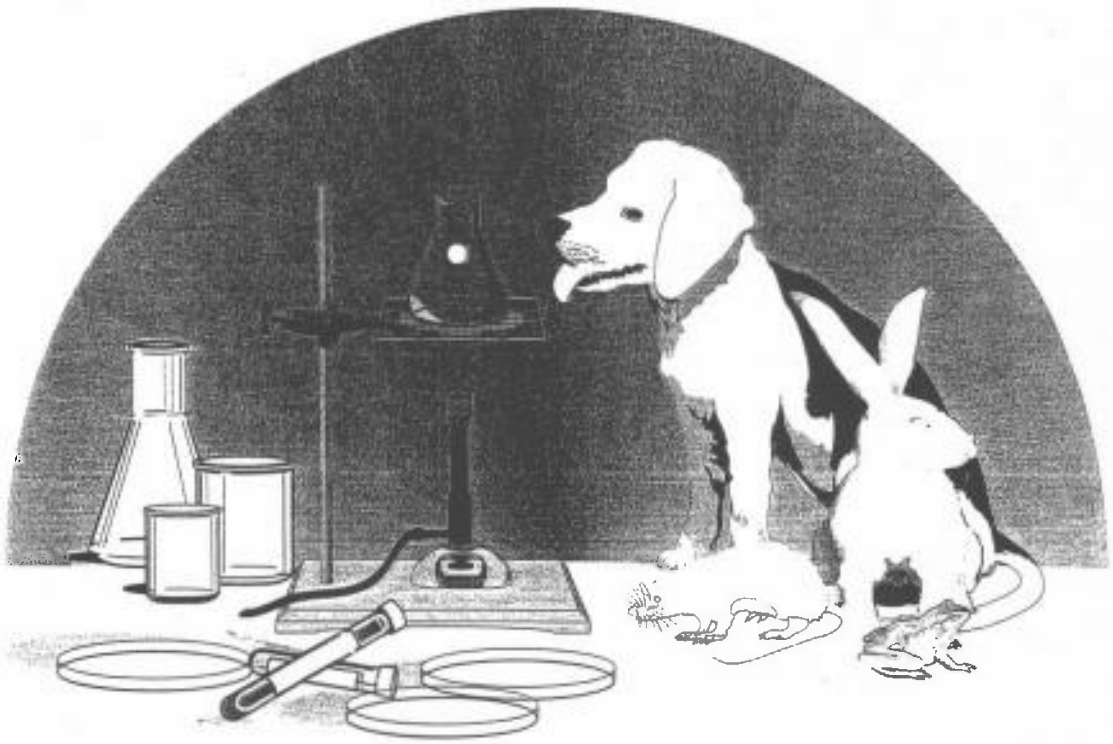
# AVMA Animal Welfare Forum:

## Veterinary Perspectives on the Use of Animals in Research



**November 4, 1994, Rosemont, Illinois**

*The following papers were submitted by the speakers at the 1994 AVMA Animal Welfare Forum, held at the Westin Hotel O'Hare in Rosemont, Ill. The opinions presented in these papers are those of the authors.*

*The Forum concluded with the presentation of the 1994 AVMA Animal Welfare Award to Dr. Robert A. Whitney of Steilacoom, Wash.*

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*The AVMA Animal Welfare Forum is an annual event planned by the Animal Welfare Committee, under the direction of the Executive Board. For additional information about the Forum or the Animal Welfare Award, please contact the AVMA Division of Scientific Activities.*

# Opening remarks

Dr. Sherbyn W. Ostrich
President-Elect

For the Fifth AVMA Animal Welfare Forum, which addresses the welfare needs of laboratory animals, we have gathered an array of speakers who will present both ends of the spectrum of philosophies on the use of animals in research, as well as the problems in providing for the welfare of these animals. The contribution that animals have made to the progress of medicine and surgery is of such magnitude that it is difficult to measure. Without them, humankind would still be living in fear of the horrors of such diseases as poliomyelitis, tetanus, and smallpox. We would know little about physiology, pharmacotherapeutics, and basic biology. We would not be beneficiaries of the knowledge that laboratory animals have given us that allows us to perform the surgical techniques that have saved countless human and animal lives.

Close examination of the welfare of laboratory animals is certainly proper, for these animals have made and continue to make possible alleviation of the suffering that our ancestors endured without benefit of the knowledge that has been provided by research animals. We should continue to strive to improve the welfare of laboratory animals in every way possible, because their lives are sacrificed so we can continue to improve the quality of life for other animals and human beings. We must surely continue to use animals to gain the knowledge to overcome disease, but we who have the responsibility for these animals must continue to treat them with the respect and kindness they deserve, and never lose sight of the goal to obviate the need for their use.

# An ethical perspective on animal research

Carl Cohen, PhD

I am honored to be here, at a meeting of the AVMA for a reason those who invited me could not know: my father, Jacob H. Cohen, was a Doctor of Veterinary Medicine, having graduated from the Cornell University in 1912. His Cornell banner hangs today in my office at the University of Michigan. With your indulgence, I dedicate these reflections to him. He loved animals and was dedicated to them. With his life's work, and with moral objectives in mind, I would reflect with you for a short while on the ethical aspects of biomedical research in which nonhuman animals are used as subjects. Two major items are on my agenda: first, I will briefly recapitulate the principle arguments commonly presented as moral objections to animal research, and respond concisely to those objections; and second, I will argue that research in which animals are used is not merely morally permissible, but that it is entirely right, and for some persons and some institutions, is a strong moral obligation.

From the School of Medicine, University of Michigan, Ann Arbor, MI 48109.

The commonly expressed objections to the use of animals in biomedical research are, in essence, of 2 kinds.[1] First is that family of objections based on the conviction that research in which animals are used violates the rights of animals. Conduct that violates the rights of others, if it is voluntary and deliberate, is morally wrong. Therefore (the critic contends), all research in which animals are used as subjects is ethically wrong, and ought to be forbidden or stopped. Arguments of this kind are usually not intended merely to ensure the humane treatment of animal subjects; they are objections to all uses of animals, including all uses of them in

biomedical research. Those who present such criticism, as they themselves say, do not seek larger cages, but empty cages.[a]

Arguments of this kind are profoundly mistaken. They rely on a confused conception of rights. They apply moral concepts and an ethical framework that is, in truth, intelligible and coherent only in a human, moral community, to the world of animals. I have presented the extended response to this argument in detail elsewhere[1]; the thrust of that response briefly follows.

We have obligations to animals, of course. But it is a mistake to infer, from the existence of an obligation, that the subject of that obligation has a right against us. Many of the obligations that we all have—to our students, friends, family, pets—are not grounded in the rights of those students, friends, and others, but arise from our commitments to them, and from the special relations between us and them.

For every right, there is, indeed, a correlative obligation. If you have a right against me or us, then I (or we) have the obligation to respect that right. But the moral proposition that all rights entail the obligations of others cannot be converted simply. Indeed, the converse is false. Rights and obligations are not reciprocals; the relations between them are not symmetric. Unfortunately, confusion on this point is very common. It is the mistaken supposition that wherever there is a genuine obligation, there must be some right held by another, that leads zealous critics to hold that rats have rights, as do fish, and perhaps trees, and whatever else may deserve our protection in the interest of other human beings.

Rights—claims or potential claims of one moral agent against another—are intelligible only within a community of beings who recognize general principles of duty as distinct from interest, who can apply general principles of duty autonomously, and who are therefore capable of recognizing the internal aspects of a voluntary act: its intent, and the moral qualities that can arise only from that intent. Therefore, with full understanding of the sentience of animals and a full appreciation of our obligations to care assiduously for them, I would insist, quite plainly, that animals do not have rights. They have interests, of course, but not every interest yields a right. Animals have feelings and suffer pain, of course, but sentience in itself yields no rights. Our obligations to animals arise partly because they can feel pain and distress, and we have a duty, as moral agents, not to cause needless pain. But it is an error—a serious and dangerous error—to conclude from the physical interests of rodents or primates that they are moral agents, as human beings are moral agents.

For one human being to kill another, in most circumstances, is a profound moral wrong. Human beings have natural rights, as human beings, on which we would be morally wrong to infringe. This wrong is not a matter only of the law of the state; outrageous conduct, even in the name of the state, may be "a crime against humanity," and we prosecute such crimes. But animals kill and eat one another constantly; theirs is a world of predation, and in that world, there is no moral fault in the predator. In summary, arguments against the use of animals in research based on the violation of their alleged rights arise from a mistaken application of human moral concepts to a realm in which such concepts do not apply.

The second set of objections to the use of animals in biomedical research abandons reliance on alleged animal rights; these arguments are founded on utilitarian principles. Proponents argue that the pain and distress we inflict on animals are excessive and unwarranted. These critics conclude that if utility is the standard of moral judgment, research in which animals are used cannot be justified.[b] Arguments of this form, in all their varieties, also fail utterly, for 2 reasons.

First, in such arguments, the pain caused by animal research is mistakenly assumed to be weighed, in the moral calculus, as equivalent to the pain of a human being. The argument fails to distinguish the differing moral status of the beings involved. There is the very greatest moral difference, you and I will agree, between the killing of a human child and the killing of a mouse. But proponents of such arguments find those who make this distinction to be speciesists—a name that (because in English, it plays on the terms "racist" and "sexist") sounds highly disreputable. But we here are all speciesists, of course. I put the matter bluntly: all those (in or out of the research community) who are not speciesists, who fail to make needed moral distinctions among species, will also almost certainly fail to fulfill their real duties to the members of the human species.

Second, utilitarian objections are profoundly mistaken because they do not involve correctly weighing all the consequences, good and bad, of using and not using animals in research. Killing or hurting animals is surely a moral negative, but sometimes that negative is an unavoidable byproduct of work that has very wonderful consequences. To be fair and rational, the general appraisal of research using animals must include weighing thoughtfully all that has been accomplished and all that can be accomplished only through their use.

Some utilitarian critics are simply ignorant of the central role of animal research in medicine. That ignorance, which is unfortunately very widespread, is itself morally blameworthy when it supports irrational attacks on biomedical research. But the moral blameworthiness of critics who are not ignorant is yet greater. There are those who, sincere in their passion to protect animals against pain, refuse to acknowledge publicly what they know privately about the reasons for the uses of animals; who repeat sensational claims about animal re-

search that they know to be false; and who sometimes make accusations against animal research that they know, or ought to know, to be unjustifiable.

In any thoughtful utilitarian analysis, then, the moral argument against animal research collapses completely. Indeed, the conclusion to which careful utilitarian reasoning compels us is that research in which animals are used is a great good for humankind, and is morally right.

Whatever the explanation for the development of moral differences between human beings and animals may be, those moral differences are a reality that cannot be denied. Those differences make a difference in our judgments and in our conduct. For example, we may not experiment on human beings without their freely given and fully informed consent. But the moral status of animals is such that the quest for their informed and voluntary consent to cooperate in the achievement of the ends of the investigation is an absurdity.

In addition, human beings rightly do to animals what animals cannot have the right to do to us. We exterminate roaches and rats. Although sometimes rats eat human babies, rats have no right to do so; indeed, they are totally incapable even of conceiving of any moral status for the things they do. Rights, as explained earlier, are not the kinds of things that rats, or other animals, can be intelligibly said to possess.

Finally, human beings can do wrongs that animals cannot. An act is culpable or blameworthy when the deed is done with a guilty mind. In primitive societies, animals were sometimes punished for crimes, but we understand full well that no rat or monkey ever committed a crime, because animals by nature do not possess the state of moral awareness necessary for the attribution of iniquity or wrongdoing.

The moral divide between human beings and animals, whatever its natural history, is vast and unbridgeable. The argument against animal research based on animal rights or on an alleged "scientific" continuity among species is, therefore, without merit.

I submit that research in which animals are used as subjects is not merely ethically permissible and right, but is, in some circumstances, a duty. It is a duty for those who commit themselves, professionally and publicly, to the care and well-being of human beings. It is also a duty that falls with special weight on commercial firms that profit from the production of drugs used in the care of human beings.

The benefits that accrue to all of us from the sale and use of pharmaceuticals carry with them some weighty obligations to the community. We are morally obliged to determine, with the highest reasonable degree of scientific reliability, that the drugs we put forward for clinical trials in human beings are safe or not toxic. Toxicologic studies are therefore a major activity and principle duty of every pharmaceutical company. Without use of the animals that are absolutely central in toxicologic studies, we would fail, and fail irresponsibly, in our duty to protect human subjects in subsequent investigations.

We also are morally obliged to determine, with the highest reasonable degree of scientific reliability, that the drugs we put forward for clinical trials in human beings are efficacious—that they do what we expect them to do, or at least that our evidence to support a claim of efficacy is the best that is in our power to obtain. To this end, the use of animals is not simply a possible way to proceed; it is, in many if not most cases, the only way to acquire reliable evidence of efficacy before human subjects become involved. Of course, even when animal studies are concluded, we cannot be completely confident of the effectiveness of any drug until trials with human beings have been performed. But if we did not engage in animal studies as preparation for those trials, we would certainly fail to fulfull our moral obligations to human beings.

Without some good evidence of efficacy, we could not justifiably put human research subjects at risk. Refraining from animal studies in the investigation of efficacy, therefore, must result in our inability to test, to market, and to prescribe drugs that may eventually prove of enormous value to humankind.

It is this point, I believe, that so many in the general population of North America and Europe simply have not grasped. There are millions who genuinely care for animals and who readily grant our higher duties to human beings, but who simply do not understand the central role of animal subjects in pharmaceutical research. I recapitulate here what every person at this gathering knows well, and what all who think about research with animals ought to weigh with care: In testing the efficacy of a new drug, there is no replacement for trials in which live organisms are used. Not tissue samples, chemical analyses, computer simulations, or anything else can replace the living organic being in research from which accurate results will directly affect human lives. Therefore, when we first administer any new drug to a live organism, that administration must be an experiment. We will not distribute (or be permitted to distribute) new drugs to the general public without the most scrupulous experimentation in advance. The risks of that experimentation cannot be imposed on human subjects without preceding animal studies. Therefore, as a society, we face this absolutely inescapable dilemma: we will perform toxicologic and efficacy studies in animals in developing new drugs—or we will not develop those new drugs. Anyone who believes that it is not merely our interest, but our duty, to develop new drugs to advance human well-being must also agree that research on those drugs in which animals are used is a moral necessity. Thus, the failure to use animal subjects in biomedical research must result in a failure, by some, to fulfill their moral duties.

[a]There are many examples of deontological arguments against the use of animals as research subjects. Perhaps the best known is Regan T. *The case for animal rights*. Berkeley, Calif: The University of California Press, 1983.

[b]There are many examples of such utilitarian arguments against the use of animals as research subjects. Perhaps the best known is Singer P. *Animal liberation*. New York: Avon Books, 1975.

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# The role of attending veterinarians in laboratory animal welfare

Fred W. Quimby, VMD, PhD

The first federal law to mandate veterinary care for research animals, the Animal Welfare Act, was passed by Congress in 1966. Yet as early as 1950, the first national meeting of laboratory animal scientists was held in Chicago. Organized by 5 area laboratory animal veterinarians, this meeting led to the establishment of the Animal Care Panel, later named the American Association for Laboratory Animal Science. In 1957, the specialty of laboratory animal medicine was accorded recognition when the American Board of Laboratory Animal Medicine was incorporated. This board became the American College of Laboratory Animal Medicine (ACLAM) in 1961. About the same time that this board was founded, the first training program for laboratory animal veterinarians was established at the University of Michigan and funded by the National Institutes of Health (NIH). Michigan continues to have a superb training program funded by the NIH to this day. During this period, the first decade following World War II, when the United States was witnessing its greatest expansion in biomedical research and establishing the NIH to promote advances in medicine, our profession had already anticipated the future needs of the medical research establishment and taken steps to prepare veterinarians for this new specialty. Today, more than 1,000 veterinarians participate in this specialty and of these, 485 are active diplomates in ACLAM. In this manuscript, we'll discuss the role of the attending veterinarian under 4 headings: responsibilities and authority, special considerations associated with institutional type and size, performance evaluation, and supporting organizations.

From the Center for Research Animal Resources, Cornell University, Ithaca, NY 14853.

## Responsibility and Authority

*Legal responsibilities*—Attending veterinarians have legal, institutional, professional, and ethical responsibilities that influence the activities of these veterinarians in biomedical research programs. Contrasts between those responsibilities mandated by law and those imposed on the veterinarian by the institution often lead to confusion. The Animal Welfare Act and the Health Research Extension Act require institutions to employ veterinarians who will provide a program of veterinary care (9 CFR §40).[1] The rules state, "Each research facility shall assure that the attending veterinarian has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use." (9 CFR §40) The 3 operative phrases in this quotation are "appropriate authority," "adequate veterinary care," and "oversee other aspects of animal care and use."

The ACLAM defined "adequate veterinary care" in 1985.[2] The ACLAM believes this care involves the planning and execution of programs for disease detection, surveillance, prevention, diagnosis, treatment, and resolution. This care must include daily observation of all animals by trained personnel, and the availability and use of diagnostic facilities. Adequate care includes providing guidance to and monitoring users in handling and restraint, as well as in the use of anesthetics, analgesics, tranquilizers, and methods of euthanasia. Programs must include review and approval of preoperative, operative, and postoperative procedures, and the conduct of surgery must involve dedicated surgical suites. Programs must include promotion and monitoring of animal well-being, including physical and behavioral aspects. Among the special considera-

tions for animal well-being are socialization, acclimation, and environmental enrichment. Veterinarians should be authorized to remove any animal from an experiment that is unduly affecting the animal's well-being. Veterinarians should share in the responsibility of evaluating appropriate use of animals, together with investigators and the institutional animal care and use committee (IACUC). This description is consistent with the language of both federal rules.

The USDA requires veterinarians to be responsible for certain other aspects of program development, including an exercise plan for dogs and a plan for promoting psychological well-being in nonhuman primates. In addition, veterinarians are responsible for exemptions to the standards, which may be granted for medical or other reasons on the basis of the veterinarian's professional judgement. Furthermore, the rules require veterinarians to re-evaluate exemptions from group housing for dogs or from environmental enrichment for primates every 30 days. Veterinarians must sign health certificates for animals in transit and proof of acclimation to temperature below 50 F.

Both federal acts also require participation of attending veterinarians on the IACUC. Other legal responsibilities are embodied in various state laws, as well as codes of conduct promulgated by state veterinary licensing authorities.

*Institutional responsibilities*—Often, institutions interpret the phrase "oversee other aspects of animal care and use" as a mandate for attending veterinarians to direct laboratory animal care and use programs. Although the USDA rules clearly state "housing, feeding and nonmedical care will be directed by the attending veterinarian or another scientist with proper training and experience," (9 CFR §31) attending veterinarians usually are charged with this duty. In addition, institutional programs often require veterinarians to be the fiscal manager of the program; to assist in the design of new animal facilities; and to provide investigators with information on animal models, animal acquisition, and interpretation of all rules and regulations. Institutions may require veterinarians to coordinate an occupational health and safety program and to participate on the biohazards committee. Attending veterinarians may be expected to advise the institution on facility security issues and to take the lead on public relations issues dealing with animal care and use. In a consensus report from a recent meeting of laboratory animal veterinarians at Research Triangle Park, NC, veterinarians were cautioned against acting as the sole responsible official for institutional public relations. Attendees recommended that attending veterinarians instead participate in a public relations response team.[3]

Institutions are required to develop animal care and use committees, charged with the review of animal use protocols, semiannual reviews of facilities and programs, investigations of public complaints, suspension of research activities for noncompliance, and making recommendations for facility improvements to the institutional officials (9 CFR §31). During review of protocols, committee members must consider whether appropriate alternatives to animal use exist, whether the species and numbers of animals are appropriate, whether pain and suffering have been abolished or minimized, whether the facilities for animal use are adequate, and whether the individuals performing animal procedures are qualified. Attending veterinarians must contribute knowledge about these issues and allow the entire committee to engage in a full discussion of each protocol.[4]

Various individuals have differing views on the role of veterinarians on the IACUC. Dr. Charles McPherson recently summarized these views at a meeting of the Scientists Center for Animal Welfare[5]; according to him, investigators expect fast approval and that the veterinarian will deal with the "alternatives thing." Institutional officials expect veterinarians to protect the institution from adverse publicity. The veterinarian's boss expects him/her to know the regulations, to be an ombudsman, and to provide animal care. The public wants veterinarians to stop "crazy things," to be an ombudsman, and to provide veterinary care. Regulators, however, view veterinarians as having the same responsibilities as other members of the IACUC.

Institutions are required to provide training and instruction for personnel responsible for animal care and animal use. Guidance must be provided on humane methods for animal maintenance and experimentation; availability and use of methods that limit the use of animals or minimize distress; the proper use of anesthetics, analgesics, and tranquilizers; methods for reporting deficiencies without reprisals; and use of information resources.

Although a legal mandate for the veterinarian to provide these educational programs does not exist, institutions often impose this responsibility on attending veterinarians. Whenever possible, attending veterinarians should involve a wide range of faculty and staff in this program to broaden the knowledge base, expand personal experience, and introduce alternative ideas.

Many attending veterinarians also seek an avenue for scholarly work; however, the responsibilities of attending veterinarians often may leave little or no time to develop independent research programs. Well-funded departments of comparative medicine in which several veterinarians share the laboratory animal medical service are an effective mechanism for providing an academic track for laboratory animal veterinarians. Membership in other academic departments impose additional teaching responsibilities, another mechanism of performance evaluation, and a requirement for extramural research funding and scientific productivity necessary for advancement to tenure. The issue of tenure vs

nontenure appointments, along with the additional obligations and expectations of a tenure-track position, should be weighed carefully by each attending veterinarian. Likewise, the benefits to the institution of having the attending veterinarian fully participating in academic programs should be weighed carefully by institutional officials. If a decision is made to employ laboratory animal veterinarians in tenure-track positions, the institution is obliged to provide the time necessary for scholarly work.

*Professional and ethical responsibilities*—First and foremost, attending veterinarians have a professional obligation to remain competent. The responsibilities of attending veterinarians require that knowledge cover not only a broad range of subjects, but also be in-depth regarding medical issues of many different species. There are more than 240 species of nonhuman primates alone. In addition, although many think of mice, rats, dogs, rabbits, and hamsters as the laboratory animals, many institutions also house large numbers of fish, reptiles, amphibians, wild mammals, and birds.

Guidelines for postdoctoral educational and training programs have been developed by the National Research Council, in which specific knowledge and experience in the medicine of laboratory animals, as well as in anesthesiology, experimental surgery, and radiology, is recommended. In addition, education on laboratory animal management and care, animal models of human disease, conservation of endangered species, protection of public health, and biologic characteristics of individual species is recommended.[6] These subjects are embodied in residency training programs funded by the NIH and other organizations, and are recognized as essential by the ACLAM.[7] Continuing education is an important obligation in this field.

Ethical dilemmas are commonplace and often relate to the many responsibilities and conflicting expectations of others, as previously highlighted by Dr. McPherson. Our principles of veterinary medical ethics clearly state: "Veterinarians should consider first the welfare of the patient for the purpose of relieving suffering and disability while causing a minimum of pain or fright. Benefit to the patient should transcend personal advantage or monetary gain in decisions concerning therapy."[8] When veterinarians have a vested interest in the outcome of research, they should excuse themselves from IACUC review and from making final judgement on alleviation of pain and suffering during the course of experimentation. In such cases, alternate attending veterinarians should be assigned these responsibilities.

The Veterinarian's Oath advises us to use our "scientific knowledge for the benefit of society through the protection of animal health, relief of animal suffering, the conservation of livestock resources, the promotion of public health and the advancement of medical knowledge."[9] However, recent innovations in molecular genetics allow us to create laboratory animals that will replicate life-threatening human illnesses. The recent development of transgenic mice with amyotrophic lateral sclerosis or cystic fibrosis are examples.[10,11] The institutional program provides an opportunity for an appropriate response to such an ethical dilemma. Veterinarians are obliged to consider the methods available to reduce pain and suffering and to recommend special husbandry procedures when appropriate. The IACUC is obliged to consider aspects of experimental technique that may minimize suffering. Reasonable endpoints can be established, which allow subjective assessment for the termination of an experiment. The rationale for estimating the numbers of animals to be used should be reviewed, and the qualifications of the investigators examined. In some cases, investigators may be asked to seek additional expertise or to hire a consultant. In the end, a majority of the IACUC must be convinced that benefits outweigh the costs, and the attending veterinarian's input is a legal and ethical imperative.

## Special Considerations Associated with Institutional Type and Size

Research facilities of various sizes generally offer differing problems and challenges to attending veterinarians. In large research universities, veterinarians often are confronted with a great variety of species and for some, little or no published information regarding veterinary medical care is available. Biologic features and husbandry of these species may be better understood by the investigator than by veterinarians. At large universities, students are enrolled in graduate programs, and special considerations for their training is essential. When animals are used for teaching purposes, special training must be provided to teaching assistants. In both the above cases, increased monitoring by the veterinary care staff may be essential.

In some instances, animals are housed in many small, noncentralized facilities under the administration of an investigator. These facilities pose challenges to veterinarians in terms of facility maintenance, environmental control, personnel training, microbiologic monitoring, and a host of other factors. However, in terms of isolating a unique species or hazard, these satellite facilities may prove beneficial. Large universities often have programs in areas such as occupational medicine, environmental safety, public relations, engineering, purchasing, and attending veterinarians often are involved in coordinating the activities of such services.

Small teaching colleges often lack adequate financial and personnel resources, thus requiring veterinarians to engage in a broader range of responsibilities, with less opportunity for intracollegiate consultation. Facility renovation grants, avail-

able from the National Center for Research Resources (NIH), may be required to augment the program, and attending veterinarians should consult with their colleagues at other institutions for advice. Laboratory animal veterinarians must engage the IACUC to provide a comprehensive and fair appraisal of the existing facilities and programs and their limitations, and of options for correcting problems. As always, administrative support for programs is essential.

## Performance Evaluation

Nowhere are a veterinarian's activities more thoroughly scrutinized than in laboratory animal medicine.[12] Within the institution, the chief executive officer, college deans, department chairpersons, faculty, and staff are evaluating an attending veterinarian's decisions. Administrative support is essential as a display of commitment to the program, and to reinforce the veterinarian's authority. The IACUC is required by law to review the entire animal care and use program semiannually and to submit a report to the institutional officials, outlining any deficiencies found and a program for their correction.

Inspectors from the USDA make unannounced site visits and review facilities and programs, including protocols, minutes of the IACUC, and veterinary record-keeping. In some states, state agency officials or societies for the prevention of cruelty to animals also visit. The Public Health Service may organize an ad hoc committee to review a facility and its programs in the event of public complaints. In some locations (eg, Cambridge, Mass) a municipal veterinarian visits and inspects the facilities and the veterinary care programs. Laboratory animal veterinarians in industry may have, in addition to the above agencies, the FDA or EPA inspectors reviewing their programs.

In 1967, a nonprofit, nongovernmental organization was formed to conduct voluntary reviews of facilities and programs and to accredit those in compliance with all rules and regulations. This organization, the American Association for Accreditation of Laboratory Animal Care (AAALAC), now has accredited more than 580 institutions. The benefits of AAALAC accreditation include an objective evaluation and assurance that the facilities and programs conform to the Guide.[13] Accreditation also conveys public confidence and meets NIH assurance prerequisites.

## Supporting Organizations

To provide a comprehensive animal care and use program, an attending veterinarian needs support. Veterinary education is enhanced by collegial relationships and continuing education programs fostered by such groups as the ACLAM, American Association of Laboratory Animal Science (AALAS), the AVMA, the American Society of Laboratory Animal Practitioners, the American Committee of Laboratory Animal Diagnosticians, and the Association of Primate Veterinarians. In many instances, laboratory animal veterinarians are joined by veterinary pathologists, anesthesiologists, surgeons, clinical pathologists, and veterinarians certified in preventive medicine, to deliver a program of animal care and use. The technical staff is best served by AALAS, which provides 3 levels of technician certification. For laboratory animal managers, the Lab Animal Managers Association provides professional meetings and publishes *LAMA Lines*.

Financial and published resources, are available through the NIH, the Institute of Laboratory Animal Resources (of the National Academy of Sciences), the International Council for Laboratory Animal Science, and World Health Organization (the latter 2 are sponsoring centers of excellence in laboratory animal science worldwide). In addition, the World Veterinary Association sponsors international meetings and publications for laboratory animal medicine and animal welfare.[14] This group also provides assistance to veterinary associations in the formulation of national policies on animal care and use.

Industry has played a key role in supporting laboratory animal programs in this country and others. United States' corporations have taken the lead in providing pathogen-free animals of known genetic constitution. Laboratory animal veterinarians still play a prominent role in many of these companies. Animal housing, equipment, and environments have all benefitted from the ingenuity of US enterprise. Investigators and the public have benefited from these innovations.[15]

## Conclusions

Laboratory animal veterinarians must maintain a broad knowledge of subjects relevant to the field. They often are assigned responsibilities that exceed their authority. In larger institutions, the lines of authority may be complex and vague, with veterinarians simultaneously reporting to deans, directors, vice-presidents, and chief executive officers. Unfortunately, opportunities for interpersonal conflicts are many, and ethical dilemmas also occur. Job performance is evaluated by every official, and financial support may not keep pace with administration-imposed responsibilities. The magnitude of the job may interfere with the conduct of scholarly work. Over the past decade, as a result of increased animal activist activities, institutions have assigned increasing public relations responsibilities to veterinarians, many of whom now worry about personal liability and safety.

However, despite these obstacles, this occupation is exciting and challenging. Attending veterinarians may take pride in improving the quality of life for research animals, in contributing to the advancement of knowledge, and in fostering a safe workplace.

One group of employees who share many of

the problems confronted by veterinarians are often overlooked. An attending veterinarian's animal care program is only as good as its staff. Members of a highly motivated, devoted, and knowledgeable animal care staff are truly the unsung heros of most animal care and use programs, and they deserve our profession's support and praise.

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# Innovations in research animal care


Denna M. Benn, DVM


Standards for laboratory animal care have traditionally been based on the physical requirements of animals, almost to the exclusion of their social and behavioral needs. Research facilities in the 1960s and 1970s addressed concerns regarding nutrition, reproduction, diseases, and sanitation. Husbandry standards were primarily developed to reduce experimental variables, to ensure reproducibility of experimental results, and to meet the convenience of researchers and animal care staff.

In the 1980s, our attentions turned to animal well-being and to improving the conditions in which research animals were kept. Instead of focusing on the absence of pain and distress in laboratory animals, research facilities were being required to investigate and implement housing systems that meet animals' social and behavioral requirements. Achievement of psychological well-being, defined as "a state of harmony, both physical and psychological, of an animal with itself and its environment," became a primary concern.[1]


From Animal Care Services, University of Guelph, Guelph, Ontario N1G 2W1.


This increased attention on psychological well-being developed for a number of reasons. We recognized that reducing stress of laboratory animals minimized their suffering, and that the care of the animals is as important to research results as the data collected in experiments.[2] Regulatory requirements also were increased. The USDA animal welfare standards were amended in 1985 to include concern for the psychological well-being of primates and the provision of exercise for dogs. The Canadian Council on Animal Care also published a document outlining the social and behavioral requirements of experimental animals.[3] These requirements led to increased interest in innovative housing and care for laboratory animals.

## Importance of Innovative Housing and Care

Innovative housing and care allows animal care staff to be active participants in providing the best possible environments for their animals. It legitimizes the staff's need for greater involvement with the animals and permits the caregivers to become

more knowledgeable about housing systems and animal behavior. The latter is of particular importance, because changes in behavior are often the first signs that an animal is in distress or suffering.[4] Providing enriched environments also encourages stronger bonds between the caregivers and their animals, which in turn, result in enhanced individual animal care.

Implementing enriched housing programs and policies assists the scientific community in meeting its ethical responsibilities toward the animals used in research. By focusing on the well-being of animals, appropriate animal housing systems can be chosen to which animals can adapt without suffering. Opportunities are increased to provide the appropriate stimuli and environments that will result in a natural repertoire of behavior and decrease the incidence of abnormal behavior, such as stereotypies.

Animals raised in enriched environments have been reported to have increased learning abilities and marked structural and biochemical changes in the brain.[5,6] On the other hand, stress attributable to impoverished housing can result in distress and considerable physiologic or pathologic changes in animals. This stress can lead to questionable data and conclusions, which might have been prevented if animals living in optimal housing conditions were used.[7,8] Thus, providing for the well-being of animals by enriching their environments is desirable, to control extraneous variables and to obtain meaningful data.

Public perception of the care given to research animals is also a consideration, and a positive impression can be helpful in the public's acceptance of scientific endeavors in which animals are used. When enhanced animal housing and care can be provided, the public is more likely to understand the importance given to the care of animals used in research and to recognize the depth of concern shown toward the animals. Researchers and animal care staff can use environmental enrichment programs as an opportunity to be recognized by the public for the care and treatment of animals.

## Strategies for Environmental Enrichment Programs

The purposes of environmental enrichment are to provide a complex social and physical environment and to create incentives for animals to express their natural repertoire of behavior. This type of housing also must provide flexibility and allow for modifications, so that animals can be given some control over their environments. Innovative housing therefore gives animals opportunities to think, and change or choose their surroundings.

To provide the conditions that a particular species prefers requires knowledge about the natural history of the species; the particular strain and individual animals; normal behavioral patterns; food-gathering styles and preferences; and past experiences in housing conditions, keeping in mind that naive animals may not be as dexterous in activities as are animals raised in enriched housing. The first step is to assess the priorities of the research facility, to determine which animals to work with initially and where to implement environmental enrichment. To successfully introduce innovations in animal housing and care, an interdisciplinary approach is encouraged, which will include animal care staff, technicians, scientists, behavioralists, and institutional administrators.[2] All proposed changes should be discussed to ensure that the research aims are not jeopardized and that all viewpoints and ideas are considered. Initiating changes slowly and acclimatizing the animals are important.[9] Once enrichment is initiated, animal care staff and researchers will begin to anticipate change and become more comfortable with the process. Thereafter, systematic and organized evaluation of environmental enrichment strategies and the resulting behavioral changes in laboratory animals is imperative.

An environmental enrichment program must provide for the social and physical needs of animals. Social needs can be met through interactions with conspecifics, as well as with human beings. Social interaction with conspecifics is especially important to the more gregarious species used in research, which seek physical and physiologic comfort from each other.[3,10,11] Increase in longevity has been reported for group-housed, compared with singly housed, rats.[12] Social isolation usually causes distress to animals and should be avoided wherever possible. However, if isolation of animals is necessary to fulfill the research aims, permitting visual, auditory, and olfactory communication should be attempted.[3,8,13,14]

Special provisions are required to ensure that group housing of social animals will be successful. These provisions include escape routes, visual and physical barriers, and choices of living space, to minimize adversive encounters and to lessen territorial or aggressive instincts. Provision of activities, appropriate-sized caging, and stable social groups are also imperative for success.[15,16] Group housing of males of some species, such as rabbits, may result in aggression unless they are castrated before puberty.[10] Male mice are also territorial, and enhanced housing conditions may lead to increased aggression.[3]

The importance of interactions between human beings and animals and the social affinity of domesticated and laboratory animals for human beings is often ignored.[17,18] Animal care personnel serve an important social role in the care of laboratory animals. Domestic animals often prefer human contact over a toy.[19] Not only do caregivers provide leadership, defense, shelter, and food, but they have a stabilizing effect on their animals. They hold a dominant status in the social structure of the group. Failure of personnel to perform in this

role can lead to handling problems, intergroup aggression, and stress.[20]

Time therefore must be permitted for animal care staff to have greater involvement with their animals and to foster bonding. Socialization is especially important for singly housed animals, and programs may need to be formalized to provide regular sessions, such as grooming and walking dogs.[16]

It may be argued that social bonding of research animals to their caregivers can be undesirable, for experimental purposes or for the uneasiness and distress that the personnel may experience. However, lack of socialization in those animals that expect such bonds to develop makes such animals difficult to handle and may introduce social and emotional stress that is detrimental to the research results.[7] Personnel involved with animals usually want the opportunity to bond with animals, even though emotional discomfort may result when the animal must be killed for research.[21] However, to foster such bonds, research facilities must be supportive of the animal care staff and the conflicts that such staff face.

The physical housing needs of laboratory animals include space, complexity of caging, food, toys, toilet needs, and music. Problems identified with traditional laboratory animal housing are lack of activities and space provided. Animals need the appropriate stimuli and facilities to allow them to perform species-specific behaviors. For this reason, one must look at the housing from the animal's perspective. However, avoiding projection of human needs and wants on animals is also important, because such thinking may not enhance the quality of animal life either.[22]

Laboratory animals are usually housed in highly populated, sterile environments, with smaller primary enclosures than these animals would have access to in nature. Many species, such as rabbits, spend most of the time in bare environments sitting in their cages.[10] Pressure on laboratory facilities to provide more space has been increased, so that animals can be more active in a laboratory setting. Increased muscular strength, decreased incidence of foot lesions, increased amount and quality of sleep, as well as increased longevity, have been reported in rats kept in larger cages.[15]

However, even when more space is given to some animals, they do not utilize it.[23] Nothing to do in the extra space is the problem. Space utilization by guinea pigs is enhanced when they are given sheltered areas.[24] Therefore, along with space size, the complexity of the primary enclosure is important and specific for each species. Physical stimuli and objects must be included that will give a more natural environment, promote expression of behaviors such as exploration and manipulation, and provide enough space to meet basic locomotor activity needs.[7] Providing gerbils with appropriate bedding and nesting materials allows them to dig tunnels and to build nests. Nests or bolt holes for mice, resting boards and tubing for rabbits, and solid-bottom caging for rodents also have been used as enrichment devices.[3] An advantage of habituating animals to complex environments at an early age is the reduction in stress when novel situations are encountered later in life.[8] Improved learning and more normal behavior also have been reported in rats raised in naturalistic environments.[25]

Food-gathering activities also can be used to provide environmental enrichment. Animals often prefer to work for their food and will do so even when free-choice food is provided.[26] They learn to perform a task and are rewarded, thereby gaining a sense of control and competence.[7] Food treats such as dog bones, seeds, and fruit also can be given to reward good behavior. Foraging for food items is another strategy used to occupy the animals' time, giving them "occupations" and control over their environments.

Toys have been used successfully to augment and enhance environmental enrichment programs by promoting exploratory and play behavior. However, this strategy is not effective when used as the primary enrichment focus. Toys must be changed frequently to avoid boredom.[10,16,19] They can be used for a large number of species including dogs, cats, rodents, and rabbits, and preferences for toys vary among species, breeds, and even individuals within a breed.[19] The objects may be loose in the cages or suspended off the ground to minimize soiling and possessive aggression and hoarding.[10,16]

Animals also have toilet needs that can be better met in enriched environments. Animals should not be forced to defecate and urinate where they sleep and live. Providing greater space and giving animals choices allows them to meet their elimination behavioral needs. Such choices include urinals for mice and litter pans for rabbits. Offering cats a fleece to sleep on stops them from sleeping in their litter pans.[19] Even cages with wire floors force animals to eliminate in their living quarters, where they must smell the odors, and for animals with highly developed olfactory senses, this may be stressful.

Another aspect of the physical environment is music, which may be valuable in protecting animals from extraneous sounds outside their room. Music also can habituate animals to the sound of human voices and appears to have a calming effect.[3]

A final consideration in developing a housing strategy is providing animals the ability to exert control over their surroundings. Allowing animals to make choices reportedly increases their health and well-being, and improves social interaction with conspecifics.[7,8] Examples of control could include a choice of sleeping and resting locations, nesting materials, food and bedding types, and toys. Invasive procedures should not be performed in animal rooms, so that animals realize they are safe within their home environment.

The benefits of environmental enrichment and innovative housing for laboratory animals are many. The needs of the animals are met, giving them "occupations" and allowing them opportunities to express a more complete repertoire of behavior. As new policies are promoted for improved care of laboratory animals, opportunity is increased for individual animals to be given increased contact time and to be treated with greater sensitivity and awareness by the animal care staff. In addition, animal care personnel feel better about their workplace, realizing that they are able to make a difference in the living conditions and quality of life of their animals. The relationships formed between the research team and the animals expedite data collection and reduce the stress associated with experimental procedures. The use of more physiologically and psychologically stable animals ensures better data collection and good scientific results. Such a program can lead only to a positive public image, whereby research institutions and personnel are recognized for their concern and sensitivity toward the animals in their care.

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# Development of a natural-habitat breeding facility for nonhuman primates

William R. Morton, VMD; Randall C. Kyes, PhD; Kelly B. Kyes, PhD; Glenn H. Knitter, BA; Dondin Sajuthi, DVM, PhD; Diah Iskandriati, DVM; Joko Pamungkas, DVM

The use of animal models for understanding and developing treatments for human disease has long been accepted as standard practice in experimental medicine. Nearly all of the vaccines and surgical techniques in use today were tested first on animal models. Currently, experimental medicine faces a number of challenges, most notably the human acquired immunodeficiency syndrome (AIDS). A relevant and practical animal model is an indispensable tool for the study of AIDS pathogenesis and for the development of effective vaccines and therapies.

Since the identification of the human immunodeficiency virus (HIV) as a member of the lentivirus family, interest in the study of animal lentiviruses as been renewed. Currently, simian immunodeficiency virus (SIV) infection of macaques remains the only established model for the study of primate lentivirus infection and pathogenesis. Five subgroups of SIV have been described. Prototype viruses of the first subgroup have been isolated from sooty mangabeys ($SIV_{smm}$), rhesus macaques ($SIV_{mac}$), and pig-tailed macaques ($SIV_{mne}$). Other subgroups of SIV have been isolated from African green monkeys ($SIV_{agm}$), mandrills ($SIV_{mnd}$), Sykes monkeys ($SIV_{syk}$), and chimpanzees ($SIV_{cpz}$). These viruses share similar cellular tropism, genomic organization, and ultrastructural features with HIV. In particular, members of the $SIV_{smm}$ subgroup, namely $SIV_{mac}$, $SIV_{smm}$, and $SIV_{mne}$, share high degrees of genetic homology with HIV-2 (70 to 85% predicted amino acid identity in various gene products).[1] This observation led to the hypothesis that HIV-2 and $SIV_{smm/mac/mne}$ share a common ancestor that caused prevalent, but nonclinical infections, among sooty mangabeys in West Africa.

Experimental transmission of SIV in macaques has been used to model the 3 major routes of HIV infection in human beings: blood-borne, mucosal (sexual), and perinatal transmission. The inoculum is usually cell-free virus (culture supernatant), but also may include infected cells, whole blood, blood mononuclear cells, cells from lymph nodes, and other tissues from infected animals.

Most of our experience with SIV infection and pathogenesis derives from transmission of cell-free viruses by IV inoculation. Infection by this route is usually reproducible and quantitative, with well-defined endpoints of infectivity. Following the initial infection of primary targets, presumably circulating $CD4^+$ mononuclear cells, an acute phase generally ensues within the first few weeks, characterized by fever, rash, diarrhea, peripheral lymphadenopathy, viremia, antigenemia, and transient decrease of peripheral $CD4^+$ mononuclear cells.

Genital or rectal mucosal transmission of SIV has been used as a model for sexual transmission of HIV. Persistent infection has been induced by atraumatic infusion of cell-free virus ($SIV_{mac251}$) into the vagina or penile urethra.[2] Perhaps because of the intact mucosal membrane barrier, the amount of virus required to initiate a persistent infection by these routes appears to be $10^3$- to $10^4$-fold higher than that required for IV infection. Macaques infected through the mucosal surface also seem less likely to develop the acute disease progression, as observed in some IV infected animals. Initial infection following mucosal inoculation may be sufficiently localized to allow development of systemic immunity; however, once infection is established, all infected macaques eventually develop typical AIDS-like diseases, as seen in IV infected macaques.

Infection through rectal mucosa also has been reported.[3,4] As in vaginal transmission, infection through rectal mucosa requires $10^3$-fold higher amounts of cell-free virus inoculum than that for IV infection. Because of the small number of macaques tested and the limited number of studies performed, disease course following intrarectal inoculation has not been fully described. Preliminary results indicate that after intrarectal inoculation at high doses ($10^3$ to $10^4$ times the IV infection doses), infection follows a similar course as that in animals infected IV (ie, viremia, seroconversion, and eventual development of AIDS-like disease). In a study performed at the Washington Regional Primate Research Center, macaques inoculated intrarectally with a low dose (1 to 10 times the IV infective doses) of $SIV_{mneE11S}$ developed an atypical disease course.[4] These macaques were seronegative, virus was not detected on cocultivation of blood mononuclear cells, and results of polymerase chain reaction analysis were positive only transiently. Nevertheless, one macaque developed AIDS-like disease 19 weeks after inoculation, one had a decrease in $CD4^+$ cells, and one had virus detected 3 years

From the Regional Primate Research Center, University of Washington, Health Sciences Building, SJ-50, Seattle, WA 98195 (Morton, RC Kyes, KB Kyes, Knitter, Iskandriati, Pamungkas) and the Primate Research Center, Bogor Agricultural University, Jalan Lodaya II/3, Bogor, Indonesia (RC Kyes, Sajuthi, Iskandriati, Pamungkas).

after inoculation. These are highly unusual findings. However, HIV-1 has been reported to be isolated from asymptomatic, seronegative homosexual men.[5,6] Further investigation of the infection and disease course in intrarectally inoculated macaques as a pathogenesis model is therefore important.

Experimental transmission of SIV from a female macaque to her fetus also has been reported.[7] Twelve pregnant macaques were inoculated with $SIV_{mne}$ during 1 of 3 parts of pregnancy. Of the 7 live neonates, 2 were infected, in keeping with the rate of maternal-fetal transmission of HIV in human beings. As is commonly observed in HIV-infected infants, accelerated disease course was observed in the SIV-infected macaques, which developed AIDS-like disease and died within 3 and 6 months of birth. Because of the relatively low rate (2/7) of transmission, this model may be practical for vaccine or drug studies. For these purposes, intra-amniotic infection of fetuses may prove useful.[8]

As these studies revealed, macaques serve as an exceptionally good host species for studying infection with immunosuppressant viruses and pathogenesis of subsequent disease. The ultimate goal of our AIDS-related research, however, is to develop vaccines that protect against the immune-destroying effects of primate lentiviruses. Macaques are now used as the primary testing resource for all new AIDS-related vaccines. To assure adequate macaque resources for AIDS-related research efforts, a new concept of breeding facility has been developed.

## Tinjil Island Natural-Habitat Breeding Facility

In 1986, the US Primate Research Consortium (consisting of the Regional Primate Research Center at the University of Washington, Bowman Gray School of Medicine of Wake Forest University, and the Oregon Regional Primate Research Center) joined with the Institut Pertanian Bogor (IPB, an Indonesian agricultural university) to establish a collaborative program of research and training in primatology (including virology, pathology, cardiovascular disease, behavioral biology, and ecology). Foremost among the projects was the development of a natural habitat breeding facility for long-tailed macaques (*Macaca fascicularis*) on Tinjil Island. This breeding program originated, in part, in response to a 1981 World Health Organization meeting convened to address the feasibility of establishing, in source countries, national programs designed to manage primate populations as sustainable (or renewable) resources so as to ensure permanent conservation of the various species, and maintain the supply of primates for essential biomedical research.[a] More immediate goals of the breeding program were to provide specific-pathogen-free, purpose-bred offspring for use in AIDS-related research at the University of Washington Regional Primate Research Center and in biomedical research directed at specific health concerns of Indonesians, conducted at the IPB. Initial construction of the island facilities began in 1987, followed by the release of the first group of macaques onto the island in 1988.

## Location and Habitat

Tinjil Island is located approximately 16 km off the south coast of West Java, at approximately 7° 0' S, 105° 45' E (Fig 1). The island is approximately 600 ha in size (6 km long and 1 km wide) and consists primarily of lowland, secondary tropical rain forest and coastal vegetation. The terrain is somewhat flat, with the highest point approximately 25 m above sea level. More than 75 species of plants have been identified on the island, 28 of which produce fruits or foliage known to be edible by the macaques. At least 2 natural fresh-water sources exist on the island.

Native fauna on the island consist of numerous species of insects; several species of land crabs and frogs; at least 3 species of snakes (including *Python reticulatus*, reticulated python, and *Agkistrodon rhodostoma*, a pit viper); at least 5 species of lizards (including *Varanus salvator*, a monitor lizard); approximately 22 species of birds; a species of rat; and at least 2 species of bats (including a large fruit bat and a small insectivore). Prior to the introduction of the long-tailed macaques in 1988, the island was uninhabited by human beings or nonhuman primates.

## Facilities and Logistical Support

The base of operation on Tinjil Island is located near the eastern end of the island and consists of several permanent buildings and huts that provide living accommodations and office space for resident staff (approx 10 individuals), visiting scientists, and students. There are also storage facilities for support equipment (ie, electric generator, all-terrain vehicle) and supplemental food provisions for the monkeys (including bananas, papayas, corn, and sweet potatoes); a communications room with a two-way radio system; and a temporary holding cage (12 × 3 × 2.5 m, partitioned into 3 rooms) for housing macaques prior to removal from the island.

There are 11 feeder/catch cages (12 × 6 × 2.5 m) distributed around the island that function as provisioning sites and trapping facilities for the periodic capture of macaques for health assessment or transfer to research facilities (Fig 1). To date, only 9 cages located throughout the eastern and central thirds of the island have been used for routine provisioning and trapping. Fresh-water wells have been dug next to most of the cages to provide additional water sources for the macaques. A desalination system also has been established on the island to supplement the fresh-water sources.

A system of 10 transects has been cleared that provides access to most of the island (Fig 1). The

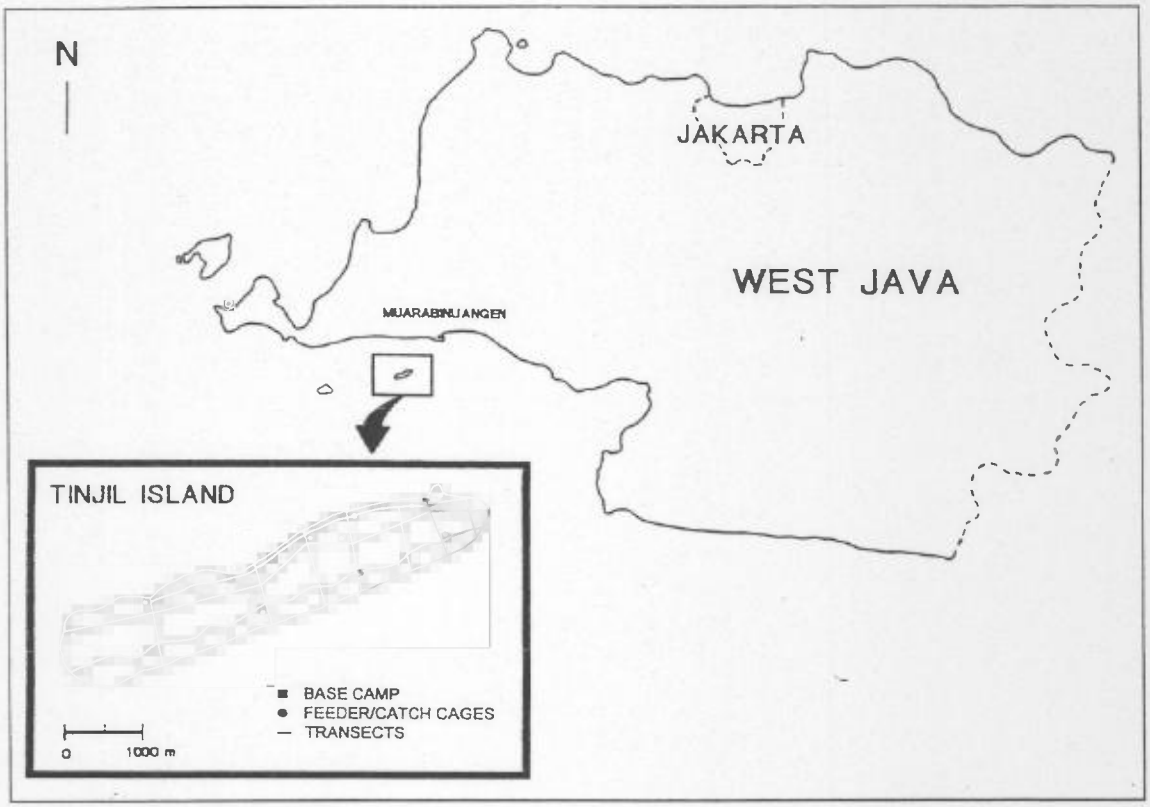


*Figure 1—Location of Tinjil Island.*

*Table 1—Macaques screened and released onto Tinjil Island*

| Group* | No. screened (males/females) | No. released (males/females) | Date of release |
|---|---|---|---|
| 1 | 200 (9/191) | 51 (1/50) | Feb 21, 1988 |
| 2 | 208 (33/175) | 15 (5/10) | Apr 29, 1988 |
| 3 | † | 58 (7/51) | June 26, 1988 |
| 4 | † | 13 (2/11) | July 10, 1988 |
| 5 | 200 (21/179) | 10 (0/10) | Sept 28, 1988 |
| 6 | † | 66 (13/53) | Mar 14, 1989 |
| 7 | † | 48 (1/47) | Apr 26, 1989 |
| 8 | 186 (39/147) | 125 (29/96) | Oct 21, 1989 |
| 9 | 226 (0/226) | 89 (0/89) | June 26, 1990 |
| 10 | 101 (0/101) | 3 (0/3) | June 4, 1991 |
| 11 | 23 (1/22) | 20 (1‡/19) | Sept 5, 1994 |
| Total | 1,144 (103/1,041) | 498 (59/439) | |

*Release groups do not represent established social groups. †Macaques from the previous group that required additional screening before being accepted or rejected for release. ‡Male born during screening and released with its dam.

trails are numbered at 25-m intervals to aid in identifying the location of macaque group encounters during periodic population surveys. The trails also provide convenient access to the feeder cages for daily food provisioning with the use of an all-terrain vehicle.

Logistic support for the Tinjil facility originates at the IPB transit base camp located in Muarabinuangen (approx 18 km from Tinjil Island), a small fishing village on the south coast of West Java (Fig 1). The transit facility consists of a large two-story building that provides ample accommodations for staff and visitors, office space, and a meeting room. Adjoining buildings offer equipment storage, drydock facility, laboratory space, and a temporary holding facility for macaques. The transit base camp also has a floating dock and covered dry dock for boat maintenance. Two inboard-diesel-engine boats are available to ferry equipment, supplies, personnel, and macaques between the island and mainland.

The Tinjil Island facility was established and managed during the first 4 years of operation by Chuck L. Darsono, DSc (Hon), a private entrepreneur who has been active in primate breeding and export for a number of years. Since January 1992, management of the facility has been the responsibility of the Pusat Studi Satwa Primata (Primate Research Center) at the IPB.

## Primate Population

*Screening and release*—Between February 1988 and June 1991, 478 adult long-tailed macaques (58 males and 420 females) were released onto Tinjil Island to establish a permanent breeding population. The macaques were captured in West Java and in the provinces of Lampung and Southern Sumatra. On capture, the macaques were placed in small group cages and transported by truck to the quarantine facilities in Cengkareng (CV Primates-Indonesia), West Java, for quarantine and health screening. Since January 1992, the quarantine/screening procedures have been conducted at the IPB quarantine facilities in Bogor. Recently, 20 additional macaques (19 adult females and 1 male neonate) were released onto Tinjil Island as part of a plan to increase the breeding stock to 1,000 macaques (Table 1).

On arrival at the quarantine facility, the macaques were individually housed in stainless-steel cages, and an initial evaluation was performed that included a physical examination, age/sex determination, and tuberculin skin test (macaques with a positive reaction were removed from the group). The macaques also were treated for common primate intestinal parasites, and each macaque's thorax was tattooed, to aid in identification on the island. Throughout the quarantine period, the macaques were fed commercially prepared monkey biscuits, fresh fruit, and water ad libitum.

A unique aspect of the Tinjil primate population is its specific-pathogen-free status. Because a portion of the offspring bred on Tinjil Island are intended for use in AIDS research, the breeding population must be free of immunodeficiency viruses. Therefore, before release onto the island, each macaque underwent a thorough viral screening process,[9] as described subsequently.

During the first week of quarantine, a blood sample was taken from each macaque and an indirect ELISA for simian retrovirus (SRV) type D was performed, using the serum. Macaques in which antibodies were found by ELISA were removed from the group. All remaining macaques (without antibodies to SRV) then were tested for SRV by use of virus isolation.[10] Cocultures of WBC and Raji cells were assayed for virus, by observation of cytopathic effect and immunofluorescence testing. Macaques in which virus was isolated or those with indeterminate or questionable test results were removed from the group. All remaining macaques (without SRV and antibodies) then were held for at least 8 weeks, and retested by ELISA. Macaques with antibodies to SRV following this second ELISA test were removed from the group. In the remaining macaques, immunoblotting was used to test for SRV, and macaques in which SRV was detected were removed from the group. All remaining macaques (without SRV) were transported to Tinjil Island. Macaques that did not meet the screening criteria were used in other research projects not requiring SRV-free macaques. The entire quarantine/screening process normally lasted 3 to 5 months.

*Population demographics*—An annual survey/census of the macaques on Tinjil Island has been conducted since 1990.[11,12] From the results of the 1994 survey,[b] the macaques are distributed throughout the island, with a disproportionate concentration in the eastern third of the island. Unlike those located elsewhere on the island, macaques in the western third are easily frightened and very difficult to observe. Overall, an estimated 17 to 18 groups have formed on the island, 11 of which can be reliably identified by tattoos and/or physical features of group members.

Group size, composition, and reproduction have been estimated from a sample of 4 of the 10 identified groups. These 4 groups frequent the feeder cages, thus permitting the most complete counts of group members. On the basis of data collected during August 1994,[b] mean size for the 4 groups was 53 members (SD, 21), with a mean of 6 adult males and 27 adult females/group. The number of offspring in these groups, although increasing, fluctuates considerably, as a result of the periodic offspring removals which began in 1991. Although variation in the literature regarding group size in *M fascicularis* is considerable, our data are consistent with estimates from other studies.[13,14]

Most of the groups observed on Tinjil Island are organized in the characteristic multimale (adult) composition, although 2 groups have been observed consistently with only 1 adult male. The sample groups are composed of adults from at least 3 and as many as 7 different release groups (released between 1988 and 1991; Table 1). These sample groups have remained stable over the past 5 years, with minimal exchange of group members. Only 2 adult males and 1 adult female (of different groups) have been observed to leave and join new groups. The circumstances surrounding these emigrations are unknown.

Reproductive estimates suggest an annual birth rate (over a 5-year period) of between 57 and 67%.[b] These percentages are considered conservative estimates of the yearly birth rate, accounting for approximately a 10-month period.[12] Recent data, however, indicate that births occur during all 12 months of the year, thus revealing lack of seasonal reproduction on the island, consistent with results from other studies of *M fascicularis*.[15-17]

If the estimated birth rate is applied annually to the adult female population released on Tinjil Island since February 1988, the cumulative number of offspring born on the island to date is approximately 1,332 macaques. This figure, however, does not include possible $F_2$ Tinjil offspring produced by 4- to 6-year-old $F_1$ Tinjil females born during the first 3 years of operation, nor does it account for death/survivorship. To estimate current population, factors such as these must be considered. Recent application of a computerized population modeling program[c] estimates the current offspring population at approximately 700 macaques.[d] This number has been adjusted to reflect the 370 offspring permanently removed from the island to date. Total population on Tinjil Island is currently estimated between 1,000 and 1,100 macaques.

Estimates of group size, composition, and reproduction generated from the sample of identified groups frequenting the feeder cages may be somewhat biased. Primate groups receiving supplementary feeding may have higher birth rates than unprovisioned groups.[18-20] Furthermore, provisioning also may support an increase in group size. Estimates derived from the sample groups, therefore, may not be representative of the remaining population (a portion of which has not received provisioning).

*Table 2—Offspring captures on Tinjil Island*

| Status | No. of macaques (males/females) by capture date | | | | | | |
|---|---|---|---|---|---|---|---|
| | June 1991 | December 1991 | July 1992 | May 1993 | December 1993 | June 1994 | Total |
| Captured | 56 | 56 | 65 | 59 | 54 | 130 | 430 |
| Died during capture/holding | 0 | 0 | 2 | 3 | 1 | 1 | 7* |
| Released back to island | 6 | 6 | 18 | 5 | 9 | 9 | 53 |
| Removed from island | 50 (28/22) | 50 (24/26) | 45 (22/23) | 51 (27/24) | 54 (29/25) | 120 (76/44) | 370 (206/164) |

*Five macaques were lost to pythons that gained access to the temporary holding cage, and 2 others died (while in temporary holding) of exposure during an unusually severe and extended period of stormy weather. No deaths have occurred during actual trapping.

*Table 3—Deaths among offspring captured and removed from Tinjil Island*

| Period | No. of deaths (% of total No. of macaques) |
|---|---|
| Trapping on island (n = 430)* | 0 (0) |
| Temporary holding on island (n = 430) | 7 (1.6) |
| Quarantine at Bogor (n = 370) | 4† (1.1)† |
| In shipment (n = 305) | 0 (0) |
| At destination (n = 305) | 0† (0)† |
| Total | 11 (2.7) |

*Values in parentheses are total No. of macaques. †During first 6 weeks.

## Offspring Capture and Removal

To date, 6 offspring captures/removals have taken place on Tinjil Island, the first in June 1991. A total of 370 juveniles (206 males and 164 females) between 1 and 3 years of age have been removed from the island, 245 of which have been sent to the Washington Regional Primate Research Center for use in AIDS-related research (Table 2).

All 6 captures have been conducted at the feeder/catch cages, sites of routine provisioning located throughout the eastern and central thirds of the island. During the capture period, daily (morning) provisioning is provided while a staff member hides in a blind approximately 50 m from the cage. When several juveniles have entered the cage, the worker pulls a string that releases a spring-loaded cage door, thus trapping the macaques. In the past, capture periods have lasted as long as 6 weeks to trap 50 to 60 offspring. Recently, modification of the capture schedule and improvements in the trapping techniques have resulted in a more efficient capture process. Two capture periods per year are scheduled (spring and fall), each about 4 weeks in duration. Trapping is conducted at 2 to 3 different cages each day, thus allowing at least 4 days between trapping at any one cage. An offspring removal quota (limit), generated from the census data, is set at the beginning of each year, to ensure a self-sustaining population.

Once offspring are captured, they are placed in the temporary holding cage at the island base camp. For each macaque, sex and weight are determined, a blood sample is obtained for SRV antibody testing, general health is checked, and the thorax is tattooed. These data are entered in a computer database that is being compiled to help monitor the island population. Offspring judged to be too young for removal from the island are returned to their respective social groups following assessment. Although, in the past, offspring were sometimes transported to the quarantine facility in Bogor for final evaluation before shipment, current protocol requires maintaining the macaques in same-age social groups on Tinjil Island until the day of shipment. By transporting the macaques directly to the airport in Jakarta, we hope to minimize the macaques' risk of exposure to SRV. Throughout the period of capture and holding, veterinary staff remain on the island to treat any health problems that might arise. All offspring screened thus far have had negative test results for tuberculosis and SRV, thus assuring the integrity of the specific-pathogen-free breeding population on Tinjil Island.

Survival rate among the macaques captured and removed from Tinjil Island has been excellent (Table 3). Of the 430 total offspring that have been captured since 1991, no deaths or injuries have occurred during actual trapping. A total of 7 macaques have died while in temporary holding on the island: 5 were lost to pythons that gained access to the holding cage, and 2 others died of exposure during an unusually severe and extended period of stormy weather. Steps have been taken to reduce the recurrence of such problems. Of the 370 total offspring that have been removed from the island to date, 4 have died while at the quarantine facility in Bogor (on the basis of total mortality up to 6 weeks after arrival). No macaques have been lost in shipment or in quarantine at their destination (on the basis of total mortality up to 6 weeks after arrival).

## Research and Training

Although the Tinjil Island facility has achieved recognition as a primate resource program, the facility, in fact, serves as more than just a breeding operation. The island is quickly becoming recognized as an active field station that offers excellent opportunity for primate research and field training. During the past 4 years, more than 45 students from the IPB, as well as from several other major Indonesian universities, have conducted research

projects on Tinjil Island covering a range of topics, including primate behavior, ecology, conservation, and management. An annual field course in primate behavior and ecology has been conducted since 1991[e]; participants have included students, faculty, and staff from the IPB and staff members from the Indonesian Directorate General of Forest Protection and Nature Conservation. Activities such as these play an important role in promoting a greater understanding of primatology and an awareness of the need for effective conservation and management practices.

## Conclusions

The success of the Tinjil Island natural-habitat breeding program has prompted the Indonesian government and state forestry company (Perum Perhutani) to consider designating other islands as breeding sites, modeled after the Tinjil facility. Natural-habitat breeding of primates in the country of origin represents a unique approach to meeting the continuing demands of primate supply in a conservationally sound and economically efficient manner. Breeding programs such as that on Tinjil Island also have assumed a sense of urgency, in light of the Indonesian government's recent (April 1994) legislation banning the export of wild-caught primates. Such programs now represent one of few remaining county-of-origin primate resources available to the biomedical community.

Although *M fascicularis* remains an important and useful model in which to study primate lentivirus, researchers at the University of Washington have recently demonstrated that the pig-tailed macaque (*M nemestrina*) is susceptible to infection by HIV-1.[21] This discovery marks the pig-tailed macaque as a valuable model for the study of acute HIV-1 infection, as well as for testing vaccines and antiviral agents. Compared with long-tailed macaques, however, the number of pig-tailed macaques available for biomedical research is very limited, accentuated even more by the Indonesian ban on the export of wild-caught primates.

In response to the potential for a shift to the *M nemestrina* model for AIDS research, the University of Washington Regional Primate Research Center, in collaboration with the Primate Research Center at the Bogor Agricultural University, plans to establish another natural-habitat breeding facility for specific-pathogen-free pig-tailed macaques. As the search for a suitable island habitat continues, a compound breeding facility for pig-tailed macaques has been established in Bogor. The colony includes nearly 175 breeders and approximately 150 offspring. All breeders were subjected to the same virus-screening protocol described earlier. Once a suitable island is found, all or a portion of the colony will be transferred to that location to establish a natural-habitat breeding facility.

Natural-habitat breeding will undoubtedly become one of the primary resource options for maintaining the availability of high-quality, bred-for-purpose primates for use in important biomedical research around the world. The facility established on Tinjil Island should serve as a useful model for future primate resource and conservation programs.

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# Private practitioner's perspective on animal research

Thomas E. Vice, DVM

Animal rights and animal welfare have become political issues that create a great deal of confusion for the average citizen. The organized animal rights movement and organized veterinary medicine have major philosophic differences on these issues, but both know where they stand. The problem is in articulating these positions to the public. Confusion is created between the meaning of rights and welfare, and often the animal rights activist uses this confusion to further this movement's agenda. That agenda is seldom, if ever, revealed to the public when animal welfare is discussed. Nowhere is this confusion more prevalent than in the animal research arena.

My first exposure to animal research was in 1963, when I became staff veterinarian for the Southwest Foundation for Research and Education in San Antonio, Tex. I was the first veterinarian the Foundation had ever hired. My first day on the job, I had to evaluate an extremely sick baboon that was comatose. With a great deal of zeal, I started my examination of this baboon by taking its rectal temperature. When I asked the rest of the staff the baboon's normal temperature, I was stunned when no one knew. As I proceeded with my examination, collecting heart rate, respiratory rate, and drawing blood for a CBC, I encountered the same blank expressions when I asked for normal values. After a literature search, I found that normal physiologic values were unknown in this species. Not knowing what was normal certainly made dealing with the health problems of these baboons much more difficult.

This difficulty also led to my first major assignment at the Foundation: writing grant proposals for baseline studies in baboons. As a result of these and other studies, veterinarians involved in primate medicine today are able to determine abnormal from normal and do a much better job of caring for baboons.

In 1963, laboratory animal medicine was in the very early stages as a specialty in veterinary medicine. At that time, institutions involved in animal research were not required to have a veterinarian on their staff or even as a consultant, and many had neither. In my 6 years at the Foundation, I had many conflicts with researchers over the issue of the welfare of their animals. I often found that budget cutting almost always was at the expense of the animal-care end, not in the laboratory. I sometimes had to deal with scientists whose end—whether it was personal, in the way of recognition; or societal, in the way of knowledge—justified any means needed, no matter how insensitive or inhumane. I think that such cases were not that uncommon in most institutions involved in animal research at that time.

In those days, animal welfare and animal rights

From the Broadway Animal Hospital, 8221 Broadway, San Antonio, TX 78209-1996.

were not public issues. They certainly are today, and in no small way because abuses were allowed to continue uncensored and unregulated. There were no guidelines for the research community to follow and no principles of humane care for it to live by. Animal rights as an organized movement certainly gained a great deal of its momentum from this arena.

To give you a balanced view of my background, in 1989 on New Year's Eve, I was asked by People For the Ethical Treatment of Animals (PETA) through Primarily Primates in San Antonio to go to the Delta Primate Center and examine one of the Silver Spring, Md, monkeys named Billy. Billy was a quadriplegic and was considered to be in critical condition by the veterinarian at Delta, who recommended euthanasia. Because of a court order, Billy could be euthanatized only with PETA's consent. I was selected as acceptable to both sides, to make the final determination. After my examination of Billy, I called PETA and recommended euthanasia, and agreed to stay and supervise the procedure, as well as a final determination to be done under anesthesia, as proposed by the National Institutes of Health. After 2 hours of deliberation, PETA called me back and refused to give permission, and even asked me not to disclose my recommendation to the Institutes. It was obvious to me that the welfare of this monkey had little to do with PETA's decision; the monkeys represented their power base and they were not going to let go. In my opinion, this situation was another example of the means being justified, in someone's mind, by the end.

The care and treatment of research animals today is much better than it was just a few years ago. This improvement was primarily because of the pressure brought by the animal rights movement. Veterinary medicine, instead of being proactive, has been reactive to this problem. We sort of dropped the ball. The first AVMA Animal Welfare Forum was held in 1990. The first AVMA position on animal welfare was approved in 1981.

In my opinion and realm of experience, most people, including my colleagues in private clinical practice, agree with the AVMA's policy on animal welfare and favor the responsible use of animals. The problem is that animal rights activists are doing a much better job of reaching the public—and politicians—than we are. Unfortunately, most private practitioners do not perceive this issue as a major problem. I attended 2 sessions at the AVMA meeting in San Francisco on "animal welfare, animal rights, and animal research" given by Drs. Jerrold Tannenbaum and Paul Armstrong, and was the only private practitioner at those sessions. I have to confess that I was unaware that the AVMA positions and policy on animal welfare were included in the AVMA directory until I was informed of such after a telephone call to Dr. John Boyce. I would bet that most veterinarians, especially those in practice, have never read this material and many, like me, are unaware of its existence.

One of my early bosses told me not to bring him a problem unless I had some solution. Here are my suggested solutions. Publish regular columns in a number of veterinary periodicals (eg, *Journal of the Association of Avian Veterinarians, Veterinary Forum, Veterinary Economics*), not just in the *JAVMA*, on ethical and animal welfare considerations in veterinary practice. Include programs at state and local veterinary medical association meetings. Develop a media kit for use in dealing with this subject at local and state levels. Monitor and publicize animal activist actions when and where they are in conflict with AVMA policy and positions on animal welfare.

No one yet has given me a convincing argument that we do not need animal research to continue our progress in human and animal medicine. In my opinion, if the animal rights activists have their way, we would no longer exist as veterinarians–not a viable option to me!

# Consistency in treatment and moral concern

Nedim C. Buyukmihci, VMD

This is a discussion of the issue of fair and consistent treatment of living creatures. Although it is specifically about the use of nonhuman animals in research by human beings, the principles can be applied to other aspects of human and nonhuman animal interaction. My premise is that human beings do not have a prima facie right to use other animals, if they are unwilling to apply the same treatment to fellow human beings. That is, human animals, when acting as moral agents, do not have a moral right to use other animals in ways they would not permit themselves or, in particular, human moral patients, to be used. This premise, I believe, is the crux of the argument. Most arguments on this subject start with the premise, usually tacit, that human concerns tower above those of others. Such arguments, therefore, provide a biased theory or discussion of moral concern and fail to deal with the issue in a serious and fair manner.

What I discuss is based on ideal circumstances. When I refer to interactions between human beings, for example, I realize that not all people treat each other with respect, nor hold to the highest moral principles. However, to consider a moral principle invalid simply because not all adhere to it would be inappropriate.

I did not always hold the views I express now. I have been involved, either principally or as a spectator, in the following uses of nonhuman animals for part of my life: research, testing, education, food, fiber, entertainment, fishing, and "pest" control. In the area of vision research, I received several large grants from the National Eye Institute, one of the branches of the National Institutes of Health, all as principal investigator, and published numerous scientific papers. I believed that the use of nonhuman animals by human beings was permissible, albeit with the usual and trite caveat that they should be treated "humanely." I had not, however, carefully explored the ethical considerations of this value judgment.

Over the past couple of decades, I slowly have eliminated my overt and intentional involvement in the exploitation of nonhuman animals. Although it did not come about at once, I eventually came to realize that all arguments in support of harming, in the broadest sense, and killing nonhuman animals for human purposes, except in immediate life-and-death dilemmas, fundamentally are flawed, particularly from a moral perspective. The major defense put forth is that human beings, or other animals, derive benefits from this use. Even a charitable interpretation of such arguments is that the end justifies the means. This notion, however, is something we have rejected when it comes to our interaction with each other, and I see no compelling reason not to apply the same moral proscription to our interaction with other animals.

There is no question that the primary issue is one of morality. If it were not, we would be compelled, on a purely scientific basis, to use human beings for all research aimed at understanding human diseases or for tests of drugs for toxicity, for example, even if it meant harming or killing these human subjects. That this practice would provide human beings as a whole with far greater benefits and safety, and far more quickly, is irrefutable, because there are too many species differences to rely on extrapolation from one species to another. This research would be immoral, however, and I do not advocate such behavior. As I will later argue, such treatment, if applied to nonhuman animals, logically must be considered immoral for precisely the same reasons.

For human beings, we do not accept the notion of a master race, or of an inferior race that could be used in the stead of others. We also do not believe that having the strength or other ability to overcome someone gives us the right to exploit that person, nor do we allow the prospect of benefits to the human species as a whole, no matter how monumental, to guide our conduct toward each other. We refrain from harming each other, not just out of fear of retaliation, but because these proscriptions are part of our moral code.

In the case of nonhuman animals, most human beings disregard this moral code. In the name of science and other activities, we subject other animals to things we would consider highly unethical and immoral if we did them to each other. No one, however, has ever put forth a rational, nonself-serving argument that nonhuman animals are not deserving of the same degree of moral concern we have for members of our own species.

Our sense of morality in dealing with each other stems from our highest capacity for benevolent action, transcending the largely amoral situation in nature. This morality is not limited to, nor simply the result of, the fact that we are dealing with human beings. If I labeled a chair a "human being," you easily could appreciate the difference

From the Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California, Davis, CA 95616-8745.

in moral consequences between gratuitously cutting off a leg of the chair and cutting off a leg of a person. Doing such to a chair has no moral significance: it does not matter to the chair that a leg has been removed. It does matter, however, and greatly so, to the human being whose leg was removed, regardless of whether anesthesia and analgesia were provided.

The reason harming another human being is wrong, therefore, is not simply because he or she is a human being per se. It is wrong because of certain qualities a human being possesses that are important to consider and protect. A person is an individual who has a life that fares better or worse, depending on what happens to her or him; no such claim can be made for inanimate objects. A person has value that is independent of her or his utility to another; the value of an inanimate object generally is negotiable. A person has interests, pursuit of which is a source of enjoyment and denial of which is a source of frustration; no such claim can be made for inanimate objects. In part, these are the bases for the so-called inalienable rights we give each other. Even people without concept of right or wrong and without obligations to others (so-called moral patients) are granted these minimal rights. I refer to children, the permanently comatose, or the mentally handicapped.

Like human animals, other animals are not inanimate and do have lives that fare better or worse, depending on what happens to those lives; their lives can be enriched or impoverished. Also like human beings, other animals have interests, although they may be difficult to define and may be different from those of human beings, just as those of one person may be substantially different from those of another. Nonhuman animals can experience painful and pleasurable stimuli and most can probably suffer in the general way in which human beings do.[1,a] When you examine the issue without prejudice and with humility, there do not appear to be any morally relevant differences between human beings and other animals that justify denying other animals similar rights, consideration, or respect, on the basis of their interests or whether what we propose to do matters to the individual animal.

Physical or intellectual equality is not a mandatory criterion for proposing equal consideration. Inalienable rights are not accorded because all people are created equal. Quite the opposite, they are a means of protecting disadvantaged individuals from tyranny at the hands of those superior in certain traits. These differences between various people (eg, intelligence or physical strength), as well as differences in gender or race, are biological, and are irrelevant from a moral perspective. The major differences between nonhuman animals and human beings also are biological—usually a difference in degree, not in kind. But more to the point, essentially all characteristics stated to be important and uniquely human actually are shared, to some degree, with many other animals and do not even exist in some human beings. Language (in a broad sense, not just the artificially narrow human construct), thinking, intelligence, and other things that people try to declare as separating human beings from other animals, even though these are morally irrelevant, are present in many other animals.[2-5] For example, experiments have revealed that nonhuman animals can seriate and that they use at least some of the important information management processes exploited by human beings.[6] Other arguments put forth by some (eg, that other animals do not have political systems or do not compose symphonies) are nonsensical, vacuous, or irrelevant from a moral perspective, and are rejected by those who view this issue in a rational and thoughtful manner.

On the basis that all mammals can experience pain and suffering, the phrase arose, ". . .a rat is a pig is a dog is a boy."[b] Those arguing against equal consideration for other animals frequently quote this phrase out of context, attempting to portray those who use it as not valuing human life. This portrayal is absurd for many reasons, not the least of which is that the critical first part of the phrase, which puts it in the context of pain and suffering, is ignored. To equate human beings and other animals in this context is scientifically correct and in no way demeans human beings. Rather, it raises the status of other animals and emphasizes the biological and moral similarities between all mammalian species. Even those who support vivisection, for example, believe at least the physical aspect of this analogy; they argue that rats are models of boys when justifying experiments on the rats.

Those who defend the harming and killing of nonhuman animals in research state that the animals are treated "humanely." This defense flies in the face of common sense. To be humane is to have sympathy for another, to have mercy, to be tender and kind. If you provide pain relief after you have broken the spine of a cat for an experimental study, in what way can this be considered humane? If it were not for you, there would have been no pain in the first place. Regardless of your beliefs about the propriety of using nonhuman animals in research, the use of the word "humane" in this context is inappropriate if the animal is harmed or killed, even if done painlessly. Those who argue otherwise should reflect on whether they would consider similar treatment of a human child "humane," even if the intent was to understand a disease so that other human beings could be helped. Bear in mind that there only is one definition of the word "humane"; it is not defined one way for human beings and another way for other animals.

When the preceding argument is discussed, many will point out that people suffer daily from various diseases. This reality cannot be denied, and I share their concern for the misery those people endure. Appealing to the suffering of or potential harm to a human being (or other being of interest),

however, simply is not adequate from a moral perspective. Why is one group of animals (human beings, in this case) more important than another?[c] Is it the fault of the other animals being used, harmed, and killed in research that human beings also are subject to disease and death? Why do we believe that because we suffer, innocent others must pay a price? In that context, the harming and killing of other animals in the name of science appears to be an expression of unconscionable selfishness on our part, something that opposes all the best qualities of human nature.

When you critically and honestly evaluate the situation, it becomes clear that we use other animals not out of some moral imperative or because it is right, but rather because we believe we will benefit from such behavior and because we have the power to dominate the animals. We tacitly act on the morally repugnant principle that might makes right. The question that should be raised by those purporting to be acting morally in such instances, therefore, is not whether benefits are derived or whether there are adequate alternatives to various uses of nonhuman animals. The real question is whether our domineering behavior is appropriate for such a highly developed, intelligent, and potentially compassionate species such as ours. If we consider ourselves to be so much better than other animals, we behave in a most despicable and self-degrading manner by subjugating and destroying those "below" us.

People often ask questions such as, "Who would you save in a situation where your mother and your dog were in mortal danger?" Such questions, although interesting, do not bear on the question of whether human or nonhuman life is more valuable. Rather, they speak to the question of which individual is more valuable to another individual. Suppose that the situation was a life-or-death scenario between 2 human beings, your daughter and someone else's daughter. I believe that most people would choose their own child over another. This choice does not mean they are callous or that they do not value human life; they simply have a closer, more familiar, and more compelling relationship with their own child.

What are we to do if we do not use nonhuman animals in research? Such a question presumes that progress is not possible without such use. Many even state that most or all advances in medicine have depended on use of nonhuman animals. Such statements are pure speculation on their part. A good scientist would ask if a controlled study had compared advances with and without the use of nonhuman animals; such a study is virtually impossible retrospectively. Nevertheless, I believe that the issue of alternatives is primarily one of mind-set. We are an incredible species with respect to our capacity to change our environment, to develop means by which to overcome natural obstacles to understanding biological processes. We do ourselves a great disservice and minimize our abilities when we claim that we have no alternatives except to rely on the subjugation of unconsenting beings.

The present level of sophistication for ethical human studies is considerable. For example, Kiyosawa and coworkers,[7] using human volunteers and positron emission tomography, demonstrated a regional reduction in cerebral glucose metabolism in patients with optic neuropathy. Uematsu and coworkers[8] have studied patients with refractory seizure disorders and who were undergoing evaluation for therapeutic brain surgery. These patients had had subdural electrode grids implanted. Cortical mapping was done by electrical stimulation of the cerebral cortex, to learn important neuroanatomic details of the human motor cortex, information virtually impossible to derive from studies of other animals.

Other investigators[9-11] have used positron emission tomography or magnetic resonance imaging to measure activity-related changes in regional cerebral blood flow, to identify brain regions active in human beings during reading or playing the piano. This combination of cognitive and neurobiologic approaches has provided information about the functional anatomy of perception, attention, motor control, and language in human beings, again, something not likely to be possible with nonhuman subjects.

These types of studies provide us with information about human brain structure and function that will be invaluable in understanding and treating human disorders. They also reveal that claims that nonhuman animals are absolutely necessary for research are simply not true. These and other methods can be used in numerous other disciplines. I cite these studies not just to point out specific examples of alternatives to nonhuman animals, but more importantly, to emphasize what could be done if there were a change in mind-set, a change from viewing other animals as mere tools to considering them as deserving of the same respect as human beings. If we changed our attitude in this respect, we could concentrate our efforts in improving available alternatives and developing new ones. Necessity would become the mother of invention. We could begin the journey out of the dark ages of violence and destruction perpetrated on unconsenting and, presumably, unwilling animals in the name of science.

When contemplating or discussing the issue of nonhuman animals used in research, the most important point to consider is that these animals are living beings who share with us the drive to live freely. They are not here for us; they are simply part of the complex web of life on this planet. Their value does not depend on their utility to us. Harming or killing these animals in the name of science does not make it noble or right. Our own sense of morality demands that our treatment of them be fair and just.

[a]Although most people do not consider this an important issue when it comes to invertebrates, there is evidence that such a view is narrow and scientifically unsupported.

[b]Newkirk I, People for the Ethical Treatment of Animals, Washington, DC: Personal communication, 1994.

[c]Whereas you may balk at considering human beings and dogs, for example, moral equals, you cannot rationally argue that morally relevant differences exist between one dog and another. All the substantive ethical considerations that would apply in protecting a dog of one status, such as one that is a human companion, would apply equally to a dog in another situation. This logic would make any argument supporting the destruction of one group of dogs to "save" another morally bankrupt.

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# The future of animal research


Bonnie V. Beaver, DVM, MS


A visionary can only look at the future through the thick and foggy globe of a crystal ball. Vision is never perfect until after an event has occurred. To predict the future, one can study current trends, events in other countries, and recent advances in related disciplines, and one can brainstorm with insightful colleagues. In the end, however, the vision is still foggy, and the prediction just that—one person's opinion of what the future might bring.

From the depths of history through the foreseeable future, animals have been used in research for 2 primary reasons—to learn more to help animal populations and to learn more to help human beings. Examples of learning how to understand human diseases as a result of learning about similar conditions in animals are many. The opposite also has been true—animals have benefited because of knowledge gained from plagues and diseases of the human population. Although the names of the specific diseases, surgical procedures, or drugs will change, these 2 situations will continue. Animals and human beings can each benefit from animal research, but the approaches will change over time.


From the Department of Small Animal Medicine and Surgery, College of Veterinary Medicine, Texas A&M University, College Station, TX 77843-4474.


## Animals Helping Animals

Predictions of benefits to the animal populations is the first stop in a vision of the future. A great deal still needs to be learned about contemporary problems, to better serve the animal community. For example, heartworm disease in dogs is still treated with IV injections of sodium thiacetarsamide. Although veterinarians know much more about this parasite's physiologic features and life cycle for use of preventive drugs, safer and more efficacious drugs for treatment are still needed. As other examples, is the increased incidence of autoimmune diseases related to better diagnostic capabilities, to the increasing number of proteins used in animal vaccines, or to environmental pollutants? When will veterinarians be better able to diagnose and treat feline infectious peritonitis?

Only a few years ago, parvovirus appeared as an important killer of young pups, and equine monocytic ehrlichiosis (Potomac fever) hit the horse population. Much detective work was needed to determine the cause of each of these conditions, and much more to develop ways to protect the an-

imal populations. There will be a new "parvo" in the future. Finding the cause and the cure will depend, in part, on animal research.

Even old diseases cause new problems. Canine distemper was recently reported to be devastating lion populations. In Tanzania, this disease has already killed up to a third of the lions in one study area.[1] Although whether to interfere in the course of this situation is truly controversial, scientists must consider the importance of a similar occurrence in rare or immunodeficient species such as mountain gorillas or cheetahs.

By way of another example, the urban dog strain of rabies in coyotes has become of such a concern that the governor of Texas recently declared a rabies emergency. Veterinary public health researchers are actively involved in the challenge tests of an orally administered rabies vaccine for coyotes, with the hope that it can be used to stop the outbreak before infected coyotes reach the denser populations of domestic dogs in Austin and San Antonio.

## Animals Helping People

Human health will remain dependent on animal research. Although devastating viruses like the human immunodeficiency virus have resulted in epidemics throughout recorded history, approaches to understanding these agents have changed. An animal model, like the feline immunodeficiency virus, will still be needed to halt the tragedy, whether through development and testing of vaccines or in finding therapeutic regimens. Ethical concerns about testing such vaccines in human beings[2] will force these alternative studies.

Drug resistance by tuberculosis and other microorganisms has received a great deal of press lately. More virulent strains of *Streptococcus* A and others have resulted in Michael Creighton-like stories of flesh-eating bacteria. Although these issues are in the headlines in the contemporary pages of the scientific[3] and lay press, similar issues will face us in the next century, too. If the scare is great enough, society will demand a cure, regardless of the cost to nonhuman animals.

Although drugs are usually tested in animals before being used in human beings, there is a push by some for this not to be done. A recent development with tamoxifen, however, may result in a reassessment of this strategy. Since the mid-1970s, tamoxifen has been used in women as treatment and prevention for breast cancer. Because of this drug's chemical structure, preusage animal trials were not deemed necessary. Only within the last 2 years, have researchers using rat models linked liver, endometrial, and breast cancers to this drug. The 8,000 women currently enrolled in the National Cancer Institute trial will ultimately determine the complication rate of this drug.[4] Consider what the legal, moral, and ethical backlash will be if human findings are as negative.

## Societal Demands

Unless there is an international crisis to trigger the self-preservation, find-an-answer-regardless nature in human beings, the trend of improving humane care and welfare for research animals will continue well into the next century. Innovative ways have already been incorporated into research facilities: from large amounts of human interaction for dogs to environmental enrichment devices for chimpanzees and to a view of fish for research cats. The AVMA's position has been and will continue to be toward this end. "The AVMA recognizes that animals play a central and essential role in research, testing, and education for continued improvement in the health and welfare of human beings and animals. The AVMA also recognizes that humane care of animals. . .is an integral part of those activities. . .. The use of animals is a privilege carrying with it unique professional, scientific, and moral obligations."[5]

Because there is still much to be learned, continuing to study the animals used in research to best understand their behavior and responses to stress will be important. Even now, studies being done at the University of Georgia may force a reassessment of canine vaccine research on the basis of newer behavioral and physiologic data on stress responses.

Although there is no way to please all sides in the use of animals in research, the trend of better study designs in which fewer animals are used more efficiently will continue. Alternative approaches will be used, as the strengths and weaknesses of each system become better recognized. Tissue cultures, DNA probes, and computer models have been widely discussed and have gained acceptance for certain types of research. The paradigm of how animals are involved in research also has been shifted. No longer is testing every concept on an individual animal necessary; the focus of most investigations now is the various components of an organism, rather than the whole.[6] Studying viruses at the cellular level, computer modeling of drug structures, and use of tissue cultures, so that a single animal contributes to many tests, instead of many animals contributing to a single test, are examples. Ever-expanding DNA technologies mean that transgenic animals can supply real models for human diseases like amyotrophic lateral sclerosis (Lou Gehrig's disease)[7] and insulin-dependent diabetes mellitus,[8] with species that adapt well to a laboratory setting, have short normal life expectancies, are relatively inexpensive to maintain, are genetically identical, and can be raised in appropriate quantities to produce meaningful results. Through such methods, DNA will be able to be transferred into cell cultures and into plants, to provide a whole new experimental model.

## The Veterinarian's Role

The veterinarian's role will remain diverse as the use of animals in research changes. Laboratory

animal specialists will continue to be involved in the proper selection of animal models and in the care of research animals. The needs of transgenic animals will add ethical and scientific challenges to this role. Other veterinarians will be involved with the development of newer knowledge. Behaviorists will define species needs and effects of stress more specifically.[9] Pharmacologists, internists, and surgeons will develop and test new ideas and reevaluate old ideas in new species. Practitioners will identify the newest threats to animal health, identify the ineffective vaccines or drugs, refer naturally developing models when purpose-bred animals are not appropriate, and educate clients about new developments for a higher quality of animal life.

Over time, the foggy haze over the future will clear. Until then, the value of these predictions is no more than that from any other mere mortal. New and exciting approaches to solving existing and evolving problems are many, but in the surrounding enthusiasm, it is important to consider the other contributors—the animals.

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