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Building a Culture of Animal Welfare: Past, Present and Future

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Abstract

Medina L. Building a Culture of Animal Welfare: Past, Present and Future. ARBS Annu Rev Biomed Sci 2008;10:T104-T111. Animal research has contributed significantly to advances in science and medicine and will continue to play a key role in biomedical research. However, there is growing public support for animal welfare and animal rights. Public concerns about animals are partly responsible for increases in regulatory oversight and the drive to find alternatives to animal research. A careful look at the past, present and future of animal welfare within the biomedical sciences will show that there has been tremendous progress in developing a widespread culture of animal welfare but that more progress is required. In the end, each institution and individual involved with animals in science must do their part to build a culture of animal welfare which not only upholds high standards but promotes the alternatives of refinement, reduction and replacement (3Rs) whenever feasible.

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1. Introduction

In the past century, and especially over the past 50 years, a growing emphasis has been placed on animal welfare around the world. In the United States a very significant reason for this growing interest is a dramatic change in how individuals perceive animals. This shift is largely due to a change in demography. Much of the population has moved from rural environments where they would have been exposed to agricultural animals to more urban environments where their exposure is often limited to pet animals (G. Golab, AVMA, personal communication). The United States Department of Agriculture (USDA) commissioned the philosopher, Bernard Rollin, to expound the reasons why U.S. society's view of anticruelty had changed so drastically in the last half of the 20th century. He listed five social and conceptual reasons but then stated "they are not nearly as important as the precipitous and dramatic changes in animal use that occurred after World War II. These changes include huge conceptual changes in the nature of agriculture and a significant increase in animal research and testing (Rollin, 1995, 2004)."

Concurrently, there has been a significant increase in the number of animal welfare and animal rights organizations. Animal welfare organizations promote responsible, humane care for all animals and recognize that people have moral responsibilities to ensure animal welfare for animals that are used for human purposes (Blackwell & Rollin, 2008). Animal rights extremist organizations promote a philosophy that animals should be given equal rights to humans and they strongly oppose what they consider to be the exploitation of animals for human purposes, such as biomedical research. "Between 1960 and today, the number of active animal rights groups has grown from about 15 to more than 250 in the U.S. alone. The Foundation for Biomedical Research (FBR) estimates there are about 20 major national animal rights groups that focus exclusively or primarily on animal research (M. Stebbins, FBR, personal communication)." Globally, there are over 900 independent animal welfare and/or animal rights organizations in over 150 countries (WSPA-USA, 2008).

The past 50 years have also seen significant advances in science and medicine. Examples include the development of lifesaving vaccines (polio, rubella), cardiovascular bypass surgical procedures and treatments for many ailments such as diabetes and cancer. Many of the advances have been based on data from animal research. Although a majority of the public may not understand how research with mice can benefit humans and other animal species, there is plenty of scientific data to prove the importance and validity of animal research. FBR reports that "seven of the last ten Nobel Prizes in medicine have relied at least in part on animal research (FBR, 2008)." A majority of human medical advances are eventually adopted for veterinary use and thus result in enhanced animal welfare practices. For example, scientists have learned more about recognizing and responding to pain and distress in a wide variety of animal species.

Throughout this period of advancing scientific and medical knowledge, there has been a parallel increase in animal welfare regulatory oversight, development of training programs for laboratory animal care specialists and development of alternative research and testing methods (Quimby, 1994). These changes have all played a role in the biomedical research community's growing interest and commitment to enhanced laboratory animal welfare.

This paper provides a brief overview of how society has been moving towards adopting a stronger culture of animal welfare. Primary emphasis will be on the culture of animal welfare within biomedical research programs with a brief review of the past, where we are at present, and where we might be headed in the future.

2. Past

A review of animal protection history shows that a majority of cultures adhere to a code of ethical conduct with regards to animals. Even one of the earliest recorded laws, the Code of Hammurabi, 1780 BC, includes mention of animal protection: "not even a dog that entered the city could be put to death untried (Johns, 1910)". The rise of organized animal protection agencies in the U.S. began in the last half of the 19th century (Wolfe, 2003). It is clear that the vast majority of animal welfare laws exist in response to public concerns and perceptions about the care and treatment of animals. A review of the Animal Welfare Act (AWA) shows that the original law was passed in 1966 in direct response to public concerns about animals used in research (Schwindaman, 1999). Since then, public interest in animal

welfare has continued to grow as evidenced by the following statement: “By the early 1990s, the U.S. Congress had been consistently receiving more letters, phone calls, faxes, e-mails, and personal contacts on animal-related issues than on any other topic (Rollin, 2004).”

Animal welfare concerns were also being recognized and addressed from within the biomedical research community. The Animal Care Panel (ACP) was founded in 1950 by five research veterinarians that recognized the need to develop expertise with laboratory animals to ensure optimal animal welfare and good science (Brewer, 1999). In 1967, the ACP was changed to the American Association for Laboratory Animal Science (AALAS) (Wolfle, 2003). AALAS members are dedicated to the humane care of laboratory animals and to quality research that benefit people and animals. Likewise, the American Board of Laboratory Animal Medicine (ABLAM) was founded in 1957 and renamed in 1961 to the American College of Laboratory Animal Medicine (ACLAM) to encourage education and research in laboratory animal medicine and to establish standards for laboratory animal veterinarians (Wolfle, 2003). In 1965, the American Association for Accreditation of Laboratory Animal Care (AAALAC) was founded by leading veterinarians and researchers to raise the standards for laboratory animal care through a voluntary assessment and accreditation program based on the *Guide for the Care and Use of Laboratory Animals* (NRC, 1996) or current revision. In 1996, AAALAC changed their name to the Association for the Assessment and Accreditation of Laboratory Animal Care, International to reflect their commitment to improve life sciences and animal care and use practices around the world (Wolfle, 2003). Currently, there are more than 770 animal care and use programs in 29 countries that have earned AAALAC International accreditation (AAALAC, 2008).

In 1985, the Improved Standards for Laboratory Animals amendment to the AWA was passed and established new concepts in the regulation of research facilities. This amendment mandated the formation of an Institutional Animal Care and Use Committee (IACUC), relief of pain and distress, limits on survival surgeries, exercise for dogs, psychological well being for nonhuman primates and the creation of the Animal Welfare Information Center (Kulpa-Eddy *et al.*, 2005). These changes were promulgated to ensure more rigorous oversight of laboratory animal care and use practices and higher standards for animal welfare.

Animal welfare within biomedical research programs continues to improve. Although analgesics are given more consistently to larger species than to small rodents undergoing surgery, recent studies report behavioral changes indicative of pain in rats undergoing laparotomies without analgesics (Roughan & Flecknell, 2001). As scientific studies elucidate these pain reactions and the biomedical research community becomes more adept at recognizing subtle behavioral changes in rodents, analgesia practices will continue to improve.

Rollin defends the biomedical research community when he states, “Now it is clear that researchers are not intentionally cruel. Rather, they are motivated by plausible and decent intentions: to cure disease, advance knowledge, ensure product safety, develop advanced surgical techniques for use in human health (Rollin, 2004).” He acknowledges that despite this lack of intention that they may still inflict suffering on the animals they use (Rollin, 2004). The biomedical research community must acknowledge that at times laboratory animals feel pain or distress. In fact, a majority of animal research is quite innocuous but some research does cause animal pain or distress because of the diseases or biological processes that are studied. In those instances, the ethical obligation is to use nonanimal alternatives if available, but if not available, ensure the fewest animals are used and minimize animal pain and distress by using supportive care and the rigorous application of humane endpoints.

3. Present

The current generation of animal care, veterinary and research staff has never worked in a program where laboratory animal welfare wasn't emphasized. Individuals in the animal research field understand that animal welfare is a priority not only because ethical science demands it but also because loss of public support could be devastating to future scientific and medical progress. As science has taught us more about how to improve animal welfare, public concern has brought a greater focus to animal welfare issues globally. A 2007 opinion survey in Britain revealed that 76% of the general public accepts animal experimentation as long as there is no unnecessary suffering caused to the animals (MORI, 2007).

In research programs across the world, minimum animal welfare standards are no longer viewed as best practices. Rather, programs are going above and beyond these minimum legal requirements and guidelines to establish unique ways to enhance animal welfare. One way they accomplish this is by adopting alternatives, also known as the 3Rs of refinement, reduction and replacement, as first described by Russell and Burch (1992). Many institutions have created special positions or committees to focus on environmental enrichment, alternatives and animal welfare initiatives that go above and beyond the mandatory IACUC oversight. Examples of the “above and beyond” approach include Merck’s Animal Alternatives Committee (James *et al.*, 1995), and Abbott’s Caring for Animals in the Research Environment (CARE) Committee (L. Medina, unpublished data). These institutions and many more have recognized that it is no longer good enough to adhere to the laws and guidelines; instead they are contributing to furthering animal protection practices in biomedical research. Thus, many institutions are funding alternatives research and developing animal welfare award programs to reward staff that initiate and promote alternatives.

There are more organizations globally that focus on promoting alternatives such as the Center for Alternatives to Animal Testing (CAAT), the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) and the United Federation of Animal Welfare (UFAW). These organizations vary in their missions, but most fund research projects to advance the knowledge or application of one or more of the 3Rs. Other organizations have been created as part of a government’s commitment to examining how to validate alternative methods for drug safety testing (Laroche *et al.*, 2007).

An important area of progress today is pain management for laboratory animals. The increase in biomedical research has contributed to veterinary and human medical knowledge and enabled significant enhancements to animal welfare. For example, as recently as the early 1990’s, veterinarians did not routinely provide analgesia for cats undergoing spays. Less than 20 years later, it would be unacceptable to forgo analgesics.

A growing number of scientists agree that unrelieved pain induces secondary negative affects, such as fear and anxiety in animals (Phillips, 2007). Research investigators hesitate to adopt alternative practices without scientific evidence to prove that these changes will not negatively impact their study data. The Australian Code states, “The underlying presumption in the selection and use of a pain management protocol is that, while pain and distress cannot easily be evaluated in animals, investigators and teachers must assume that animals experience these in a manner similar to humans unless there is evidence to the contrary (see section 1.20 of the Code) (NHMRC, 2008).” The question about whether analgesics add an unacceptable variable to certain types of animal research is systematically being answered by scientists who run side-by-side studies to show if analgesics affect animal study data. ACLAM’s position statement on pain and distress in laboratory animals clarifies, “Pain is an undesirable variable in most research projects and, if not relieved, can lead to unacceptable levels of stress and distress in animals (ACLAM, 2008).” Each scientific scenario must be carefully analyzed as some animal models could be invalidated by analgesics that induce changes in pain receptors. Whereas analgesic use for laboratory rodents was rare in the late 1990s, it is a much more common practice today, but it’s not as widespread as it should be. A recent report indicates that, “although the use of analgesics has increased over the past ten years, the overall level of post-operative pain relief for laboratory rodents is still low (Richardson & Flecknell, 2005).” This is an animal welfare issue that needs more attention. IACUCs and animal welfare committees must not continue to accept the response, ‘we think that analgesics might affect our data’. The animal research community must take responsibility to ensure the most current knowledge about rodent pain control is used and studies must be performed to validate rodent analgesic use in research to promote animal welfare.

The creation of advanced technologies such as automatic blood sampling has led to less pain and distress in laboratory animals and thus more consistent data. Instead of restraining animals for each blood sample collection, the animals are surgically implanted with vascular catheters, provided analgesics and allowed time for recovery. Then the vascular catheter from the animal is attached to tubing which runs through a computer-run blood-sampling machine. Animals may move in their home cages and often sleep through the majority of the blood samples, thus avoiding the acute stress from restraint. Studies with rats have shown that automated blood sampling plus oral analgesics results in reduced corticosterone,

which is often elevated with acute pain or distress (Goldkuhl *et al.*, 2008). These refined methods may also reduce animal use because crossover pharmacokinetic studies can be conducted in rats that previously would have required separate sets of animals.

Replacement methods are also being embraced as they become available and are validated to provide data that was formerly produced in animal studies. There are a growing number of examples of alternatives such as the *in vitro* Limulus Amoebocyte Lysate (LAL) assay as an alternative for the rabbit pyrogen test (Ding & Ho, 2001). There are a growing number of high-throughput *in vitro* assays used to screen compounds for cardiovascular safety, such as the hERG assay. This assay replaces some, although not all, animal studies required by the Food and Drug Administration as part of an integrated cardiovascular risk assessment for new compounds (Porsolt *et al.*, 2005).

Each year, more animal research programs are going above and beyond the minimum standards to seek voluntary accreditation by AAALAC. In addition, companies that use contract laboratories for animal studies are routinely performing audits to ensure that these suppliers are adhering to animal care laws and guidelines. All of these measures have contributed to building a culture of animal welfare in animal research programs internationally.

4. Future

As the world becomes smaller and smaller through increased technology and travel, globalized standards for animal welfare will become more prevalent. One of the more significant indications of global concern about animal welfare was the 2005 addition of animal welfare guidelines to the international Animal Health Code (Kahn, 2007) by the World Organization for Animal Health (OIE). OIE is comprised of more than 170 member countries and its primary focus is to prevent the spread of epizootic animal diseases through increased transparency and collaboration among members. There are eight guiding principles for animal welfare outlined in the Animal Health Code with a majority of these principles being applicable to laboratory animal research programs worldwide. The OIE animal welfare principles include the internationally recognized 'five freedoms' and '3Rs' as well as the statement "that the use of animals carries with it an ethical responsibility to ensure their welfare to the greatest extent practicable (OIE, 2008)."

Advances in laboratory animal welfare will continue with increased resources and attention being devoted to this important issue. Alternatives that have been developed will continue to gain widespread acceptance by countries that are in close communication and collaboration to ensure harmonization of scientific and regulatory practices. For example, the European, U.S. and Japanese centers for the validation of alternative methods have worked together to accept alternative skin irritation/corrosion toxicity tests through rigorous review and scientific validation (ICCVAM, 2008). Future enhancements of high throughput screening will allow even greater screening of compounds without animals to select a few for further development in animal studies. Potentially, bioreactors, bacteria, insects and worms will play larger roles in early drug discovery work as we learn how to gain the most knowledge out of simple living systems and extrapolate them to data that is applicable to human and nonhuman mammals.

Additionally, non-animal surgical or technical training tools will become more common in veterinary, medical and undergraduate coursework. Highly complex, anatomically similar models of human and animal body parts are being created and used for various types of training ranging from endotracheal intubation to cardiovascular stent placement. Teachers should embrace these changes as long as they meet the needs of students but insist on retaining certain animal training practices if there is evidence to show that some training is optimized when performed with animals. One compromise is when animal shelters invite veterinary students to perform spay and neuter surgeries. Student surgical training is achieved while animal welfare is advanced.

Computers will play an increasing role as our advances in intelligent design allow us to build increasingly complex systems. To date, there is no computer that mimics the enormously complex and numerous cell-cell interactions and biochemical communications that exist within a living person or animal. However, there has been great progress in our understanding of molecular biology, genetics and in developing human subsystems for use in research. These advances provide powerful tools for research that avoids unnecessary use of animals. It cannot be emphasized enough that despite this progress

animal research will remain a vital part of an integrated research program to help further clarify the complex scientific and medical questions that remain to be answered (Williams, 2006). Thus, the research community must remain ever vigilant and committed to making science more humane and less dependent on animals, whose involvement in this noble endeavor is nonetheless not voluntary.

5. Concluding Remarks

Innovation in research methods will result in refined techniques that reduce animal use, reduce pain and distress and replace animal models. Humane science is the goal. Establishing clear lines of responsibility, humane endpoints, and a thorough plan for monitoring and intervention strategies helps to prevent, minimize and alleviate pain and distress in laboratory animals (NIH, 2008). There are still opportunities to improve but overall the international biomedical research community has made tremendous strides in adopting practices that promote a culture of animal welfare. Animal welfare is not only an ethical imperative but also important for good science and for the continued support of the public. Biomedical research continues to unravel many of life's mysteries and assist with the discovery and development of lifesaving healthcare products for both people and animals. The challenge remains for individuals and institutions involved with animal research to invest more into animal welfare research so that additional alternatives can be discovered and humane science will continuously advance.

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7. About the Author

Leticia (Letty) V. Medina, DVM, DACLAM - Letty obtained her Bachelor's of science degree from the University of Notre Dame. She earned her DVM from Texas A&M University and completed a postdoctoral fellowship in Laboratory Animal Medicine at the University of Illinois at Chicago. She is a Diplomate of the American College of Laboratory Animal Medicine (ACLAM). She is currently the Manager of Animal Welfare & Compliance, Abbott Laboratories, Abbott Park, IL, where she is responsible for helping to assure the welfare of laboratory animals used in the discovery and development of new pharmaceutical and diagnostic products. She serves as the Vice Chair for the IACUC and Chair of the Corporate Animal Welfare Committee. She provides leadership for the companies global animal welfare initiatives. Dr. Medina serves as an ad hoc consultant for the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC). She is also a Council member of the Institute for Laboratory Animal Research (ILAR). She has given numerous invited presentations and authored several book chapters, papers and abstracts on many facets of laboratory animal care. She is passionate about educating individuals about the importance of animal welfare in biomedical research and the benefits of biomedical research to both people and animals.