



Animal Welfare Information Center

Newsletter

Spring 1994
Vol. 5, No. 1
ISSN: 1050-561X

Special Issue:

FARM ANIMALS IN RESEARCH AND TEACHING



(Photo by Tim Allen)

Welfare Considerations for Farm Animals	p. 2
Recognition of Pain in Farm Animals	p. 5
Principles of Laboratory Animal Science Review	p. 7
Large Animal Anesthesia	p. 8
Post-Operative Care and Analgesia	p. 11
Future Development of USDA Standards	p. 14

Welfare Concerns for Farm Animals Used in Agricultural and Biomedical Research and Teaching

by

Janice C. Swanson, Ph.D.
Department of Animal Science and Industry
Kansas State University
Manhattan, KS

Introduction

Animal welfare issues are often thought to be easily dissipated by the production of scientific arguments and evidence. However, animal welfare is not only a scientific issue. Politics, philosophy and ethics, and aesthetics can influence societal expectations concerning the use, care, and treatment of animals (b). Because of the multiple influences that come to bear on the issue, it is nearly impossible to reach agreement on a precise definition of animal welfare (6,9). However, there seems to be a general consensus that there are two central themes, the state of the animal itself and broader sociological factors. An approach used within the scientific community is to use the term “*animal well-being*” when referring to the actual welfare status of the animal, and “*animal welfare*” when referring to broader sociological and ethical concerns (5). When encountering concerns regarding farm animal use in research and teaching, there is a need to address the broader sociological and ethical expectations as well as the scientific.

Agricultural Research and Teaching

Farm animals used for agricultural research require strict attention to their care, husbandry, and maintenance of protocol requirements under a variety of conditions (a). The research environment may vary from fairly extensive (e.g., grazing study) to very intensive (e.g., metabolism trial). It is expected that the research animals will not be subjected to unnecessary pain or distress and will be observed for the development of signs of distress. Social (e.g., isolation) or physiological (e.g., sensory) deprivation tends to raise concerns and questions about the necessity of the procedure and potential benefits of the research. Agriculture is typically perceived as an applied science and when research protocols require greater manipulation (e.g., invasive procedures) questions arise concerning the potential application of results and the skill of the researcher(s) involved. For example, field or standing surgery often poses questions regarding potential harm to the animal due to lack of aseptic conditions or adequate pain control. Other surgical procedures such as fistulation, laparotomies, cannulation, etc., are sometimes performed by persons other than veterinary surgeons (e.g., trained Ph.D. or graduate students), which present issues concerning proper training and oversight (14). Pre- and post-operative care, pain recognition, and management are critical to animal well-being. Handling, equipment use and condition, and methods that are current with good practice are important from both a research and welfare perspective (7). Concerns often arise when observation notes deficiencies in any of the areas mentioned above and effects on animals are perceived.

Teaching in agricultural schools and colleges also presents concerns for the animals and the safety of the students. A wide variety of teaching activities occur from basic

“hands-on” experience such as leading animals to fairly technical physiological laboratories. Handling animals that are relatively large requires that instructors are knowledgeable about the species with which they are working and safety precautions that need to be considered to protect students and animals. Concerns arise regarding the instructor’s competency in animal behavior, husbandry, handling methods, and technical skills. Also of concern are suitability of teaching facilities, holding quarters, transportation to and from instructional sites (if required), equipment, student manipulation, provision of space and essentials such as food and water (if held for long periods). Demonstrations of invasive procedures in upper level techniques courses require instructors to be sensitive to animal needs and student concerns. Euthanization techniques should be in accordance with the American Veterinary Medical Association’s recommendations for approved methods of euthanasia (15). Instructors should be familiar with state-of-the-art methodology and have demonstrated skill in performing the technique before being allowed to teach students.

Finally, dedication to exercising the 3 R’s (reduction, refinement, and replacement) when working with potentially painful procedures can serve as appropriate guidance for agricultural teaching and research. All teaching and research protocols should be submitted and reviewed by the Institutional Animal Care and Use Committee (IACUC).

Biomedical Research and Teaching

Farm animals have made valuable contributions as models in biomedical research (4,a). Organ transplants, pharmacokinetics, vaccine efficacy, etc., are just a few examples of how farm animals have been used. Special concerns arise when animals who are not customarily bred and raised in laboratory settings are used for experimental manipulations under such conditions. Flooring, housing, isolation, handling, and specialized equipment are all concerns. Experimental manipulations may require extensive contact with the animal for long periods of time, therefore, standard field equipment, traditionally used in agricultural practice for short-term restraint purposes, is not practical in many laboratory settings (11). Frequent handling of the animal and familiarization with equipment and routines may be necessary to alleviate distress in laboratory settings. Surgical facilities (especially for large species such as cattle and horses), proper use of analgesia and anesthetics, and pre- and post-surgical care are of utmost concern.

Like agricultural teaching, similar concerns can be echoed regarding the use of farm animals in biomedical teaching. Appropriateness and goals of the exercise, skills of the instructor, techniques used, facilities, etc., should be considered. However, in biomedical teaching it is more likely that the animal will be subject to greater manipulations and invasiveness. The 3 R’s are expected to be considered in teach-

ing protocols that are potentially painful. Consideration should be given to reducing the number of animals used, looking for alternative teaching technologies, and using the most appropriate techniques and equipment for the intended purpose.

Compliance standards under the AWA and/or Public Health Service (PHS) policy must be met for farm animals used in biomedical activities. All protocols must be reviewed by the IACUC.

Assessing Farm Animal Well-Being

Assessing the well-being of farm animals requires that adequate measures have been identified and agreed upon, and are quantifiable (b,c). In agricultural settings, farm animal well-being has traditionally been assessed by productivity (e.g., growth, weight gain, feed intake, etc.), various health parameters (e.g., disease incidence), a limited number of physiological measures (e.g., cortisol), and animal behavior (e.g., stereotypies, vacuum behaviors). The science of animal welfare is still in its infancy, and current investigations are revealing the complexities of well-being assessment (9). Researchers, although diverse in their proposals of best measures, are in general agreement that a multi-disciplinary approach is needed to assess and define animal welfare in order to understand, alleviate, and prevent suffering (13). The concept of animal suffering is controversial (2). Duncan (3) suggests that welfare is determined primarily by how an animal "feels." To suffer, animals must 1) be sentient, and 2) have the ability to be aware of their suffering. Research into cognition, perception, motivation, and the emotional states of animals can provide insight into welfare problems. Others, however, suggest that feelings are too subjective to provide reliable information and that more objective measures based on biological functioning, such as a pre-pathological state (8,10), would be more accurate.

While welfare assessment is very much in debate, reasonable observations can be made to help assess welfare in research and teaching settings. It is reasonable to assume that animal well-being is of a physiological and psychological nature, and that both need to be monitored to the best of our abilities. Aside from the considerations previously stated, careful observations of the animals and of human-animal interactions can provide helpful feedback. Depression, anorexia, injury, aggressiveness, self-mutilation, sickness, and fear responses can be indications that the animal's psychological and/or physiological well-being is impaired. Thorough knowledge of protocols will assist in determining whether such manifestations are expected (e.g., disease research) and addressed, or unexpected and in need of attention, or worse, symptomatic of neglect and poor research conduct. Animal caretakers, instructors, and researchers all need to develop a keen eye for their animals and address problems in a timely manner.



(Photo by Tim Allen)

Public Accountability

During the last 20 years, public concern about the use of animals for experimental and educational purposes has focused on the biomedical community. Federal legislation such as the Animal Welfare Act (AWA) provided impetus behind institutional accountability for the care and use of common laboratory species.

Agricultural animals used in biomedical research are covered by the AWA at this time, but with no specific standards for their care and use. If used experimentally for the purpose of improving food or fiber production, they are exempted from the AWA regulation.

The Public Health Service (PHS) policy sets standards of care for all warm-blooded vertebrates used in PHS-supported work. General standards of care for common species of livestock are outlined in the *National Institutes of Health (NIH) Guide for the Care and Use of Laboratory Animals*. Although appropriate for the care of livestock under the experimental settings of biomedicine, the *NIH Guide* falls short of addressing the unique attributes of agricultural production research (1).

Although general concerns about the well-being of farm animals used in either biomedicine or agriculture can be thought to parallel one another, differences do exist in the goals of agricultural and biomedical research and teaching that require guidelines and standards to maximize welfare to differ (12). Agricultural research must have the ability to use its current industry practices as a control in order to address problems in either a basic or applied sense. The ultimate goal is the production of a food product and practices that can be applied in the field. Although application of the 3 R's has been advocated in agricultural teaching and research, there are limits. Replacement of animals is often not an option

and may have limited use in teaching or research protocols. For example, when attempting to answer specific questions concerning specie productivity, no other model will be acceptable.

In biomedical research, farm animals are generally used as models for human systems or conditions, and the production or testing of products (pharmaceutical, etc.). There tends to be greater experimental manipulation of the animal in biomedical procedures, and housing and handling requirements are generally more intensive with rigid standards for laboratory upkeep. The experimental criteria for the use of these animals will vary.

In the mid-1980's a consortium of animal scientists, members of the government and veterinary community, etc., cooperated to develop the *Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching*. The *Ag Guide*, as it is presently referred to, is meant to provide institutional accountability, responsibility, and com-

pliance guidelines for farm animals used in agricultural teaching and research. Prior to the publication of the *Ag Guide*, there was no vehicle by which welfare concerns could be formally addressed, nor uniform guidelines that agricultural institutions could refer to. Presently the *Ag Guide* has been adopted by a majority of agricultural institutions for setting policy on institutional animal care and use (Mench, personal communication), and the American Association for Accreditation of Laboratory Animal Care has adopted the *Ag Guide* (specie care and husbandry sections) for accreditation of farm animal research facilities.

Maintaining the welfare of similar animals for different purposes in contrasting environments poses a problem with consistent application of guidelines for their care and use. Hence, the potential utilization of three documents (AWA, *NIH Guide*, and *Ag Guide*) to ensure their welfare. IACUC's should be well acquainted with all three documents to know under which conditions each of these documents should be applied.

Conclusion

In closing, I wish to reflect on the idea that no issues would exist if it were not for human concern and commitment to animal welfare. Laws, standards, and guidelines are ways in which the research and teaching community can be held accountable to the public for their actions. Animal protection groups frequently seek to strengthen and provide increased oversight of research activities in an attempt to represent the interests of the animal being used. Whereas, the biomedical and agricultural community seek to reach a compromise between human and animal interests that will provide societal benefits yet fulfill expectations regarding animal care and use. I venture to say that most issues concerning the care and use of animals in research and teaching are propelled by the dynamic exchanges between protectors and users of animals, each of which has made contributions to enhancing farm animal welfare.

Endnote

Listed below are cited literature and selected references of the recent articles and proceedings that address farm animal welfare issues. All have been used extensively for the production of this paper.

Literature Cited

1. Curtis, S.E. (1992). "Agricultural animal guidelines." *Proceedings from a SCAW-sponsored conference, Agricultural Animals in Research, held September 6-7, 1990, Washington, DC.* Scientist Center for Animal Welfare, Bethesda, MD, pp 11-12.

2. Dawkins, M. S. (1980). *Animal Suffering*. Chapman Hall, London, pp. 10-26.

3. Duncan, I. J. H. (1993). "Welfare is to do with what animals feel." *Journal of Agricultural and Environmental Ethics*, 6 (Special Suppl. 2):8.

4. Ediger, R.D. (1992). "The use of farm animals in biomedical research." *Proceedings from a SCAW-sponsored conference, Agricultural Animals in Research, held September 6-7, 1990, Washington, DC.* Scientist Center for Animal Welfare, Bethesda, MD, pp. 51-53.

5. Fraser, D. (1993). "Assessing animal well-being: Common sense, uncommon science." *Food Animal Well-Being*

1993 - Conference Proc. and Deliberations, April 13-15 1993, Indianapolis, IN. Purdue University, Office of Agricultural Research Programs, West Lafayette, IN, pp. 37-54.

6. Gonyou, H. W. (1993). "Animal welfare: Definitions and assessments." *Journal of Agricultural and Environmental Ethics*, 6(Special Suppl. 2):37.

7. Grandin, T. (1992). "Handling and transport of agricultural animals used in research." *Proceedings from a SCAW-sponsored conference, Agricultural Animals in Research, held September 6-7, 1990, Washington, DC.* Scientist Center for Animal Welfare, Bethesda, MD, pp. 74-84.

8. McGlone, J. (1993). "What is animal welfare?" *Journal of Agricultural and Environmental Ethics*, 6(Special Suppl. 2):26.

9. Mench, J. A. (1993). "Assessing animal welfare: An overview." *Journal of Agricultural and Environmental Ethics*, 6(Special Suppl. 2):68.

10. Moberg, G. P. (1993). "Using risk assessment to define domestic animal welfare." *Journal of Agricultural and Environmental Ethics*, 6(Special Suppl. 2):1.

11. Panepinto, L.M. (1992). "The minimum-stress physical restraint of swine and sheep in the laboratory." *Proceedings from a SCAW-sponsored conference, Agricultural Animals in Research, held September 6-7, 1990, Washington, DC.* Scientist Center for Animal Welfare, Bethesda, MD, pp. 85-87.

12. Stricklin, W.R., D. Purcell and J.A. Mench. (1992). "Farm animals in agricultural and biomedical research." *Proceedings from a SCAW-sponsored conference, Agricultural Animals in Research, held September 6-7, 1990, Washington, DC.* Scientist Center for Animal Welfare, Bethesda, MD, pp. 1-4.

13. Swanson, J.C. (1994). "Farm animal well-being and intensive production systems." *Journal of Animal Science* (in press).

14. Swindle, M.M. and A.C. Smith. (1992). "Regulatory issues in experimental surgery in farm animals." *Proceedings from a SCAW-sponsored conference, Agricultural Animals in Research, held September 6-7, 1990, Washington, DC.* Scientist Center for Animal Welfare, Bethesda, MD, pp. 54-57.

15. "1993 Report of the AVMA Panel on Euthanasia." (1993) *Journal of the American Veterinary Medical Association*, 202(2):229-249.

Selected References

a. Mench, J.A., S. Mayer, and L. Krulisch, (Eds.). (1992). *Well-being of Agricultural Animals in Biomedical and Agricultural Research*, Scientist Center for Animal Welfare, Bethesda, MD.

b. Mench, J.A. and Stricklin, W.R. (eds.), 1993. "An International Conference on Farm Animal Welfare: Ethical, Technological and Sociopolitical Perspectives" and "Scientific Perspectives." *Journal of Agricultural and Environmental Ethics*, volume 6 supplements 1 and 2, 153pp. and 116pp.

c. *Food Animal Well-Being 1993 - Conference Proceedings and Deliberations, April 13-15, 1993, Indianapolis, IN.* Purdue University, Office of Agricultural Research Programs, West Lafayette, IN.



Recognition of Pain in Farm Animals

by

James E. Breazile, M.A., D.V.M., Ph.D.

*Professor of Veterinary Physiology and Director of Laboratory Animal Resources
Oklahoma State University, Stillwater, OK 74078*

The study of pain in laboratory animals through the past 40 years has presented us with a progressive development in our understanding of the means by which noxious stimuli elicit neural activity, and the neural pathways through which this activity reaches and terminates within the brain. At the same time, we have experienced a growth in our intellectual and philosophical consideration of pain in animals and have become more concerned about the role of pain in production of stress and discomfort in all laboratory animals (6).

The inclusion of farm animals into these considerations has been a fairly recent but not unforeseen development. The explanation for delay in the inclusion of farm animals fully into the arena of research, teaching, and testing animals likely resides in the desire to isolate these practices from production practices. There are many common practices in production of animal meat and fiber that would not be considered acceptable under the current guidelines for care and use of laboratory animals. It is necessary, however, that these practices be considered on their own merit in an attempt to apply current Federal guidelines to the use of farm animals in research, teaching and testing.

It is my philosophy (and one that I think should be emphasized within our Institutional Animal Care and Use Committee (IACUC) membership) that there is a basic level of humaneness that must be applied to all species used in research, teaching and testing. I feel that this level also applies to production practices. Beyond this level, other considerations of pain perception and humane treatment are determined by the protocol applied to the animal. In the following discussion, I wish to raise some consideration of factors influencing the nature of pain sensations in animals in general, and particularly in farm animals. I hope that these considerations may be helpful in establishing the characteristics of that basic level of humaneness as it is applied to a specific research, teaching or testing protocol.

Pain has been recognized through the centuries as a word that describes a wide range of unpleasant experiences in humans (8). It has continually been recognized that it is difficult for humans to share what they have felt as a pain sensation, and to describe this experience to their own satisfaction. Realizing that the concept of pain perception is derived entirely from our human experience, and that we by necessity have extrapolated this concept to animals, leaves one with little wonder that there are difficulties in interpreting sensory and meaning phenomena within this extrapolation.

There was a time, not so long ago, when pain scientists were relatively comfortable with their understanding of the anatomic, physiologic, and behavioral aspects of pain perception in animals (3). Specific "pain pathways" had been identified within the spinal cord and brain that underlie pain perception and the behavior it elicits. These were taught to veterinary medical students, to be memorized as the anatomic basis for pain perception in animals. Elaborate behavioral studies were conducted to confirm that these pathways did indeed serve as the anatomic substratum for pain perception (3). It was generally considered that wherever pain was to be evoked in an animal, anesthesia and/or analgesics would be applied. These were the days before there was a great deal of attention given to the need for extensive considerations of pain induction by the methods applied in the use of animals in research, teaching and testing.

It was clearly recognized that there were anatomic substratum differences between non-primate laboratory animals and humans. These anatomic substratum differences appeared to represent degrees of neurologic differentiation. They were interpreted to represent differences in the specificity of central nervous system structures in the processing of neural information concerned with pain perception (4). There could not, however, be allowed the consideration that there might be a difference between the actual sensation experienced in humans

and animals. The difficulty that these anatomic differences produced was that the only pain perception that we, as investigators, or oversight persons of IACUC responsibility, have ever experienced is our own pain. If we did not perceive pain, if this pain was not unpleasant to us, and if this pain did not induce suffering and distress in us, we would not be considering whether or not it occurs in laboratory animals.

It is necessary to assume that animals perceive pain with all its variations in intensity, sharpness, dullness, localization, or diffuseness, exactly as it is perceived by human beings. If this premise does not hold, then it is impossible to study pain in animals, because there would be no standard against which it could be measured. It was, and still must be accepted, therefore, that if a given stimulus evoked a pain sensation, emotional and escape reaction in a human, and if the application of that stimulus will evoke a similar emotional or escape reaction in an animal, that stimulus produces pain perception in the animal. It must be emphasized that it must be considered that pain perception does not differ from that perceived by a human being in the same situation.

If, however, we are to use the human as the standard, it is necessary that we clearly characterize the standard before it is applied. There are some characteristics of pain perception that are well known through everyday experience in humans that are basic to our ability to determine, quantify, and characterize pain perception in animals. I do not think that we can abandon the anthropomorphic basis of evaluating pain in animals. This is the only basis we have. I do feel, however, that it is necessary that we apply this basis from a realistic point of view. The emphasis that I would like to make is that there are some differences in our lives from those of farm animals that do make a difference in the significance of pain perception.

The difference that I would like to emphasize is our anticipation of pain and the impact of this anticipation on our perception. We learn, through per-

sonal experience, or the experience of others, to anticipate pain in certain circumstances. Although animals may learn through experience, they are not generally preconditioned, to the degree experienced by humans, by the experience of others. Whether or not pain perception would normally be elicited by a given circumstance, if we think we will perceive pain, then when the stimulus is applied, we *will* perceive pain. Some of you may have been in the old U. S. Marine Corps (before the 60's), or may have joined a fraternity in college in which hazing was common. The experience with the blow torch, hot iron, and application of ice that you were certain burned a hole in your skin typifies this conditioning. This preconditioning often makes it difficult to evaluate pain perception in humans. A stimulus that is apparently innocuous in one human subject may induce an excruciating painful experience in another.

A good example to illustrate the effect of preconditioning and the difference it makes in suffering or distress is the comparison of a human who has undergone laparotomy, and intra-abdominal surgery, to a laboratory animal (rat, dog, cat, or farm animal) undergoing that same surgery. The human, through anticipation, anguish, and concern for the pain to come, often suffers the pain even before the act of surgery occurs. I have never experienced an animal, except in cases where multiple serial surgeries are performed, that demonstrated any degree of anticipation to surgery. After the surgery, the typical animal is on its feet, eating, running, grazing, whatever is natural for it to do. The human, on the other hand, is slow to recover, complains of much pain, and takes days to weeks to recover. This difference, not only in pain, but also the distress produced by it, is an important consideration in the evaluation of pain perception in farm animals from a strictly anthropomorphic point of view. It is clear that in these circumstances, we depart from the strict anthropomorphic interpretation of pain and distress in animals, but let the animals "speak" for themselves through their behavior.

The sensations that are described as pain in humans, and assumed in animals (due to their anthropomorphic responses to situations in which these sensations are generated), represent a wide spectrum. We can quickly recognize that there are differences in the

sensation produced by a pin prick or a burn, and one produced by neuralgia. These not only represent differences in type of sensation evoked, but also represent different stimulus modes through which the sensation is induced.

At one end of the pain sensation spectrum are the well-known protective sensations. These are usually evoked by "applied stimuli" such as burns, needle sticks, electric shock or other stimuli that are noxious to cells and tissues. In farm animals used in research, teaching, and testing, this "induced pain" represents the majority of sensations referred to as pain. Induced pain initiates alarm, withdrawal, escape, or attack responses that are often accompanied by vocalization in farm animals. In humans experiencing induced pain, there is a good correlation between the afferent neural activity induced in peripheral nerve axons and the intensity of subjectively perceived pain (8). The intensity of induced pain in farm animals, that is acceptable in a research, teaching, or testing protocol, is difficult for investigators and IACUC members to discern. The presence of pain-associated reflexes, along with voluntary or "willed" behavior, usually serves as the basis for judging whether or not a pain perception takes place. It is generally accepted that there is a level of pain perception that is acceptable. This allows the consideration that in trained hands, needle punctures for the normal clinical collection of blood produce an acceptable level of pain or discomfort. For each protocol, that goes beyond this level, the investigator and members of IACUC must use their judgement concerning the intensity of pain induced.

At the other end of the spectrum are non-protective pain sensation syndromes produced by organic or patho-physiological mechanisms. This type of pain sensation is generally the consequence of naturally occurring, or experimentally induced peripheral or central neuropathies (1). It can reasonably be referred to, therefore, as "neuropathic" pain. It is the sort of pain that is experienced in neuralgia, so familiar to humans (11). Such neuralgias may be induced in animals by disease processes, or by experimental processes (7). Polyneuropathies, diabetes, toxin or viral induced, can result in the production of intense pain perception in humans, and must be considered to do so in farm animals as well. It is necessary that investigators

and IACUC members be cognizant of this type of pain induction, and its significance in producing distress that may interfere with the well-being of the animal and the outcome of the research (5). A portion of the campus educational program provided to animal research personnel should include discussion of the possibility of neuropathic pain induced by specific types of experimental protocols.

Between the two extremes of "induced" pain and "neuropathic" pain is pain that is associated with inflammation. This "inflammatory" pain is distinctly different from the two extremes, in that it is induced by mechanisms of tissue response to injury, rather than an external stimulus that would be regularly considered to induce pain perception (9, 10). The pain associated with inflammation usually requires some additional stimulus for initiation, but this stimulus need not be noxious (which implies damage, or potential damage to tissues). Even the slightest movement or lightest tactile stimulation may initiate pain perception in the presence of inflammation.

Recognition and prevention of pain-induced distress in farm animals, as in other species, is aided by a knowledge of the neuro-physiological mechanisms underlying pain sensation. This knowledge is particularly necessary to those directly responsible for use of animals in research, teaching, or testing, so that they may discern whether or not, toxins, microbiological agents or drugs used in their protocols may mask or prevent a response to pain. These animals may demonstrate a number of distress responses that are not clearly discerned as due to pain induction.

Although it is necessary that the judgement of the distress-producing capability of pain sensation be anthropomorphically based, those who use farm animals as laboratory animals and IACUC members must also be aware of protocols that are likely to induce pain in circumstances in which it would not ordinarily be expected in humans. It is equally as important that those judging research protocols on the basis of animal responses be aware of normal animal behavior. In most farm animals, unsocialized with humans, even the slightest stimulus, whether it be noxious or not, may induce vocalization, alarm, withdrawal, escape, or attack responses that could easily be ascertained as induced by pain or discom-

fort. Recognition of pain perception in farm animals, as in other species, requires a thorough knowledge of the normal behavior of that species. Chronic pain perception or chronic distress from any cause generally results in decreased appetite, motility, milk, egg or meat production in farm animals.

There is no list of signs that infallibly indicate that pain is being perceived in any given farm species. There are some characteristics of individual animals within a farm species, or often within a species as a whole, that are helpful in making this determination and of estimating the degree of discomfort that is present. If there is any doubt, however, concerning whether or not an animal is experiencing undue or unacceptable levels of pain, one should consult a veterinarian or animal husbandryman who is familiar with the species in question. Usually animal care personnel are the first to know when an animal is distressed by disease or a pain-inducing process. They should be an integral part of this evaluation.

The author may be contacted by phone at 405-744-8089, or by FAX at 405-744-6743.

References

1. Bennett, G. J. (1990). "Experimental models of painful peripheral neuropathies." *News in Physiol. Sci.* 5:128-133.

2. Breazile, James E. and Kitchell, R. L. (1968). "A study of fiber systems within the spinal cord of the domestic pig that subserve pain responses." *J. Comp. Neurol.* 133:373-382.

3. Breazile, James E. and Kitchell, R. L., (1969). "Pain perception in animals." *Fed. Proc.* 28:1379-1382.

4. Breazile, James E., (1971). *Textbook of Veterinary Physiology*, Lea and Febiger, Philadelphia

5. Breazile, James E., (1987). "Physiologic basis and consequences of distress in animals." *J.A.V.M.A.* 191: 1212-1215.

6. Breazile, James E., (1988). "The physiology of stress and its relationship to mechanisms of disease and therapeutics," in Howard, J. L.

(ed.), *Stress and Disease in Cattle, The Veterinary Clinics of North America, Food Animal Practice* 4 (3): 441-480.

7. Campbell, J. N., Raja, S. N., Meyer, R. A. and Mackinnon, S. E., (1988). "Myelinated afferents signal the hyperalgesia associated with nerve injury." *Pain* 32:89-94.

8. Cervero, F. and Laird, J. M. A., (1991). "One pain of many pains? A new look at pain mechanisms." *News in Physiol. Sci.* 6:268-273.

9. Hylden, J. L., Nahin, R. L., Traub, R. J. and Dubner, R., (1989). "Expansion of receptive fields of spinal lamina I projection neurons in rats with unilateral adjuvant-induced inflammation: the contribution of dorsal horn mechanisms." *Pain* 37:229-243.

10. Meyer, R. A., Campbell, J.N. and Raja, S. N., (1985). "Peripheral neural mechanisms of cutaneous hyperalgesia." *Advances in Pain Research and Therapy* 9:53-71.

11. Sato, J. and Perl, E. R., (1991). "Adrenergic excitation of cutaneous pain receptors induced by peripheral nerve injury." *Science*, Wash. D. C. 251:1608-1610.



BOOK REVIEW



PRINCIPLES OF LABORATORY ANIMAL SCIENCE:

A Contribution to the Humane Use and Care of Animals and to the Quality of Experimental Results

edited by
L.F.M. VanZutphen, V. Baumans & A.C. Beynen
Published by
Elsevier Science Publishers
May 1993

Reviewed by Robert Hall, DVM, Asst. Dir. for Assurance, National Institutes of Health, Bethesda, MD
[Ed. Note: Robert Hall passed away on March 30, 1994]

Developed countries around the world require that their veterinarians, technicians, and other animal care providers be adequately educated or trained to provide the husbandry and care of animals used in research. Likewise, scientists who design and use animals in their research are also being required to be educated and trained in laboratory animal science. *Principles of Laboratory Animal Science* was written as a text and basis for a graduate course for this latter group of scientists.

It is hard to conceive of a single book of less than 400 pages that covers: animal legislation; animal models; biology, husbandry, and diseases of commonly used animals; experimental design and management; factors such as stress, nutrition, microbiological contamination and genetics which impact research results; and recognition of animal pain. Yet this book succinctly does just that. A solid background in each of these fields may be necessary to fully appreciate how carefully each chapter is presented with regard to improving the researchers approach. For instance, the chapter on "Design of Animal Experiments" discusses the subject of selecting the correct number of animals to use to provide valid results. With an understanding of basic principles of biostatistics, the reader realizes that the appropriate number of animals to use can be calculated once the correct experimental design has been selected.

Occasional reference to the *Directive for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes* adopted by the Council of European Communities is the only hint that this book is targeted for European scientists. Certain standards, such as the required floor space for housing each species, are applicable only to that community. Otherwise, the information and recommendations in this book are universally applicable.

LARGE ANIMAL ANESTHESIA

by

Richard V. Shawley, DVM, MS, DACVA

*Department of Medicine & Surgery, College of Veterinary Medicine
Oklahoma State University, Stillwater, Oklahoma 74078*

This discussion reviews some of the common anesthesia problems when dealing with the large animal species used in research. This includes cattle, sheep, goats, and swine.

Neonatal Anesthesia

Frequently, research projects require general anesthesia for neonates of farm animal species. The neonate has several significant physiological differences from the adult animal that affect anesthesia. These differences include:

- The blood brain barrier is poorly developed because the junctions between endothelial cells and the choroid plexus are wider than in the older animal. As a result, induction of anesthesia may be quicker and requires less drug in the neonate than in the adult animal(1).
- X ● Hypothermia. Neonates have a greater body surface:body weight ratio (2). As a result, they lose heat more rapidly than adult animals. With hypothermia, drug metabolism is retarded and the neonate may be slow to recover, especially from injectable anesthetics that depend primarily on metabolism for complete recovery.
- Hypoproteinemia. Plasma protein levels, particularly albumin levels, are lower in the neonate than in the adult. This means that neonates are more likely to develop pulmonary edema from intravenous fluid therapy (3). Also many anesthetic drugs are protein bound. Therefore, smaller doses of anesthetics may be required in neonates (particularly barbiturates) than in adults. It is the non-bound anesthetic that crosses the blood brain barrier (4).
- Low body fat content. Fat represents a storage depot for anesthetic drugs. In the case of neonates, the lack of body fat means that redistribution of anesthetic drugs will be delayed and recovery will be slow due to prolonged plasma levels (5).
- Hepatic function and hypoglycemia. In general, the clearance of drugs by the liver is less than in the adult. Microsomal enzyme development is incomplete, resulting in the delayed clearance of drugs (6). Neonates also have poor glycogen stores; consequently, hypoglycemia can readily occur in the stressed neonate (2).

Anesthetic Techniques For Neonates

Because of the various alterations of normal drug metabolism listed above, it is often preferable to use anesthetic drugs that are minimally metabolized, namely, the inhalant anesthetics.

Because neonatal animals are more readily restrained and induction is quicker than in the adult, mask induction is easily accomplished. A mask is loosely applied to the nose and mouth and oxygen only is first administered. This reduces anxiety about the mask and also increases the arterial oxygen of the patient. After at least one minute of oxygen only by mask, the anesthetic gas is delivered. Some anesthesiologists prefer low concentration of anesthetics at first while others recommend high concentrations immediately.

Nitrous oxide can also be used to speed the induction time. If the patient is struggling severely, the quicker one can induce anesthesia the better. After the patient is anesthetized via the mask, the animal should be intubated and the endotracheal tube cuff inflated.

Another method of inducing anesthesia is nasotracheal intubation. This method works well in foals (7) and calves (8). In this, endotracheal intubation is performed with the animal awake, utilizing the nasal route. The neonate tolerates the tube in the nose and trachea amazingly well. The tube, with cuff inflated, can then be attached to the anesthetic machine and anesthetic delivered as described in the previous paragraph. The tube can be left in the nasal passage or the animal can be reintubated orally.

In summary, the neonate can readily be anesthetically managed with gas anesthesia only. Because neonates can be easily restrained and little metabolism of inhalant anesthetics occurs, the inhalants are an excellent choice for neonates. The recovery from inhalants is smooth and rapid which means the neonate can be returned to its normal environment shortly after the anesthetic procedure.

Ruminant Anesthesia Problems

Regurgitation

Ruminants are prone to regurgitate and aspirate the rumen contents with anesthesia. Regurgitation is a result of several factors. Anesthetics relax the pharyngeal-esophageal sphincter and the reticulo-esophageal sphincter. Anesthetics also depress the swallowing reflex, thereby reducing the animal's ability to protect its airway from any regurgitated material. When the ruminant becomes recumbent, pressure is applied to the rumen. This increase in rumen pressure with sphincter relaxation results in regurgitation.

To reduce the incidence of regurgitation and aspiration, fasting prior to elective anesthetic procedures is indicated. The guidelines for fasting prior to anesthesia are as follows:

- Adult cattle: withhold food for 24-36 hours and water for 12-24 hours prior to anesthesia
- Small ruminants: withhold food for 12-24 hours and water for 0-12 hours prior to anesthesia
- Ruminants less than 1 month of age are not fasted prior to anesthesia.

In addition to fasting, intubation is highly recommended. Use of a properly inflated, cuffed endotracheal tube will protect the lower airways from regurgitation.

Bloat

Anesthesia eliminates the ability of the animal to eructate. Also during anesthesia, rumen motility is reduced. These two factors lead to gas formation that, if excessive, will result in pressure on the diaphragm and a decrease in lung volume. Ventilation perfusion (V/Q) mismatching occurs during anesthesia in large animals because of gravity and blood flow changes due to decreased cardiac output (9). V/Q

mismatching is accentuated by bloat and results in a further decrease in oxygenation. Proper fasting as discussed above will diminish the incidence and severity of bloat during anesthesia.

Injury

Induction and recovery injuries such as fractures can occur even with the best of facilities but they should never occur because of poor facilities. Adequate restraint and trained personnel are essential for successful inductions of general anesthesia of large animals.

Nerve paralysis is usually due to prolonged anesthesia, with inadequate padding or positioning. Post-operative myositis may also be due to prolonged down time with inadequate padding (10). However, myositis can be due to poor perfusion of muscle during anesthesia. This can be attributed to failure to maintain adequate cardiac output and sufficient blood pressure for adequate muscle perfusion.

Preanesthetic Sedatives

Xylazine

Xylazine, an alpha₂ adrenergic agonist, can be used as a sedative in low dosage. Ruminants are very sensitive to xylazine. The dose in ruminants is approximately one-tenth that used in the horse. However, xylazine is not approved for food-producing animals.

The following dosage guidelines are for healthy adult animals not receiving any other preanesthetic drugs.

<u>Xylazine Doses:</u>	<u>Cattle</u>	<u>Sheep & Goats</u>
Sedation	0.02 mg/Kg IV, 0.05 mg/Kg IM	0.1-0.2 mg/Kg IM
Recumbency, heavy sedation	0.11 mg/Kg IV, 0.22 mg/Kg IM	0.22-0.66 mg/KgIM

Detomidine

Detomidine is an alpha₂ adrenergic agonist that has similar characteristics to xylazine. It is, however, much more potent. It is approved for use in the horse but not in food-producing animals. The suggested dosage for cattle is 20-80 ug/Kg IM (11).

Side Effects of Alpha₂ Adrenergic Agonists

The most common life-threatening side effect of alpha₂ adrenergic agonists in ruminants is bloat. Rarely is this a significant problem if the animal has been properly fasted. Treatment, in addition to sternal positioning and stomach tube passage, could include the use of an alpha₂ adrenergic antagonist.

Excessive salivation frequently occurs following the use of alpha₂ adrenergic agonists. The use of atropine is not very effective and of very short duration. Treatment of excessive salivation consists of preventing its tracheal aspiration by keeping the nose and mouth of the animal lower than the pharynx.

Bradycardia occurs with alpha₂ adrenergic agonists. Treatment with atropine is rarely necessary but will correct the bradycardia. For cattle exhibiting bradycardia due to alpha₂ agonists, the initial intravenous dose of atropine is approximately 0.02 mg/Kg. If no response is seen the dose should be repeated.

Alpha₂ Adrenergic Antagonists

These drugs are used to reverse the effects of alpha₂ adrenergic agonists. Reversal is usually rapid and complete,

however, results in ruminants with yohimbine have been variable (13) while tolazoline and yohimbine have produced variable results in horses (14). Idazoxan and atipamezole are very specific alpha₂ adrenergic antagonists but are not readily available at present.

Anesthetic Combinations For Sheep, Goats, And Cattle

The following methods of producing anesthesia are for procedures usually less than 45 minutes or for induction/intubation of gas anesthesia. Since most anesthetics are not approved for use in food-producing animals, these recommendations are for animals not entering the food chain.

Sheep And Goats

Xylazine/Ketamine

In this combination the two drugs are given according to the dose listed:

Xylazine 0.22 mg/Kg IM
Ketamine 11 mg/Kg IM

The amount of gas anesthesia during the first 15-20 minutes of the procedure would be minimal. As the xylazine: ketamine combination is eliminated, gas concentrations will need to be increased.

Cattle

Thiopental/Gurafenesin

This combination is a very reliable method of producing general anesthesia with good muscle relaxation. Guiafenesin is a central-acting muscle relaxant that can be purchased in powder form or solution. The barbiturate, thiopental, is added to the guiafenesin solution.

The dosage for healthy cattle is as follows:

Thiopental 6.6 mg/Kg IV (5 Gm max dose)
Guaifenesin 100 mg/Kg IV (50 Gm max dose)

Guiafenesin is usually prepared in a 5 or 10 percent solution with sterile water, saline or 5% dextrose. If the 5 percent solution is used, a large bore catheter (10-12 ga.) is required for rapid administration to provide a smooth induction of adult cattle.

Anesthetic Methods for Swine

Adult swine can be very difficult anesthetic patients. Both intravenous and intramuscular routes have been used for anesthetic procedures of short duration or for induction of gas anesthesia.

Intravenous thiopental or thamylyl at a dose of 9-11 mg/Kg is used for procedures of 5 to 10 minutes duration and for tracheal intubation. A combination of xylazine/Telazol® (telamine-zolazepam) can be used via the intramuscular route. The dosage is xylazine (1.1 mg/Kg) and Telazol (3 mg/Kg) given intramuscularly.

Inhalation Anesthesia

As research surgical procedures have become more sophisticated, the need for quality anesthesia of long duration has developed and the use of inhalation anesthesia has increased.

Some of the reasons why gas anesthesia is superior to injectable techniques without respiratory support include the following:

- Provides a patent airway. Gas anesthesia usually utilizes an endotracheal tube. This ensures an open airway and saves valuable time in an emergency when respiratory control is required.
- Improves oxygenation. Because oxygen is used as the carrier gas for inhalant anesthetics, arterial oxygen tension is much higher than in animals breathing air. This is of particular importance to large animals because of low oxygen tension during anesthesia.
- Facilitates control of ventilation. By using positive pressure ventilation, arterial carbon dioxide levels can be maintained near normal preventing cardiac arrhythmias that may develop with a respiratory acidemia.
- Control of the depth of anesthesia. During surgery the analgesic requirements may vary. Changes in the depth of anesthesia can be quickly achieved. If emergencies arise, the administration of inhalants can be stopped immediately and the system flushed with oxygen to hasten recovery.
- Smooth and rapid recovery. Because almost all inhalant anesthetic is eliminated via the respiratory system, recovery is relatively quick and with minimal excitement. Injectable anesthetic techniques, however, depend upon metabolism for elimination of the agent.

Inhalation Anesthetic Agents

There are two primary inhalation agents, halothane and isoflurane. Both of these agents require the use of out-of-circle vaporizers. Nitrous oxide can be used with both agents to speed induction and to reduce the amount of primary agent required to maintain anesthesia. The use of nitrous oxide, however, is not recommended for ruminants because of the risk of arterial hypoxemia and bloat.

Halothane

Halothane has a MAC (minimum alveolar concentration) of approximately 0.9 percent for most species. The MAC value is a measure of a gas anesthetic's potency. By knowing the MAC value one can estimate the maintenance level of anesthetic (vaporizer setting) required for surgical anesthesia. The vaporizer setting is in the range of 1.5-2 times the MAC value. For halothane the vaporizer setting is approximately 1.5-2 percent. The vaporizer setting may be reduced by preanesthetic and induction agents. Halothane can be used for mask inductions of neonates since it produces a relatively quick induction with minimal excitement.

The effect of halothane on the cardiovascular system has been studied extensively (15,16). Halothane is a very useful and relatively inexpensive inhalant anesthetic and will continue to be a widely used agent in all species.

Isoflurane

Isoflurane has been available since the early 1980's. The advantages versus halothane include a quicker induction and recovery with less cardiovascular depression. The incidence of dysrhythmias during isoflurane anesthesia is substantially reduced when compared to other agents (15,16). Isoflurane is relatively expensive to use when compared to halothane.

Isoflurane has a MAC value of approximately 1.3 percent. This translates to a maintenance level (vaporizer setting) of 2-3 percent. Malignant hyperthermia, previously reported in swine exposed to halothane, may also occur with exposure to isoflurane (17).

Epidural Alpha₂ Adrenergic Agonists and Opioids

Recently there has been considerable interest in the use of epidural anesthesia both for providing surgical anesthesia and for post-operative analgesia. Xylazine has been the primary drug utilized for surgical anesthesia. Xylazine has been administered epidurally, primarily at the coccygeal₁ - coccygeal₂ space, for both horses (18) and cattle (19). The onset of anesthesia is slower than that seen with lidocaine but is longer in duration. Also in the bovine, the analgesia advances forward to the flank area with the patient remaining in the standing position.

Opioids have primarily been used for post-operative analgesia. Epidural morphine in the dog has been used to provide post-operative analgesia lasting up to 24 hours. The amount required is much less than that given intramuscularly for analgesia and does not interfere with motor function or produce depression of the cardiovascular system (20). The use of epidural opioids in food animal species requires further investigation before any recommendations can be made.

References

1. Saunders, N.R. (1977). "The blood brain barrier in the foetal and newborn lamb." *Annales de Recherches Veterinaires* 8:384-395.
2. Steward, D.J. (1992). "Anesthetic Considerations for Neonates and Grownup 'Preemies'." *1992 ASA Refresher Course Lectures* 146:4.
3. Robinson, N.E. (1992). "The Respiratory System." In *Equine Anesthesia Monitoring and Emergency Care*, W. W. Muir III and J.A.E. Hubbell, (eds.), St. Louis, MO, Mosby Year Book 1992, 2:20.
4. Muir, W.W. III. (1992). "Intravenous Anesthetics and Anesthetic Techniques in Horses." In *Equine Anesthesia Monitoring and Emergency Care*, W. W. Muir III and J.A.E. Hubbell, (eds.), St. Louis, MO, Mosby Year Book 1992, 12:286.
5. Mihaly, G.W., et al. (1978) "The pharmacokinetics and metabolism of the anilide local anesthetics in neonates." *European Journal of Clinical Pharmacology* 13:143-152.
6. Baggot, J.D., and Short, C.R. (1984). "Drug disposition in the neonatal animal, with particular reference to the foal." *Equine Veterinary Journal* 16:364-367.
7. Webb, A.I. (1984) "Nasal intubation in the foal." *Journal of the American Veterinary Medical Association* 185:48-51.
8. Shawley, R.V. Personal observation.
9. Hall, L.W., Gillespie, J.R., and Tyler, W.S. (1968). "Alveolar-arterial oxygen tension differences in anesthetized horses." *British Journal of Anesthesiology* 40:560-568.
10. Lindsay, W.A., et al. (1985). "Effect of protective padding on forelimb intracompartmental muscle pressures in anesthetized horses." *American Journal of Veterinary Research* 46(3):688-691.
11. Alitalo, I. (1985). "Clinical experience with domosedan in horses and cattle." In *Proceedings of the Domosedon Symposium, Tucker, Finland, 1985*, p.17.
12. Gross, M.E., and Tranquilli, W.J. (1989) "Use of alpha-2 adrenergic receptor antagonists." *Journal of the American Veterinary Medical Association* 195:378-381.

(cont'd p.13)

POST-OPERATIVE CARE AND ANALGESIA OF FARM ANIMALS USED IN BIOMEDICAL RESEARCH

by
Mildred M. Randolph, DVM
University of Oklahoma
Health Sciences Center, Animal Resources
Oklahoma City, OK 73190

Introduction

Farm animals are being used with increased frequency in research facilities. As biomedical researchers and investigators, we must recognize and accommodate their unique husbandry needs. These farm animals should be housed in areas designed specifically for them. Unfortunately, it may not be advisable to put pigs or goats in a facility's largest dog pens. These animals will probably be less domesticated than the typical research cat or dog, and the "human contact" factor may not be as essential to their well-being. However, their needs should be considered as we prepare to house them for extended periods of time. The environment that the animals encounter, beginning with their initial entrance into the facility, can contribute to a smooth operative and post-operative period. They should be housed in the least stressful environment possible. Food and water intake, as well as social behavior, should be monitored as an indication of overall well-being. More research is needed to develop analgesics that address some of the challenges these animals present during the post-operative period. Farm animals used in biomedical research would benefit from analgesics with longer duration times, increased routes of administration and shelf-life, reduced addictive potential, and wider margins of safety. As we increase our usage of farm animals in invasive surgical procedures, we are obligated to circumvent post-operative pain and other stressors resulting from our experimentation.

Pain Perception and Analgesics

As ethology research increases, hopefully our knowledge of the expression of animal pain will increase proportionally. Being familiar with the normal behavior is imperative in assessing abnormal activity and temperament in farm animals. Parameters for "normal" behavior vary not only from one species to another, but also from one individual animal to another. It may prove to be a very expensive endeavor, both in time and money, to engage in any research protocol without first thoroughly familiarizing yourself with the normal activity of your animal model. Close communication between animal caretakers and the researchers works toward the best interest of the animal in the post-operative period. An astute caretaker's knowledge of the normal behavior for that particular age, sex, species, and individual is crucial in determining when animals are experiencing unacceptable levels of pain.

One of the best clinical assessments in distinguishing normal from abnormal behavior is the feeding pattern. Many species of farm animals experiencing pain and distress do not eat normally. However, this does not mean that any animal that seeks food post-operatively does not need pain management. When animals are housed in a group, it would be helpful to remove the post-surgical cases for daily weight checks.

A reduction of food intake will also be reflected in fecal and urine output. Too, the animal that separates itself from the rest of the animals with which it is housed may need additional attention. Other signs of discomfort may be an alteration in an animal's gait or a constant changing of position. Also, some species of farm animals (especially goats) will increase their vocalizations when in pain. Pigs are notorious for becoming either aggressive or seeking solitude when they are uncomfortable. Sheep seem to be unique in their ability to tolerate high levels of pain with only minor changes in their normal behavior. The need for researchers to learn the normal behavior of their particular animal model is easily understood.

There is a general consensus that animals perceive pain. However, as researchers we have been slow to respond to this awareness, especially when farm animals are used in biomedical research. As farm animals become increasingly popular in research, it is not only appropriate, but also an obligation for researchers to familiarize themselves with both the obvious and the more subtle signs of pain and discomfort in these large animal species.

We should assume that any procedure that would cause pain in humans will also cause comparable discomfort in farm animals. Invasive procedures causing tissue injury should be expected to result in varying degrees of post-operative pain. When this is anticipated, a plan should be in force to administer appropriate tranquilizers and analgesics post-operatively. The goal is not directed toward giving relief so much as it is toward *circumventing* pain by designing a protocol which includes adequate analgesics given prior to the onset of severe discomfort.

As we decide on appropriate analgesics, the surgical procedure must be considered. Certain surgical sites are likely to present a greater pain management challenge than others. Extensive surgical procedures involving the areas of the cervical spine, sternal approaches to the thorax, the head, eye, ear, mouth, rectal area and bones will all generally result in moderate to high degrees of pain post-operatively. Since this sensitivity has been documented in other species, we should investigate which analgesics would be most appropriate for those experiments requiring surgery in these areas.

The proper analgesic selection has much to do with the particular animal model that is being used. Some research has been performed that compares differences among common domestic farm animals and their ability to utilize various analgesics. There are species differences that influence the deposition of analgesic drugs. These differences, many of which are anatomical, will affect the selection and route of administration for various analgesic drugs. The digestive tracts of various domestic species reflect a difference in the drug deposition. For example, swine have simple stomachs with a

spiral colon. It has been reported that this feature does not greatly influence drug deposition. Yet horses, being herbivorous, rarely have an empty stomach, and there follows a reduced opportunity for the drug to be absorbed. Cows and other ruminants have large acidic environments in their digestive tracts from which many drugs are not easily absorbed. Also, many drugs are destroyed by the enzymes produced by the ruminal flora. These factors should be remembered as researchers decide on their armament of pain medicines.

Specific Analgesics

Opioid agonists (morphine, meperidine, oxymorphone, and fentanyl) and agonist-antagonists (pentazocine, butorphanol, nalbuphine, and buprenorphine) are two groups of effective analgesics. Opioid agonists probably have the best reputation for providing potent analgesia. When administered in analgesic dosages and given intramuscularly or subcutaneously, they are unlikely to cause detrimental side effects. Unfortunately, in farm animals the use of morphine and other opiates is known to cause excitement. Therefore, when opiates are used for analgesic purposes in farm animals, they are used in conjunction with other drugs.

Analgesics work best when their use is initiated to prevent post-operative pain. Low doses of analgesics given prior to full recovery mean that fewer analgesics will be necessary and that any pain will be more readily managed.

Opioid agonist-antagonists have some advantages over opioid agonists. They have limited abuse potential and are not strictly controlled. They do not produce the profound analgesic response that characterize the opiates; however, they can be very helpful in pain management. These drugs also have a "ceiling effect," and depending on the given situation, this may or may not be an advantage. Increasing the dosage of butorphanol, for example, above the optimal dose does not increase the analgesic effects or incite respiratory depression. The advantage of this is that the respiratory system is spared from further depression. However, the analgesic effects are also limited by this same "ceiling." Another advantage of these opioid-antagonists is that they can be used to antagonize opioid agonists.

Buprenorphine appears to be one of the longer acting agonist-antagonists. It has the advantage of being able to be administered by various routes (IV, IM, SC, and IP). However, the most encouraging aspect about this drug is that dose intervals are up to 12 hours in pigs, and 4-6 hours in sheep and goats.

Nonsteroidal anti-inflammatory drugs, although commonly overlooked, can be very helpful in the management and treatment of post-operative pain. Many of these drugs (aspirin, ibuprofen, and phenylbutazone) are excellent anti-inflammatory, antipyretic and analgesic agents. The disadvantage is that they modify the release of arachidonic acid, and this may interfere with experimental studies. They are not the potent analgesics that the opiates are.

Meperidine, a commonly used opioid agonist, has been found to have an undeserving reputation as an analgesic drug in farm animals. The literature is now showing that this drug has a half life of less than 1 hour, making its use in farm animals less than practical. Likewise, pentazocine has been shown to have very rapid elimination from farm animal species.

Suggested Practical Analgesics for Farm Animals Used in Biomedical Sciences

Ruminants

aspirin	50-100 (mg/kg) PO	12 hr duration
phenylbutazone	6 (mg/kg) IV,IM,PO	
buprenorphine	.005 (mg/kg)	4 to 6 hrs duration

Pig

aspirin	10 (mg/kg) PO	
phenylbutazone	2-5 (mg/kg) IV	
buprenorphine	0.1 (mg/kg) IM	12-hour duration

The Post-operative Period

The recovery period should be viewed as the final stage in the surgical procedure. Some investigators and their staff have underestimated the importance of this stage of the surgical endeavor. There can be no successful surgery with an unsuccessful recovery. Often, mistakes made during the surgical procedure come back to haunt the research staff during the recovery stage. For example, large pigs that were given excessive doses of a barbiturate experience a protracted recovery period.

Post-operative care should be assigned to a particular person on the research team. The recovery of animals used in surgical experimentation should take place in a specific area designed to meet the special needs of animals during the post-operative period.

The post-operative environment should be characterized by a room equipped with subdued lighting. The ambient temperature should be near 27-30 °C for adult animals and 35-37 °C for young animals. It is important to monitor the body temperature as well as the environmental temperature. As the animal recovers, it will regain the ability to maintain its own temperature and diminish the need for heating pads, etc. Care must then be taken to ensure that the animal does not become over-heated.

The maintenance of a patent airway is important in any recovering animal. An endotracheal tube should remain in position until the animal's swallowing reflex has returned. This dimension has increased importance in certain species, such as the pig – an animal that has a tendency to vomit.

Small ruminants (sheep and goats) should be placed in a sternal position. This position tends to reduce the incidence of overdistention of the rumen and the aspiration of rumenal contents. Repositioning to avoid hypostatic pneumonia is important if the animals are still recovering after 3 to 4 hours.

Animals recovering from surgical procedures should do so in a warm, dry environment. Farm animals should be allowed to recover on fresh bedding, such as straw. Providing a thick, non-skid surface will reduce the incidence of pressure sores and injury as the animal attempts to stand and ambulate.

One of the major problems in providing the ideal recovery room for farm animals is the recurring problem of adequate space. A large-size room is absolutely necessary for large animals as they recover from surgery. This can become a major problem in situations where up to 25 surgeries may be performed on a group of experimental goats or sheep in a single day. These animals need to be placed several feet apart while they recover. Incidents have been recounted wherein adequate space was not provided, and sheep were stacked on top of one another during recovery from general anesthesia. An unfortunate scenario developed from one such situation –

one of the sheep on the bottom died from suffocation, while many of the others had to be treated for rumenal tympany.

Optimal recovery conditions may be even more important for farm animals used in research than they are for rodents, dogs or cats. The farm animals commonly used in biomedical research (sheep, goats and pigs) are less likely to be amenable to the routine handling required in the case of any post-operative complications. It is in the best interest of the investigator to reduce the need for restraining these animals unless it becomes absolutely necessary. Therefore, maintaining a clean surgical incision and supplying clean bedding may reduce the incidence of having to treat post-operatively. As these animals recover, they are also more likely to be fearful and nervous. A non-skid floor surface in an area with reduced noise and lighting will all encourage a smooth recovery.

A time-intervalled, record-keeping system should be operational in the recovery area. At specific intervals, the heart rate, respiratory rate, temperature, and acid-base status should be monitored on each recovering animal. Such intermittent recording of various vital signs requires a commitment on behalf of the researcher and the nursing staff, helping to magnify the importance of the recovery stage to those individuals keeping records.

Summary

As researchers plan surgical procedures, post-operative analgesics should be an important consideration. Analgesics must be selected based upon the specific farm animal involved in the experiment. It should be assumed that any invasive surgery, and perhaps some minor surgeries, will require post-operative pain medication. These drugs should be given *prior* to the onset and clinical manifestation of severe pain.

The best attitude to adopt in order to avoid unexpected events in the recovery room is one of prevention. By anticipating and preparing for worst-case scenarios, recovery room technicians are forced to mentally rehearse actions to be taken in the case of an emergency. The recovery of farm animals may present a distinct problem because of the large amount of space required for a safe recovery. As researchers routinely make provisions for monitoring animals during the post-operative period, failure to make arrangements for the essential post-operative needs will become increasingly unacceptable. No environment in a research facility can ever be totally free of factors that stress the research animals. However, it is our moral and scientific obligation to reduce, for the entire duration of their stay, the chronic and extreme stressors placed upon the animals entrusted to our care.

References

Flecknell, P. A. (1987). *Laboratory Animals Anesthesia*. Academic Press, Inc., San Diego, CA.

Haskins, Steve C. and Klide, Alan M. and guest editors. (March 1992). *The Veterinary Clinics of North America*. W. B. Saunders, Philadelphia, PA.

National Research Council. (1992). *Recognition and Alleviation of Pain and Distress in Laboratory Animals*. National Academy Press, Washington, DC.

Short, C.E. and Van Poznak, A. (1992). *Animal Pain*. Churchill Livingstone, New York, NY.



cont'd from p.10

13. Thompson, J.R., Kersting, K.W., and Hsu, W.H. (1991). "Antagonistic effect of atipamezole on xylazine-induced sedation, bradycardia and ruminal atony of calves." *American Journal of Veterinary Research* 52: 1265-1268.

14. Greene, S.A., et al. (1987). "Effect of yohimbine on xylazine induced hypoinsulinemia and hyperglycemia in mares." *American Journal of Veterinary Research* 48:676-678.

15. Joas, T.A., and Stevens, W.C. (1971). "Comparison of the arrhythmia doses of epinephrine during forane, halothane and floroxene anesthesia in dogs." *Anesthesiology* 35:48-53.

16. Johnston, R.R., Eger, E.I. II, and Wilson, C. (1976). "A comparative interaction of epinephrine with enflurane, isoflurane, and halothane in man." *Anesthesia and Analgesia* 55:709-712.

17. McGrath, C.J., et al. (1981). "Malignant hyperthermia triggering liability of selected inhalant anesthetics in swine." *American Journal of Veterinary Research* 42:604-607.

18. LeBlanc, P.H., et al. (1988). "Epidural injection of xylazine for perineal analgesia in horses." *Journal of the American Veterinary Medical Association* 193:1405-1408.

19. Zaugg, J.L. and Mussbaum, M. (1990). "Epidural xylazine: a new option for surgical analgesia of the bovine abdomen and udder." *Veterinary Medicine* 85:1043-1046.

20. Bonath, K.H. and Saleh, A.J. (1985). "Long term pain treatment in the dog by peridural morphines." In *Proceedings of the 2nd International Veterinary Anesthesiology Symposium*, Santa Barbara, CA, Veterinary Practice Publishing Co., p.161.



New Publications Available from AWIC

- QB 94-02 Welfare of Experimental Animals
- QB 94-10 BST - Bovine Somatotropin/Growth Hormone
- QB 94-14 Housing, Husbandry, and Welfare of Swine
- QB 94-15 Housing, Husbandry, and Welfare of Poultry
- QB 94-16 Housing, Husbandry, and Welfare of Rabbits
- QB 94-17 Training Materials for Animal Facility Personnel
- QB 94-18 Anesthesia and Analgesia for Companion and Laboratory Animals
- QB 94-19 Animal Models of Disease
- QB 94-21 Anesthesia and Analgesia for Farm Animals
- QB 94-22 Housing, Husbandry, and Welfare of Horses
- QB 94-24 The Dog
- SRB 94-01 Animal Models in Biomedical Research: Swine

Correction

The photograph showing drill grooming behavior (AWIC Newsletter V.4 #4, p.8) should have been credited to Heidi Englehardt of Grass Valley, CA.

Future Development of USDA Standards for Farm Animals Under the Authorities of the Animal Welfare Act

by

Bonnie Buntain, DVM, MS
Director of Animal Care Staff, APHIS, REAC
and Sue Gallagher
Program Specialist, APHIS, REAC

Historical Background

The Animal Welfare Act (AWA) (7 U.S.C. 2131 *et seq.*), enacted in 1966 and amended in 1970, 1976, 1985, and 1990, authorizes the Secretary of Agriculture to promulgate standards and other requirements governing the humane handling, housing, care, treatment and transportation of certain animals by dealers, research facilities, exhibitors, carriers, and intermediate handlers. Regulations established under the Act are contained in *Title 9, Code of Federal Regulations, Parts 1, 2, 3, and 4*. From the time the Act was amended in 1970 (*Public Law 91-579*), the definition of the term "animal" has included "any live or dead dog, cat, monkey (nonhuman primate mammal), guinea pig, hamster, rabbit, or such other warmblooded animal, as the Secretary may determine is being used, or is intended for use, for research, testing, experimentation, or exhibition purposes, or as a pet. . ." (7 U.S.C. 2132 (g)).

The following animals are excluded from the term and therefore are not covered by the Act: ". . . horses not used for research purposes and other farm animals, such as, but not limited to livestock or poultry, used or intended for use as food or fiber, or livestock or poultry used or intended for improving animal nutrition, breeding, management, or production efficiency, or for improving the quality of food or fiber . . ." (7 U.S.C. 2131 (g)).

The U.S. Department of Agriculture (USDA) is authorized by the Act to regulate horses when used for biomedical or other nonagricultural research and is authorized to regulate other farm animals when the animals are used for biomedical or other nonagricultural research, nonagricultural exhibition, or as pets. Prior to 1990, USDA had not generally enforced the AWA regulations with respect to horses and other farm animals. However, with increasing use of horses and other farm animals in biomedical research and nonagricultural exhibition and comments and inquiries from members of the public and regulated industries, USDA reevaluated its policy regarding the need to extend enforcement of regulations to include these animals.

In April 1990, USDA published in the *Federal Register* its intent to begin regulating, under the AWA, farm animals used for nonagricultural (nonproduction) research and exhibi-

tion and wholesale purposes; and horses used in nonagricultural research.

Nonagricultural practices would include, but are not limited to, biomedical research to advance animal or human health; exhibition of farm animals under specified settings; or breeding of farm animals for exhibition or research purposes. Comments regarding future regulations were simultaneously solicited from the public. In order to better provide humane standards to farm animals under the Act's authorities and to respond to comments expressed by various interest groups, regulated entities, and the general public, USDA believes more specific guidelines are appropriate.

Current Standards

Currently, the Animal and Plant Health Inspection Service (APHIS) is using the existing requirements contained in Part 3, Subpart F, of the AWA regulations. These regulations are applied to farm animals as defined in the Act for nonagricultural research and exhibition, and for wholesale purposes, as well as horses used for nonagricultural research. We have become increasingly aware of the need to provide species-specific standards, when applicable, for farm animals in order to best address their individual needs to ensure proper humane care, treatment, housing, and transportation. Therefore, USDA is resuming the process of gathering information before developing regulations. We emphasize that farm animals used in production agriculture are not currently covered under the AWA nor is USDA seeking to bring the use of animals in production agriculture under its purview.

Specific standards to enhance uniform enforcement of the Animal Welfare Act are currently under consideration and development. An open exchange of ideas is needed today to develop fair, effective and scientifically sound regulatory standards, where applicable.

Open Public Forums and Federal Interagency Meetings

In an effort to canvass the concerned public for recommendations on the housing, care, handling, and unique prac-



(Photo by Tim Allen)

tices applied to nonagricultural use of farm animals, the USDA sponsored a meeting on September 28-29, 1993, in Oklahoma City, Oklahoma.

Approximately 125 people attended this meeting – the general public, research and exhibition industries, animal science and veterinary medical organizations, animal protection groups, and leaders from academic institutions and government agencies. Specific workshops were held to address: agricultural exemptions, agricultural vs. nonagricultural environment, well-being of farm animals, and special considerations for major operative procedures. The following summarizes some recommendations:

- Standards should include use of the *Guide for the Care and Use of Agricultural Animals in Agriculture Research and Teaching*, the *NIH Guide for the Care and Use of Laboratory Animals*, nationally recognized production and research facilities' standards, and international farm animal regulations.
- There should be minimum performance and design standards for farm animal well-being.
- The Institutional Animal Care and Use Committee (IACUC) and USDA should provide oversight for the use of all farm animals in research, teaching, and testing.
- Within the intent and provisions of the AWA regulations, the IACUC should decide when to grant exemptions from enforcement of AWA provisions in farm settings regardless of the intent of the research, teaching, or testing.
- Major operative procedures and post-operative recovery periods should be covered by the AWA standards (and therefore are not exempt, or referred to as "nonexempt").
- Biomedical research where animals are used as models should also be nonexempt.
- There should be uniformity in the enforcement of the standards, yet flexibility in the process.
- Multi-disciplinary team approach by IACUCs and USDA inspectors is needed to enhance compliance and enforcement of the standards.
- Specific species standards should be developed.
- Research personnel, IACUC members, and USDA inspectors should receive training and be educated in farm animal practices.
- AWIC should be a center for all farm animal welfare information.
- Endoscopic surgery for research and teaching (non-diagnostic) should be done in USDA registered facilities.
- Farm animals used in research, teaching and testing should not enter the food chain unless approved by the Food and Drug Administration.
- Animal husbandry and agriculture-related procedures (tail docking, castration, dehorning, etc.) should be exempt from AWA standards unless they are part of the scientific research protocol.
- Production agriculture farms supplying animals for research should be exempt from being USDA registered facilities.

- No animal should be used in more than one major operative procedure.
- Regulations for the transportation of farm animals should be developed.
- All surgical exercises should meet professional veterinary standards.
- Those farm animal facilities which are certified by the American Association for the Accreditation of Laboratory Animal Care should be considered for fewer USDA inspections.

In December 1993, the USDA held a meeting with Federal representatives requesting input for the development of these standards. Some of the issues and topics discussed included the following:

- Include special considerations for transgenic species.
- Use science-based standards where possible.
- Redefine the term "animal" in the Act to reflect which "animals" are to be regulated.
- Revise the definition of "exemptions" in the Act.
- Broaden the USDA authority on the use of farm animals for teaching.
- Address behavioral enrichment requirements.
- Review the current definition of "major operative procedures" under the AWA.
- Medical records should follow the animal if it is moved to a different facility.
- Address the animal identification issue.
- Define humane handling practices.
- Use tables/guides, when applicable, e.g., number of animals per enclosure.
- Limit the number of separate subparts for each farm animal species.

The Final Steps

USDA staff will prepare a regulatory work plan and seek administrative acceptance of the plan. Next, a draft of farm animal regulations will be developed for governmental clearance. The proposed regulations will be published in the *Federal Register* and a period of public comment will be allowed. Comments will be reviewed and considered, and regulations will be modified, where appropriate, before implementing the final rule of the regulations.

Society's changing values have influenced the global importance of animal well-being, including the adoption of international farm animal guidelines and regulations under specific conditions. This is clearly evidenced by recent international requirements in the European Community, Canada, and New Zealand. It is important that USDA continue its information-gathering process to assist in the development of well-balanced regulations which will ensure and enhance the humane care and treatment of animals.



Farm Animal Welfare Canada

Past, Present and Future

Workshop Organized by
The Expert Committee
on Farm Animal
Welfare and Behaviour



June 3 and 4, 1994 • University of Guelph • Guelph, Ontario

For more information call 519-824-4120 extension 2352.

USDA EEO Policy Statement

The United States Department of Agriculture (USDA) prohibits discrimination in its programs on the basis of race, color, national origin, sex, religion, age, disability, political beliefs and marital or familial status. (Not all prohibited bases apply to all programs). Persons with disabilities who require alternative means of communication of program information (braille, large print, audiotape, etc.) should contact the USDA Office of Communications at (202)720-5881 (voice) or (202)720-7808 (TDD).

To file a complaint, write the Secretary of Agriculture, U.S. Department of Agriculture, Washington, D.C., 20250, or call (202) 720-7327 (voice) or (202) 720-1127 (TDD). USDA is an equal employment opportunity employer.

United States Department of Agriculture
National Agricultural Library
AWIC Newsletter Staff
Beltsville, MD 20705

OFFICIAL BUSINESS
Penalty for Private Use, \$300
ANIMAL WELFARE INFORMATION CENTER NEWSLETTER
ISSN 1050-561X

BULK RATE
POSTAGE AND FEES PAID
USDA
PERMIT NO. G95

If changes are required to your mailing address, enter them on the address label and return it or a copy of it to the above address. If you wish to be removed from the mailing list for this publication check here and return this page or a copy of it to the above address.

ANIMAL WELFARE INFORMATION CENTER
NEWSLETTER (ISSN 1050-561X)
is published quarterly and distributed free of charge by the National Agricultural Library. The Animal Welfare Information Center Newsletter provides current information on animal welfare to investigators, technicians, administrators, exhibitors, and the public. Mention of commercial enterprises or brand names does not constitute endorsement or imply preference by the U.S. Department of Agriculture. Articles appearing in this newsletter do not necessarily represent positions or policies of the U.S. Department of Agriculture or any agency thereof.

Tim Allen, Editor
D'Anna Berry, Production and Layout
Michael Kreger, Assistant Editor
Phone: (301) 504-6212
Fax: (301) 504-6409 Internet: AWIC@NALUSDA.GOV