

Meeting 10 Summary
10/4/04

Thanks to those of you that attended the meeting in October. It was productive-we discussed granting information, training, maintaining the Primates Inc mission, variability, and pain perception. I apologize for the length of this summary, but I think you will find it informative. It ends with a very important review of pain and distress☺

Next Meeting:

Wednesday, November 3rd at In the Company of Thieves with a 6:15pm start time.

Granting Information:

Last month, I compiled animal welfare granting information. I divided up the different potential grants into 3 categories: 1. start writing and following directions, 2. write for more information, or 3. Obtain more information from website. If you would be interested in helping me out with this endeavor, please email me directly and I can send you the granting information to choose from.

Searching for common ground-Animal Welfare: follow-up discussion regarding a recent comment.

Primates Inc will maintain its stance of studying and promoting animal welfare. It will be difficult to make this connection with everyone as a public organization since we will be presenting to many people with different views. We will stick to our mission and will let the goals of Primates Inc speak for what we are trying to do.

Jordana from the Primate Center provided a follow-up message to the previous meeting summary regarding a statement I made in the previous meeting summary:

Dear Supporters of Primates, Inc.:

In her last e-mail, Amy wrote:

“I want you all to know that I will do whatever it takes to prevent Primates Inc from being labeled as animal rights.” To that effect, please join me in supporting any and all efforts on behalf of animals everywhere that are carried out in a professional and informative way, with respect to everyone who supports both life-saving research that benefits humans and animals, and shares similar goals for animal care, if not always the same methods: Animal welfare in research facilities, or involving research animals, cannot always be carried out in the same way as in zoos or sanctuaries, due to differences in the overall missions of various facilities. However, being open to new ideas and methods is always the key to good communication and to getting things done.

I have seen many people over the past eight years try new approaches to animal welfare, both inside the Center and out, and I have seen these approaches work most effectively when the rationale behind them is not driven by an animal rights ideology (the desire to end all use of animals by humans), but rather by the desire to improve conditions for all animals living in a variety of environments--research facilities, the wild, zoos, sanctuaries, shelters, etc. If you donate to any animal-related causes, and if you haven't done so already, you might wish to track overall donations to various entities, to find out whether or not your money is directly helping animals, if that is your goal. Please let me

know if I can assist in this area. Helping educating the public on the differences between animal welfare and animal rights is a key mission of groups like the National Association for Biomedical Research, Americans for Medical Progress, and the National Primate Research Centers Consortium of Public Information Officers. My best wishes to your future endeavors. Please feel free to keep me posted and contact me at any time.

Sincerely,
Jordana Lenon

Training: Amy discussed, Viktor Reinhardt's paper on training:

Reference: Reinhardt, Viktor. Training nonhuman primates to cooperate during handling procedures: a review. Obtained from:

http://www.awionline.org/Lab_animals/biblio/at55.htm

For brevity's sake, I am only including the summary, introduction and a short discussion. Please see the full article for more detail and to obtain references.

Summary:

There is ample published evidence (46 reports) that nonhuman primates do not need to be forcefully restrained during common handling procedures. Twenty-six reports provide detailed information of how primates can be trained to voluntarily cooperate - rather than resist - during blood collection, injection, topical drug application, blood pressure measurement, urine collection, and capture. Such training techniques minimize distress reactions, thereby safeguarding the subjects' welfare and increasing the validity of research data collected.

Introduction: Traditionally, nonhuman primates are being regarded as unpredictable and vicious animals, posing a serious danger of zoonoses transmission through bites and scratches to all those who handle them. Hence, it is a commonly endorsed and recommended practice to apply forced restraint when handling primates not only during complex procedures such as blood pressure measurement and blood collection, but also during simple procedures such as drug injection and capture.¹⁻¹⁴ Bites and scratches, however, are frequent despite the rigorous precautions.¹⁵⁻¹⁷

Involuntary restraint is accompanied by numerous changes from normative behavioural and physiological reactions. Such deviations include: alarm vocalization, fear vocalization, defensive threatening, defensive aggression, acute diarrhea, struggling, respiratory rate increase, heart rate increase, catecholamine increase, cortisol increase, prolactin increase, luteinizing hormone decrease, testosterone decrease, metabolic acidosis, immune suppression, leukocytosis, enzymatic shifts, drowsiness, and exhibition of neurotic behaviours.^{18,19} Individuals respond differently to restraint, thereby introducing additional nonexperimental variables into the research data.²⁰ This problem has traditionally been dealt with by using more experimental animals in order to improve statistical significance. Training techniques that reduce or eliminate such sources of variability have, therefore, the potential of reducing the number of animals required in a given protocol.²¹⁻²⁹

The Primate Research Institute of Kyoto University stipulates that unnecessary physical restraint should be avoided.³⁰ The International Primatological Society also underscores that restraint procedures should be used only when less stressful alternatives are not

feasible.³¹ Prentice *et al* make it a principal rule that physical restraint should be used only after alternatives have been considered and found to be inadequate.³² Training the animals to cooperate - rather than resist - during handling procedures is an *adequate alternative* which: reduces or eliminates data-confounding stress responses thereby enhancing the quality of data collection,^{16,19,33-44} decreases the risk of injury,^{16,45-51} reduces the amount of time and the number of personnel required to perform a procedure,^{38,40,48,52-55} provides mental stimulation not only for the animal subject but also for the care personnel,^{42,46,49,50,54-61} and fosters a human-animal relationship that is based on trust rather than fear.^{48,62}

For the present review of the literature, *training* nonhuman primates to cooperate during procedures is defined as: *teaching* the subject to *voluntarily* respond to a key situation in predetermined fashion and *accept* the handling procedure. This definition implies that the subject is not coerced but is *free to resist* the handling. All publications included in this review provide background information not only of the species but also of the gender and age of the subjects.

Discussion. We discussed that there are some methods that do exist that are historical in nature that could be replaced with other methods that are being used. The topic of tb testing came up...I read that there were some methods/alternatives to provide tb testing such as once/ year during physical or administer tb testing on in the chest area (comment: con-chest can be furry and can vary in sex-skin color). I will try to find the article I read on tb testing.

The other method is the chairing of nonhuman primates. We all could agree that the training and rewarding the animal to voluntarily enter the chair would be far less stressful on the animal than providing involuntary restraint. Since the less-stressful methodology already exists in some laboratories, it should be used as a model for the USDA to disseminate this information to the laboratories in order to work towards standardizing methods.

More enriching to Less enriching?

As many of you know, I am on the Laboratory Animal Refinement and Enrichment forum. Recently someone wrote in and asked a very interesting question. I decided it should be brought up at the meeting since it is a very complex issue. Please email me with any follow up comments that you might have so I can include them in the next meeting summary and also send to LAREF.

Question:

Dear LAREFers

Recently a colleague stated an interesting point of view. He thought that producing primates in large outdoor corrals and then bringing them inside into small cages (during research studies) creates stress similar to that experienced by wild caught monkeys. The obvious causes being social disruption, restricted space of less complexity and an alien indoor environment. This despite captive bred individuals being habituated to humans and some operational procedures, which, he claims, wild caught monkeys also habituate to. In his opinion if monkeys are to be produced for biomedical research, that should be

in indoor communal cages, with exposure to environments resembling those in which they are going to be used or maybe even spend most of their lives. I would be keen to learn of your opinions, particular from those who operate such a breeding and housing system.

Jürgen,

PS: this is not about conservation but purely from the welfare point of view.

Dear Jürgen,

Although I don't have experience with corral housing, I have heard about it and its necessity to maintain a population of research monkeys. Your message interested me, because I was interested in the sale/transfer of monkeys between research facilities and reasoned that they should move from less-enriching to more enriching facilities so nothing is taken away from what they are used to; only added to. With this rationale, I guess the corral thing would be a problem. It is common, though and probably unavoidable. I would also say that if a monkey is raised in group outside until it has to go inside, that it is at least learning valuable behavioral interactions from its troop to help produce more naturalistic behavior.

There is, however, the notion of adaptability and habituation and that monkeys can adapt to any environment given enough time. I am not into the 'shell shocking' though where the monkey is just transferred and that is it. I think they should be exposed for small amounts of time to the inside and given rewards while they are in there. The key is to look for their willingness to go inside. I have heard stories of people being able to train specific animals to come out of their groups by color-coded targeting. Perhaps if there were more training on hand, these animals could come in to habituate during the morning and then be reintroduced to the group in the afternoon.

I hope you don't mind, but I brought this issue up at a Primates Inc meeting last night to get some other ideas... I had just provided a summary on the training review Viktor had written: Training nonhuman primates to cooperate during handling procedures: a review, obtained from:

http://www.awionline.org/Lab_animals/biblio/at55.htm and so we were inspired to try to relieve some of the unnecessary stress that still occurs in labs. We reasoned that the corral housing transfer would be ok if all of the monkeys went through an incremental habituation period. If all of the animals had the same habituation/housing/upbringing history, then they should be ok as a group of subjects in the same study. The group also agreed that all monkeys are individuals and react to stress differently. So, if they were all trained and habituated, they should act similar to their environment and this would help add to the validity of a study by reducing variability for that institution.

Have a good day,

Amy Kerwin

Evelyn- pain & distress review:

**Note: Due to the fact that a full text copy of this article is not available either on the web, or in PDF format, this summary provides you with the full introduction, verbatim, as well as a synopsis of the debate that follows the introduction.

Introduction from the article *Pain and Distress in Research Animals: A Panel of Experts Debates the Issues* as written by B. Taylor Bennett, DVM, PHD, and published in *Lab Animal* January 2002 (volume 31, no. 1, pages 34-42).

On June 22, 2000, the Committee on Regulatory Issues in Animal Care and Use of the Institute for Laboratory Animal Research held a workshop entitled, "Definition of Pain and Distress and Reporting Requirements for Laboratory Animals." Shortly after the workshop, the Animal Plant and Health Inspection Service of the United States Department of Agriculture (USDA-APHIS) published a request for comments, stating that they were "...considering several changes to the Animal Welfare regulations to promote the humane treatment of live animals used in research, testing and teaching and to improve the quality of information we report to Congress considering pain and distress." They proposed to accomplish these two goals by adding a definition of "distress" to assist research facilities in recognizing and minimizing distress in animals, and by developing a different categorization system to more accurately depict the nature to pain and distress and to serve as a tool to measure efforts made to minimize animal pain and distress in research facilities.

Since that time, the issue of pain and distress in laboratory animals, and how to define these factors and report them in the annual report required of all research facilities registered with the USDA, has been the subject of much discussion both informally and as part of several organized conferences. Here, the editors have assembled a panel representing different viewpoints within the field to comment on six specific questions concerning pain and distress, our knowledge of these two conditions, the possibility of defining distress in the regulations and the impact that inclusion of this definition and changing of the annual reporting format to include distress would have both on the animals used in research and the research institutions.

The perception of pain and distress in humans and animals is a complex phenomenon that tends to be very individual in nature. The specific stimuli that lead to the perception of pain and, to some degree, distress are less variable. This has naturally led to an anthropomorphic approach to assessing pain and distress in animals used in biomedical research. Pain and distress are medical conditions, the symptoms of which can be treated by a variety of methods, including the use of drugs. In a research environment, it is not only important to recognize and treat the symptoms of pain and distress, but also to be able to identify the cause(s) in order to minimize them, reduce the nonexperimental variables, and improve the quality of the data generated.

As the panelists point out, our knowledge of pain and how to manage it has increased significantly in the last several decades, in part due to research conducted on laboratory animals. Our knowledge of distress and how to manage it is, comparatively speaking, in the early stages of development, and it is important that additional research with a free flow of communication between the researchers and the clinicians be encouraged and supported. Whether the addition of a regulatory definition will help the institutions recognize and minimize distress in animals or simply add to their regulatory burden is still open to debate, as indicated by the panel members.

The issue of pain and distress and how to minimize them in experimental animals is a topic that will continue to be debated with or without a regulatory definition. Minimizing pain and distress reduces nonexperimental variability and thus reduces the number of animals used. To minimize pain and distress requires that we continue to refine the methods used for caring for and using laboratory animals. To accomplish this goal, veterinarians and investigator must work together to prospectively evaluate each protocol with the potential for producing pain and distress, and then monitor the animals to assess the accuracy of their prospective judgments. When events occur that were not expected in the prospective analysis, veterinarians and researcher should strive to find the cause of these events. Whenever possible, they should report those events in the scientific literature to add to the knowledge base that serves as a basis for minimizing pain and distress in the animals that must be used for research.

The discussion that follows (**in this case, a synopsis presented at the Primates Inc Meeting #10) does not provide a simple conclusion to the debate or pain and distress, nor about the reporting mechanism that should be in place to document them. It does point out that there are no simple answers, and emphasizes that need for a “long period of dialogue and communication about distress among researchers, IACUCs, veterinarians, and technicians.” In the meantime, we should carefully consider how the animals will benefit by changing the existing regulations, and, as always, “we should always give the animals the benefit of the doubt.”

**The discussion was in question and answer format. Lab Animal printed a synopsis of each individual’s answer to each question. To try to maintain brevity, what is below, is each question and a summary of the points given by the panel members.

QUESTION AND ANSWER SESSION

What do we know about pain perception in animals? Have we been adequately applying our knowledge? How do we apply it?

Overall it was stated that we are able to recognize severe pain, but not mild to moderate

We need to recognize all levels not only to limit suffering and improve animal welfare, but also to improve research results.

The Humane Society believes some, if not a great deal of pain and distress is overlooked in lab animals or its severity is underdetermined.

The Humane Society also brought up a good point about the fact that several research animals are by nature nocturnal (mice, rats, etc...) but their pain is being assessed during the daylight hours when they are least active.

It was also stated that we on a whole are still ignorant about chronic pain – determination and alleviation in both animals and humans.

Interest in pain in animals has increased a great deal. However many believe that we are not adequately applying the knowledge we have obtained over the past couple of decades. So, in order to get people to pay attention and apply knowledge, the suggestion is to teach those who work with lab animals in a positive manner about these issues.

What would you give as the definition of distress?

* Inability to adapt to stressors or from maladaptation

* Intended to capture in a single term a wide variety of ways animals can suffer beyond

physical pain

* Emotional or behavioral response to real or perceived environmental conditions. Pain and distress may occur together and the IASP includes both.

* Not satisfying needs – hunger, thirst, anxiety, loneliness, boredom, fear, etc...

However, what we must remember is that not every organism is the same. For instance, caged birds are unable to fly – this may be distressful for them.

Across the board it was agreed that the Animal Welfare Act regulations seem difficult to understand conceptually and then apply to concrete terms.

Is there significant literature to clearly define distress? If not, what additional studies are needed?

Here the panel was torn. Some believe that there is sufficient literature out there; some believe it's too limited.

They did expand by saying that distress most often results from inappropriate intervention by humans and that non-pain distress is most commonly caused by flaws in husbandry, environment and experimental design.

They suggested that the USDA should make a working definition. However, two comprehensive resources were motioned: Moberg and Mench's *The Biology of Animal Stress: Basic Principles and Implications for Animal Welfare* and The National Research Council's *Guide for the Care and Use of Laboratory Animals*.

One panel member made the poignant comment as follows: "There are still investigators who, if allowed, would ignore stress and pain. They still do not recognize that stress/pain may bias their data, even to the point of researching false conclusions."

Are complaints that adding 'distress' to the regulations would just increase researchers' and IACUC's paperwork load valid? Why or why not?

All in agreement that it shouldn't matter. More paperwork, if necessary, should be looked at as a minor trouble in retrospect if this will make lab animal's lives and data collection better.

A statement was made that said that adding distress should not add work to those already addressing distress adequately. But rather, doing this is likely to increase researchers' and IACUC's attention to distress.

If we were to replace our pain and distress classification under USDA regulations, is there a template that should be followed?

Consensus was that it should be made simple – if researchers can't understand it, they won't use it.

Some ideas and recommendations from the panel:

* Human society would like to see a four category scale from minor to severe

* Recognize that there are other ways to alleviate suffering other than anesthetics, pain killers and tranquilizers

* A suggestion was made for the use of two scales – one for pain and one for distress

* Make sure to cover all species

* Take into consideration that some IACUCs are often surprised about what causes pain

and distress (expect pain from a procedure, but the animal exhibits none, and vice versa)

* System should take into account the unrecognized forms of suffering. For example, when a social partner is removed from a pair or group.

Which would result in a greater burden of paperwork? Prospective or retrospective reporting of animal pain and distress?

Not one member of the panel cared about the amount of paperwork that would result, but rather what would result in better care of the research animals.

Opinions were split between prospective and retrospective with arguments for each:

Prospective allows for taking prior action to alleviate foreseen pain and distress

Retrospective is more accurate

*if you no longer do not want to be on this list, just hit reply and let me know! If you know of anyone who would like to be on this list, send their email to me!