Pain & Distress Report

From the Pain & Distress Campaign of The Humane Society of the United States

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The *Pain & Distress Report* is available online at *humanesociety.org/pain_distress_report.*

THE HUMANE SOCIETY OF THE UNITED STATES

humanesociety.org

Policies+Perspectives

ILAR Updates Publications

The National Research Council (NRC) Institute for Laboratory Animal Research (ILAR) recently released a report, *Recognition and Alleviation of Distress in Laboratory Animals*, examining scientific and ethical issues associated with stress and distress; causes and functions of stress and distress; transformation of stress to distress; identification of principles for the recognition, minimization, and alleviation of distress; the role of humane endpoints in situations of distress; and areas for further investigation. For more information, go to *http://dels.nas.edu/ilar_n/ilarhome/reports.shtml*.

ILAR will also be updating its *Guide for the Care and Use of Laboratory Animals*, last revised in 1996. The process, anticipated to begin in early 2008 with workshops inviting public comment from all interested parties, is expected to take approximately two years. For more information, visit *http://dels.nas.edu/ilar_n/ilarhome*.

Primate Enrichment Survey

A 2003 survey of enrichment program managers at U.S. primate breeding and research facilities conducted by Baker (2007, *Journal of Applied Animal Welfare Science, 10*(1), 49–54) asked questions about enrichment programs at their facilities, including social, feeding, structural, and manipulanda enrichment; human interaction and training; program administration; the role of the Institutional Animal Care and Use Committee (IACUC); and the impetus for recent changes. Of the 22 respondents providing data on nearly 36,000 primates, social housing was by far the most limited form of enrichment. The most common constraints on social housing included protocol concerns (77%), incompatibility of individuals (73%), lack of appropriate housing (41%), lack of time or staff (32%), and cost (14%). Facilities conducting IACUC reviews of enrichment issues reported a significantly higher proportion of animals in social housing; however, IACUC reviews did not prompt enhancements nearly as often as did regulatory or accreditation visits. Social housing of macaques has not increased significantly over the past decade, and only 36% of the facilities reported strong support of IACUC enrichment objectives. IACUC review is an underutilized mechanism for improving enrichment programs, and cross-institutional sharing of data on social housing attempts could promote program progress, since there appears to be more consistency within facilities than between them, in regards to primate socialization.

NIH Public Access Survey

The National Institutes of Health (NIH) published a *Federal Register* notice on Jan. 11 announcing a policy change regarding public access to information resulting from NIH-funded research. All peer-reviewed articles arising from NIH funds and accepted for publication on

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Noteworthy

Animal Welfare Awards Winners

The 2007 National Centre for the Replacement, Refinement and Reduction of Animals in Research 3Rs prize of £10,000, sponsored by GlaxoSmithKline, was recently awarded to Dr. Charlotte Gower of the Department of Infectious Disease Epidemiology at Imperial College London, for a new application of DNA fingerprinting that replaces animal use in research on the disease bilharzia, which affects 200 million people worldwide, and improves the research's accuracy. A Highly Commended prize of £1,000 was also awarded to Dr. John Doe from Syngenta for his publication describing an improved tiered testing approach for assessing agricultural chemical safety that will potentially reduce the number of animals used for this purpose and that major regulatory authorities are considering.

"Joint in a Test Tube" Reduces Animal Use

A new in vitro model for studying arthritis disease progression and pharmaceutical treatment drugs has been created by scientists at the University of Missouri–Columbia's Comparative Orthopaedic Laboratory. Small sections of joint capsule cartilage typically discarded after surgery on dogs are placed in test tubes and grown together to communicate as a normal joint. The new model has provided valid results and shows promise for providing insight into human arthritis without using animals.

CO_2 Causes Distress in Humans

A recent study at the University of Maastricht, the Netherlands, found that inhalation of carbon dioxide (CO_2) triggers emotional distress in humans. Self-report questionnaires used for assessing subjects after four double inhalations of increasing doses of CO_2 (from 0–35%) showed subjects panicked more as the concentration of CO_2 increased. Researchers concluded that beyond a particular threshold, increased CO_2 negatively affects mental states, highlighting the link between disrupted bodily function and mental stress (*www.sciencedaily.com/releases/2007/10/071002213433.htm*).

While this study highlights carbon dioxide causing distress in humans, there is also evidence that it is distressful to other animals, calling into question its ethical use as a sole euthanasia agent in laboratory animals.

Resources+Services

Pain & Distress Report Sent Electronically

To reduce our environmental impact, The Humane Society of the United States (HSUS) will soon be sending the *Pain & Distress Report* only via e-mail. To continue receiving it, please contact ari@humanesociety.org and provide your e-mail address. Please encourage your friends and colleagues to contact us as well.

Humane Endpoints CD-ROM

The Netherlands Centre Alternatives to animal use at Utrecht University has an interactive CD-ROM intended to increase awareness and implementation of humane endpoints. *Humane Endpoints in Laboratory Animal Experimentation* includes information about normal laboratory animal behaviors, pain and distress, clinical signs, humane endpoints, and pathology, along with an extensive glossary and examinations. For more information and to obtain the CD-ROM, visit *www.vet.uu.nl/nca/documents/humane_endpoints*.

From the Technical Literature

Vasectomy Pain in Mice

Wright-Williams et al. (2007, *Pain, 130*: 108–118) examined behavior and levels of fecal corticosterone in C57BL/6JCrl and C3H/HeN mice who were administered saline or the analgesic meloxicam at one of three doses prior to vasectomy surgery under anesthesia. Mice who received saline or the two lower doses of meloxicam had significantly higher corticosterone levels than sham-operated controls, while mice receiving the highest dose of meloxicam prior to vasectomy had levels similar to sham-operated mice. Mice receiving saline prior to vasectomy exhibited more pain-related behaviors, such as flinching, writhing, and rear leg lift, than controls and mice receiving any dose of meloxicam. C3H/HeN mice had higher pain scores and corticosterone levels than C57BL/6JCrl mice overall. Significant behavior changes occur in mice as a result of vasectomy and may be related to post-operative pain, but these can be reduced with meloxicam administration, although corticosterone levels were reduced only by the highest dose of meloxicam. While differences between strains emphasize the challenge of developing pain relief strategies for mice undergoing surgery, this study demonstrates that analgesics can be effective.

Pain Biomarkers

Peterson and Servinksy (2007, *Comparative Medicine, 57*(6): 554–562) examined central nervous system (CNS) markers for pain in mice and the ability of pain-associated factors in the blood to affect other tissues. Mice were subjected to adjuvant footpad injections or partial sciatic nerve ligation (PSL), and gene expression profiles were then analyzed to identify pain markers. Cell line growth was monitored following exposure of mice to serum from the adjuvant and PSL mice, as well as from rats who experienced surgical pain. Adjuvant injection and PSL in mice either increased or decreased transcription of certain genes, and serum from mice with PSL and rats undergoing surgical procedures stimulated the growth of tumor cell lines. It was concluded that gene expression profiles vary based on the nature of the painful stimulus, tumor cell line growth is affected by blood from rodents exposed to these stimuli, and pain can be a potential confounder in neurologic and oncologic studies.

Statistics on Animal Use+Pain & Distress

New Zealand 2006 Animal Use Statistics

New Zealand's National Animal Ethics Advisory Committee recently reported the country's 2006 animal research, testing, and teaching statistics. The total number of animals used was 318,489—a 21% increase from 2005. Sheep and cattle, rodents, and birds were among the most commonly used species. Since 2005, the number of rats and mice, fish, and marine mammals used decreased, respectively, by 10%, 24%, and 92%, while the number of sheep, cattle, and deer used increased collectively by 31%, birds increased by 61%, and the number of reptiles nearly quadrupled. The overall increase in total animals used was partially attributed to the three-year cycle of statistics reporting for long-term projects, as numbers in 2000 and 2003 were higher as well. New Zealand grades manipulations using a five-point severity scale ranging from "no suffering" to "very severe suffering"; 13% of the research animals experienced moderate to very severe suffering, a decrease of 4% since 2005. As in previous years, rodents made up the vast majority of animals in the very severe suffering category; this typically involved meeting regulatory requirements for testing.

To view the report in its entirety, go to *www.biosecurity.govt.nz/animal-welfare/naeac/annual-report/naeac-ar-06.pdf.*

EU 2005 Animal Use Statistics

Recently released animal research statistics reveal that 12.1 million animals were used in the European Union (EU) in 2005. Mice, rats, cold-blooded animals, and birds were the most commonly used species. Fundamental biology studies accounted for 33% of animal use, followed by research and development of human medicine, dentistry products, and veterinary products (31%); production and quality control of human medicine and dentistry products (12%); toxicology (8%); other research (8%); production and quality control of veterinary medicine (4%); diagnosis of disease (2%); and education and training (2%). As in 2002, no great apes were used in the EU in 2005.

An examination of the data for the 15 countries that were member states in both 2002 and 2005 (as opposed to the 25 now) shows a 3% increase in animals used when compared with 2002. Use of mice and rabbits each increased by 10% or more. The use of "other mammals" increased by 30%, while reptile use decreased by 73%.

Attitudes+Public Opinion

Animal Testing Poll Results

Of the 750 respondents to a recent independent poll conducted in New Zealand, 68% agreed that the use of animals for research and testing was acceptable as long as there was no unnecessary animal suffering, while 72% found animal use for teaching acceptable without unnecessary animal suffering. Respondents also felt research into diseases was most justified, while safety testing of cosmetics and chemicals was least justified.

UPCOMING CONFERENCES

IACUC Advanced

Hosted by the Scientists Center for Animal Welfare (SCAW)

May 7, 2008

Bethesda, Md.

www.scaw.com/iacuc-advanced.htm

IACUC 101/201 PLUS

Hosted by Florida Atlantic University

May 20–21, 2008

Delray Beach, Fla.

http://grants.nih.gov/grants/olaw/workshop.htm

IACUC Advanced

Hosted by the Scientists Center for Animal Welfare (SCAW)

June 4, 2008

Columbus, Ohio

www.scaw.com/iacuc-advanced.htm

IACUC 101/201 PLUS

Hosted by University of Minnesota, Twin Cities

June 17–18, 2008

Minneapolis, Minn.

http://grants.nih.gov/grants/olaw/workshop.htm

UFAW Animal Welfare Science Conference 2008

Hosted by Universities Federation for Animal Welfare (UFAW)

July 3, 2008

Birmingham, UK

www.ufaw.org.uk/quality-of-life.php

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or after April 7, 2008, must be submitted electronically to the National Library of Medicine's PubMed Central (PMC), to be made publicly available within 12 months of publication. Grant applications, proposals, or progress reports submitted to the NIH by May 25, 2008, must include the PMC or NIH manuscript submission reference number when citing articles that arise from their NIH-funded research. For more information, go to *http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-033.html*.

ICCVAM Report on Alternatives to Ocular Testing

The National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), on behalf of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), has released a report describing final recommendations on use, protocols, further optimization and validation studies, and reference substances for the Bovine Corneal Opacity and Permeability (BCOP) Test, the Isolated Chicken Eye (ICE) Test, the Isolated Rabbit Eye (IRE) Test, and the Hen's Egg Test-Chorioallantoic Membrane (HET-CAM). ICCVAM suggests these in vitro methods be considered prior to live animal use as screening tests for identifying potential ocular corrosives and severe irritants. ICCVAM's findings have been forwarded to federal agencies to be considered for regulatory acceptance, which could lead to a reduction in live animal use for ocular testing. The report is available at *http://iccvam.niehs.nih.gov/methods/ocutox/ivocutox.htm*.

Helpful Websites

The National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) has a blood sampling microsite that offers information on principles for refinement, advantages and disadvantages to available techniques, adverse effects and control measures, training images and videos, and more references related to blood sampling. To view the site, go to *www.nc3rs.org.uk/bloodsamplingmicrosite/page.asp?id=313*.

Recent Publications

de la Cueva, T., Naranjo, A., de la Cueva, E., and Rubio, D. (2007). Refinement of intrathymic injection in mice. *Lab Animal, 36*(5): 27–32.

Foltz, C., Carbone, L., DeLong, D., Rollin, B.E., Van Loo, P., Whitaker, J., and Wolff, A. (2007). Considerations for determining optimal mouse caging density. *Lab Animal, 36*(10): 40–49.

Novak, M.S.X., Kenney, C., Suomi, S.J., and Ruppenthal, G.C. (2007). Use of animal-operated folding perches by rhesus macaques (*Macaca mulatta*). *Journal of the American Association for Laboratory Animal Science*, *46*(6): 35–43.

Stevens, C.A., and Dey, N.D. (2007). A program for simulated rodent surgical training. *Lab Animal, 36*(9): 25–31.

Pain & Distress Report

The *Pain & Distress Report* provides laboratory animal veterinarians, technicians, oversight committees, and others with up-to-date information on issues regarding pain and distress in laboratory animals.

E-mail ari@humanesociety.org for a free subscription to the electronic version of the newsletter; copies are also available online at *humanesociety.org/pain_distress_report*. Please share this report with your colleagues and IACUC members.

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