PSU Animal Resource Program

Animal Source

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New Studies on Tribromoethanol Anesthesia in Mice

Tribromoethanol (TBE) is an injectable anesthetic commonly used in mice. TBE is sometimes referred to as Avertin, the trade name for a previously marketed version of the drug. Although TBE has been used for decades and is popular with many researchers due to its relatively fast induction and recovery times, there have been conflicting reports on its safety and efficacy in mice. Two recent studies by Lieggi, et al. in *Contemporary Topics* have attempted to evaluate recommended preparation and storage methods in addition to providing further clinical data on TBE safety and efficacy in mice.

TBE is available as a non-pharmaceutical grade powder that must be mixed with a solvent to produce a solution for use as an anesthetic. Previous reports have indicated that adverse effects, including intestinal ileus, muscle necrosis, peritonitis and death may result from intraperitoneal injection of TBE in mice. These effects have been attributed to the formation of toxic breakdown products in the TBE solution. It has been commonly recommended that stock and working solutions of TBE be stored under refrigeration in the

Pain Management, Part I: Assessment of Pain

(Over the next several issues, Animal Source will explore various pain management strategies including the assessment process, perioperative pain management, and the future of pain management.)

As recently as ten years ago, standards for assessing and controlling pain in both human and animal patients were virtually nonexistent. In the early 1990s, in response to human clinical studies showing that many patients were receiving inadequate pain intervention therapy, the medical community began developing standards of care to ensure adequate pain control. In 2001, the Joint Commission on Accreditation of Healthcare Organizations adopted standards for pain management in all accredited human healthcare organizations.

Similarly, pain management standards were established for animals in 2003 by the American Animal Hospital Association (AAHA) and embraced by the American Veterinary Medical Association. The AAHA standards state, “Continual pain is detrimental to the overall healing process as well as to the general well-being”. Unrelieved pain leads to stress, anxiety and diminishes the quality of life.

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Inside this issue:

Threats from within: Screening potential employees to guard against animal extremism.

In 2001-2002, an undercover PETA (People for the Ethical Treatment of Animals) operative was unknowingly employed by the University of North Carolina (UNC) at Chapel Hill in one of their research animal facilities. This employee secretly videotaped investigators, staff and students working with animals, primarily rodents, in the facility. In April 2002, PETA publicly accused UNC of animal cruelty and filed a formal complaint with the Office for Laboratory Animal Welfare (OLAW; the regulatory arm of the National Institutes of Health). By the time the OLAW investigation ended in 2004, PETA revealed that it had planted another spy in the UNC animal facilities and was filing a second complaint against the university with OLAW.

In 2003, PETA revealed that they had performed a similar undercover operation against a private contract research laboratory in Missouri. Once again, a newly hired employee secretly videotaped research personnel while they worked. The result of this operation was the filing of a formal complaint against the laboratory to the United States Department of Agriculture and the loss of millions of dollars in revenue, numerous business contracts and employee positions at this research facility.

While both UNC and the Missouri research laboratory admitted to some legitimate problems with animal care in their facilities, many of the PETA allegations were unsupported and contrived. Neither facility had a history of USDA or OLAW violations. Several of PETA's cruelty complaints against UNC consisted of rodent husbandry or veterinary issues (i.e., overcrowded cages) that are not necessarily associated with improper care. Compliance with animal welfare regulations is no guarantee that your facility or research will not be targeted.

How can you ensure that the staff and students you hire are not animal rights extremists in disguise? Security consulting firms and those who have experienced animal activist infiltration offer some important tips to help screen out animal extremists among job applicants.

- Verify student/applicant schools, previous employers, home address and phone number.
- Check references extensively, and in addition, call other individuals who may know the applicant or know who to contact to find out if the applicant is legitimate.
- Thoroughly interview students/applicants and engage them in conversation. Ask them about their past employment and experiences with animals. Ask practical knowledge questions designed to reveal if they really have worked around animals. Ask them to describe in detail their experience with animal research and their thoughts on the ethics of the use of animals in research.
- Look for the student/applicant's involvement in relevant organizations, clubs, societies or involvement in inappropriate causes.
- When appropriate use criminal background checks and/or self-disclosure questions on the employment application form to help identify criminal convictions.
- After an individual is hired they should have an appropriate probationary period where they are supervised with working with animals and their access to animal rooms is restricted.
- Observe new personnel closely during the probationary period for any unusual or suspicious activities. Potential things to look for include: wearing bulky clothing (for hiding camera or recording equipment); coming in early or staying late for work when it isn't necessary; looking for excuses to spend time with the animals; asking strange questions or inciting conversations about animal care.

Reference: When Animal Extremists Attack! Prevention and Response. May 2004. Midwest Regional AALAS Symposium, Columbia MO.

This article was first printed in *Animal Source,* Summer 2004.

dark to reduce the formation of these breakdown products. In addition, it has been thought that the concentration of breakdown products may be correlated with decreasing pH of the TBE solution.

Lieggi, et al. purchased TBE powder from commercial suppliers and evaluated several preparation and storage methods. They found the purity of purchased TBE powder varied with supplier and all were found to contain contaminants. However, the method of preparation and storage of stock solutions did not lead to differences in breakdown product formation, particle size or turbidity of stock and working solutions of the drug. Storage of TBE solutions at room temperature and in light resulted in decreasing pH but not increased concentration of breakdown products.

Lieggi, et al. also found that TBE produced adequate anesthesia in mice but induction time and duration of anesthesia was variable. In addition, TBE was associated with increased inflammation of the abdominal body wall with necrosis of the underlying muscle. In one experiment, 10 of 17 mice were found dead or moribund four days after injection with TBE. Examination of these mice showed intestinal ileus, peritonitis, pneumonia and bacterial septicemia. Analysis of the TBE solution used in this experiment revealed no difference in composition or contamination compared to previously used solutions. The authors postulated the increased toxicity in this experiment was due to chemical changes of the solid TBE powder during storage.

In comparison, a 1993 study by Papaioannou and Fox found that TBE produced adequate anesthesia in mice with low mortality and few pathologic changes in abdominal and thoracic organs. They did not examine the body wall histologically. However, the concentration and dosage of TBE used by Papaioannou and Fox was significantly lower than used by Lieggi, et al. and precludes direct comparison between the results of each study.

The Lieggi, et al. studies shed some light on the effect of varying methods of TBE preparation and storage but appears to raise new questions about the direct cause of pathology and mortality associated with TBE anesthesia. It remains unknown why TBE works well as an anesthetic in some cases and not in others.

Lieggi C, Artwohl J, Leszczynski J, et al. 2005. Efficacy and Safety of Stored and Newly Prepared Tribromoethanol in ICR Mice. *Contemporary Topics* **44**(1): 17-22.

Lieggi C, Fortman J, Kleps R, et al. 2005. An Evaluation of Preparation Methods and Storage Conditions of Tribromoethanol. *Contemporary Topics* **44**(1): 11-16.

Papaioannou V and Fox J. 1993. Efficacy of Tribromoethanol Anesthesia in Mice. *Laboratory Animal Science* **43** (2): 189-192.

Training for Agricultural and Wildlife Users

The Animal Resource Program offers training for individuals using agricultural and wildlife animals in research and teaching at Penn State. Training programs are tailored to meet individual research needs and goals. Specifically, workshops may include handling and restraint, sample collection, surgery, routine animal husbandry procedures, and health monitoring are available. Please call the Animal Resource Program to discuss training for your research.

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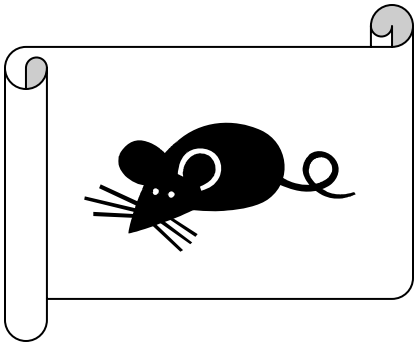

The Animal Resource Program (ARP) is committed to providing PSU faculty, staff and students with high quality, cost-effective research animal resources. In addition to suitable housing facilities and animal husbandry services for animals used in biomedical research, ARP provides veterinary and diagnostic services, personnel training and expertise in laboratory animal technology and medicine. ARP veterinarians are also available to participate in collaborative research projects with PSU investigators. Areas of interest include animal behavior and welfare, infectious disease, and pathology.

Pain Management, continued from page 1.

Assessing pain in animals is the key component of pain management, and pain scales or scoring systems are utilized in constructing objective assessments. The site http://iacuc.ufl.edu/OLD%20Web%20Site/painassessment.htm gives several comprehensive scoring schemes, each of which is developed for a specific species undergoing a given procedure and its potential complications. As such pain scoring schemes rely on human observers, personnel involved must first be familiar with the normal behavior of the species under observation to be able to identify abnormalities should they occur. Characteristics under consideration often include changes in posture, gait, hair coat, appetite and feces production, as well as deviations in physiological parameters including heart rate, respiratory rate, and temperature fluctuations. Additionally, all observers should be trained in the pain assessment process and familiar with the scoring system. The scoring systems accuracy requires consistency in application. Once the pain assessment process is completed, pain control measures can be implemented if indicated.

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Information was taken from:
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Karas, A.Z. Assessment of pain in animals-a critical part of progress. Tufts University. 2005 AVMA Annual Convention
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