

- Physiol. Behav.* **38**, 887–890 (1986).
- Ritchie, J.M. & Greene, N.M. Local anesthetics. in *Goodman & Gilman's The Pharmacological Basis of Therapeutics* 302 (McGraw-Hill, New York, 1985).
 - Danneman, P.J. & Mandrell, T.D. Evaluation of five agents/methods for anesthesia of neonatal rats. *Lab. Anim. Sci.* **47**, 386–395 (1997).
 - Wolf, S. & Hardy, J.D. Studies on pain. Observations of pain due to local cooling and on factors involved in the “cold pressor” effect. *J. Clin. Invest.* **20**, 521–533 (1941).

Richerson is the Institutional Veterinarian, The Bionetics Corporation, Oak Ridge National Laboratory, Oak Ridge, TN. Beatty is the ACUC Chairperson, Oak Ridge National Laboratory, Oak Ridge, TN.

RESPONSE

SOPs for hypothermia

Ann Marie Dinkel, RLATG & Deyanira Santiago, RLATG

Great Eastern University's policy of using the USDA's pain and distress classifications for both USDA-regulated and non-USDA-regulated species is best practice and is widely used; however, there is no regulatory mandate to use these categories for the latter group.

For years, it has been common practice to use hypothermia on neonatal rodents both for surgical procedures and as part of euthanasia. Neonates have fared well during these surgeries. Studies show that neonates do not have fully developed cortical pain memory systems¹. In addition, the Committee on Pain and Distress in Laboratory Animals found that hypothermia can be considered a type of nonpharmacological pain control on neonates. Their finding states that hypothermia can be “applicable to altricious neonates that have not yet developed effective thermoregulatory mechanisms”².

As a member of the IACUC, Bellamy has the right to question any practice that he believes may be archaic or out of the scope of the IACUC's responsibility. It is a subject that may, at this time, need to be reviewed and thoroughly discussed. Until there is factual evidence to dispute the current practice of using hypothermia for neonatal surgeries, however, the IACUC should not change the pain category for these animals from D to E without more background research on the subject.

The induction of anesthesia by hypothermia must be done carefully. Care must be

taken to ensure that animals do not come in direct contact with cold materials, that frostbite is prevented and that the animal is re-warmed slowly. To address Bellamy's concerns about the potential for pain during induction and recovery, the IACUC is within its purview to require the development of standard operating procedures to ensure animal comfort and to certify personnel as skilled in the procedure. As part of its discussions, the IACUC should develop a well-written, acceptable rationale for use of hypothermia, clearly defining how and when this process may be used. This will guide future deliberations and facilitate evaluation of future protocols using this method.

Nevertheless, each protocol should be evaluated on its own merit and its own scientific justification. If the IACUC finds that a particular protocol using that procedure is not justified or, in reviewing the details of the protocol, finds that the protocol should be categorized as a category E protocol, it certainly can act accordingly.

- Simons, S.H. & Tibboel, D. Pain perception development and maturation. *Semin. Fetal Neonatal Med.* **11**, 227–231 (2006).
- Institute for Laboratory Animal Research (ILAR). *Recognition and Alleviation of Pain and Distress in Laboratory Animals* 83 (National Academies Press, Washington, DC, 1992)

Dinkel is Adjunct Faculty at Delaware Technical & Community College, Georgetown, DE, and SUNY Delhi, Delhi, NY. Santiago is Compliance Manager of Office of Regulatory Affairs, University of Pennsylvania, Philadelphia, PA.

RESPONSE

Category definitions are limited

Harry Fyke, DVM

Hypothermia has been widely used as an acceptable method of anesthesia in altricial neonatal rodents for many years. Although it has been shown to be safe and effective¹, controversy exists as to whether it is humane.

A major concern is that during the chilling process, peripheral nerves that control movement are affected sooner than nerves that transmit sensation. This would be similar to using neuromuscular-blocking drugs that result in immobilization without analgesia². These drugs are considered unacceptable for

surgical procedures without the concurrent use of another anesthetic. Another major concern is the likelihood that rapid cooling and re-warming cause pain. This is well documented in humans and adult animals³. There is no evidence to suggest that neonates do not experience pain from this process. A modified technique for producing hypothermia, which uses an insulated sleeve, may reduce pain resulting from cooling³ but has not been shown to eliminate pain altogether.

Many researchers tend to use techniques that are familiar to them. While this may increase their own comfort level, the same may not be true for their subjects. Newer safe and effective methods of anesthesia for neonatal rodents have been described^{2–5}. Researchers should be required to provide evidence that more appropriate methods of anesthesia will confound their results before being permitted to use other methods. In fact, considering that hypothermia has been shown to cause pain in humans, USDA regulations would require a search for alternatives prior to its use in species covered by the USDA^{6,7}.

There is no mention of consultation with the attending veterinarian in this scenario. Such consultation is not only required by the regulations, but should be an integral part of the decision process any time anesthetics are used. In this case, the researcher may not be aware that hypothermia can cause many physiologic changes such as respiratory depression, decreased heart rate, metabolic acidosis, alterations in gas transport and decreased metabolism of glucose and citrate in the liver, any of which might affect study results.

Another point worth raising is that any procedure that might produce pain that could persist beyond the duration of anesthesia should include an appropriate analgesic.

The USDA pain categories mandate the placement of any painful survival procedure done under hypothermia anesthesia in category E, because this method does not use drugs. This illustrates the limitations of the present categories. There are many instances where pain can be lessened or eliminated by means other than drugs, such as acupuncture, therapeutic ultrasound and physical therapy. The USDA should consider revising pain categories to recognize the range of therapeutic options (as well as to address the issue of degrees of pain and distress).