Assessing Pain and Distress in Laboratory Animals

Introduction

A key aspect of animal welfare regulations is that pain and distress be minimized whenever possible. The cause of pain and distress could be directly related to the study (the animal is on a tumor study and the tumor growth is affecting the animal’s ambulation), or unrelated to the study (injuries resulting from fighting with cage mates). Because a variety of reasons exist for an animal to experience pain and distress, the following information is provided to help research staff:

- appreciate their personal responsibility for monitoring laboratory animals for pain and distress
- recognize, evaluate, and prevent pain and distress
- understand and adhere to protocol endpoints regarding pain and distress

What is Pain and Distress?

Pain is physical or mental suffering caused by injury or illness. Distress is a response to pain or a stressor that can inhibit the animal’s ability to cope with the situation (e.g. anorexia in response to induced disease or self-aggression in response to psychological stress).

It is assumed that for vertebrates, any procedure that would be expected to cause pain or distress in a human will cause similar pain or distress in an animal.

Personal Responsibility

All individuals working with laboratory animals have an ethical responsibility to plan for, monitor, and alleviate pain and distress in their animals. If a procedure is expected to cause pain, appropriate sedation, analgesia, and/or anesthesia must provided.

Studies must be designed to minimize pain and distress. If pain or distress is unavoidable, scientific justification must be included in the protocol and approved by the IACUC. The earliest possible endpoint compatible with meeting study objectives must be used.

Failure to plan, monitor, and treat for pain and distress can result in unnecessary discomfort to the animal, poor study data, research paper rejection, and/or mandatory staff retraining. Anyone working with laboratory animals has a personal responsibility to reduce, monitor, and alleviate pain and distress in order to preserve animal health and welfare as well as research integrity.
Recognizing Pain and Distress

Some animals do not show signs of pain as obviously as humans do which can make assessing pain and distress difficult. Prey species, such as rodents, rabbits, and livestock, may mask their signs. Therefore, investigators need to be aware of species-specific behaviors and monitor animals regularly for signs of pain and distress.

General Signs of Pain and Distress:
- avoidance of cage mates
- reduced activity
- vocalization / or silence in vocal species
- aggression
- altered gait
- hunched posture
- rough hair coat
- reduced grooming
- decreased food or water consumption
- decreased fecal or urine output
- dehydration
- labored breathing
- squinted / sunken eyes
- self-mutilation

If you see any of the above signs in a lab animal, follow procedure outlined in your IACUC approved protocol. If you are unsure how to handle the situation, call an RAR veterinarian or veterinary technician. If the situation is an emergency, page the emergency vet pager to reach the on-call veterinarian (see contacts below).

Humane Endpoints

Animal welfare regulations require that experiments are designed in such a way to prevent or minimize pain and distress whenever possible. For some experiments, pain and distress are necessary to achieve the goals of the study. In addition, there is always the possibility of unexpected pain and distress in laboratory animals. To address these issues, humane endpoints must be established. Endpoints must be described in the protocol the animal is being held under. Otherwise, universal endpoints established by IACUC will apply. Fulfillment of just one criterion can constitute grounds for euthanasia. If euthanasia is required, it must be performed via the route approved in the investigator’s IACUC protocol, or by RAR veterinary staff.

Universal Euthanasia Criteria (exceptions must be justified in your IACUC protocol)
- Weight loss: loss of 20-25% (depending on attitude, weight recorded at time of arrival, and age: growing animals may not lose weight, but may not gain normally) or cachexia and muscle wasting.
- Inappetance: complete anorexia for 24 hours in small rodents, up to 5 days in large animals; partial anorexia (less than 50% of caloric requirement) for 3 days in small rodents, 7 days in large animals.
- Weakness/inability to obtain feed or water: Inability or extreme reluctance to stand which persists for 24 hours, assuming that the animal has recovered from anesthesia.

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Universal Euthanasia Criteria cont.

- Moribund state: In rodents, evidenced by a lack of sustained purposeful response to gentle stimuli (example of purposeful response - weak attempt to get up); in larger animals, evidenced by depression coupled with body temperature below 99°F (assuming in either case that the animal has recovered from anesthesia).

- Infection: infection involving any organ system (either overt, or indicated by increased body temperature or WBC parameters) which fails to respond to antibiotic therapy within an appropriate time and is accompanied by systemic signs of illness.

- Signs of severe organ system dysfunction non-responsive to treatment, or with a poor prognosis as determined by an RAR veterinarian:
  - Respiratory: dyspnea, cyanosis.
  - Cardiovascular: blood loss or anemia resulting in hematocrit below 20%; one transfusion may be performed.
  - Gastrointestinal: severe vomiting or diarrhea, obstruction, intussusception; peritonitis, evisceration (immediate euthanasia required).
  - Urogenital: renal failure characterized by elevated BUN, creatinine or uroperitoneum.
  - Nervous: CNS depression, seizures, paralysis of one or more extremities; pain unresponsive to analgesic therapy.
  - Musculoskeletal: muscle damage, bone injury, locomotor deficits, etc. resulting in inability to use the limb, unless anticipated as part of the study.
  - Integumentary: Non-healing wounds, repeated self-trauma, second or third degree burns from heat support.

For Veterinary Assistance

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<tr>
<th>Research Animal Resources (RAR)</th>
<th>(612) 624-9100</th>
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<tr>
<td>RAR After Hours &amp; Emergency Vet Pager</td>
<td>(612) 899-6285</td>
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Additional Information

Many objective tools exist to help evaluate pain and distress. See links for additional information:

- Nestle Scoring………. [http://lan.sagepub.com/content/47/3/153.long](http://lan.sagepub.com/content/47/3/153.long)
- Grimace Scale………. [http://www.nature.com/nmeth/journal/v7/n6/fig_tab/nmeth.1455_F1.html](http://www.nature.com/nmeth/journal/v7/n6/fig_tab/nmeth.1455_F1.html)