

RECOGNITION AND ASSESSMENT OF PAIN, STRESS, & DISTRESS IN LABORATORY ANIMALS

ACUC GUIDELINES FOR ADMINISTRATION OF ANALGESICS & ANXIOLYTICS

(Excerpted from Recognition and Assessment of Pain, Stress and Distress in Laboratory Animals, Recognition and Alleviation of Pain and Distress in Laboratory Animals, NRC, Washington, DC 1992)

Introduction

The recognition of pain, pain-induced distress, and non-pain-induced distress in animals is necessary for proper clinical management of laboratory animals to ensure compliance with current guidelines and regulations. Species-specific behaviors and clinical signs are listed in this document to assist the research staff at the University of Virginia in deciding whether to pharmacologically intervene in pain and distress, and the appropriate intervention to be taken.

Recognition of Pain

Well-being in animals is associated with normal species-typical behaviors. A well animal will interact with its cage mate or handler, exhibit curiosity through exploration of its surroundings, keep itself well-groomed, show no impairment of its movement or prehension of food and water, grow normally (e.g., similar to its conspecifics) and have normal reproduction. Table 1 lists behavioral signs commonly associated with pain or distress in many animal species.

Table 1 Commonly Seen Postural and Behavioral Signs of Pain in Many Species

Sign	Explanation
Guarding	Attempting to protect, move away or bite
Vocalization	Crying out when manipulated or forced to use an affected area
Mutilation	Licking, biting, scratching, shaking or rubbing an affected area
Restlessness	Pacing, lying down, and getting up repeatedly, or shifting weight
Sweating	In species that sweat (horses)
Recumbency	Lying down for an unusual length of time
Depression	Reluctance to move or difficulty in rising
Abnormal appearance	Head down, abdomen tucked up or a hunched appearance, facial distortion or membrane pallor

An animal in severe pain may flail about, writhe, and exhibit rigidity or reluctance to move. Wounded or painful areas may be wet from excessive licking or chewing and be red and swollen. The animal may look repeatedly at the painful area. The animal may vocalize when in pain: whine, groan, whimper, grunt or growl. Not all vocalization is associated with pain as restraining an animal may elicit distress vocalization particularly in swine and nonhuman primates.

Chronic or persistent pain is different from acute pain and its clinical manifestation can be harder to recognize. Chronic pain is more likely to lead to distress and maladaptive behaviors. Signs of chronic pain include decreased appetite, weight loss, reduced activity, irritability and decreased reproductive performance. Some chronic conditions can lead to self-injurious behavior such as chewing the skin to the point of creating an open wound.

Pain thresholds are similar among all species and breeds of animals; however, the perceived intensity and tolerance of pain is highly variable among individuals. There are notable differences between animals and humans related to the site of pain. Abdominal surgery is thought to be less painful in four-legged animals than in humans because humans use their abdominal muscles to a greater extent in maintaining posture and for walking. A median sternotomy produces low to moderate pain in humans but more pain in animals because four-legged animals use their forelimbs for walking. A lateral thoracotomy is less painful in animals than humans because animals rely more on abdominal respiration and humans more on thoracic respiration. Table 2 lists common behavioral signs of pain or distress for several species.

Table 2 Species-specific Behavioral Signs of Pain as Criteria for Administering Analgesics

Species	Behavioral Sign
Nonhuman Primate	<ol style="list-style-type: none">1. Loud, persistent vocalization2. Crouched posture with facial grimace3. Ungroomed or increased grooming attention from cage mate4. Clenching or grinding teeth5. Moaning and shaking6. Feed and water refusal7. Weight loss
Dogs	<ol style="list-style-type: none">1. Stiff body movement or reluctant to move2. Hunched posture, abdomen tucked up3. Panting in cool room4. Whimper or howl5. Incessant licking of a body area6. Guard painful area by biting or scratching7. Feed and/or water refusal8. Weight loss
Cats	<ol style="list-style-type: none">1. Stiff body movement or reluctant to move2. Hunched posture, abdomen tucked up3. Incessant licking of a body area4. Unkempt, ungroomed

	<ol style="list-style-type: none"> 5. Violent reaction to touching a painful area 6. Feed and/or water refusal 7. Weight loss
Rabbits	<ol style="list-style-type: none"> 1. Appear apprehensive, anxious, dull, or inactive 2. Squeal or cry 3. Teeth grinding 4. Tonic immobility (play dead) 5. Feed and/or water refusal 6. Weight loss
Rodents	<ol style="list-style-type: none"> 1. Decreased activity 2. Pilo-erection 3. Rapid, shallow respiration 4. "Red tears" in albino rats 5. Vocalize, pitch may be above human hearing 6. Aggressive 7. Feed and/or water refusal 8. Weight loss 9. Unkempt fur (not grooming) 10. Hunched appearance
Sheep and Goats	<ol style="list-style-type: none"> 1. Dull, depressed, head held low 2. Rapid, shallow respiration 3. Grunting or grinding teeth 4. Persistent licking or kicking at an area 5. Reluctance to move 6. Standing and lying down repeatedly 7. Feed and/or water refusal 8. Loud, persistent vocalization 9. Weight loss
Swine	<ol style="list-style-type: none"> 1. Dull, depressed, head held low 2. Rapid, shallow respiration 3. Grunting or grinding teeth 4. Reluctance to move 5. Loud, persistent vocalization
Amphibians and Reptiles	<ol style="list-style-type: none"> 1. Flinching and muscle contraction (move limb away from unpleasant sensation) 2. Weight loss
Birds	<ol style="list-style-type: none"> 1. Vocalization 2. Excessive movements 3. Weight loss 4. Feed and/or water refusal 5. Eyes partially closed, wings flat, neck retracted

Effective: 10-01-01

Rev.: 04-02-02

Rev.: 05-15-07

In general, an analgesic agent should always be administered after any type of surgical procedure unless there is a scientific justification for not doing so. That justification must have been approved in the animal care and use protocol by the IACUC after considering all classes of analgesic drugs. Recommended dosages for analgesics for several species are given in Table 3. Non-pharmacological means of attenuating pain and distress should also be considered and used when appropriate. Examples of non-pharmacologic interventions include using a softer bedding material for limb pain, or providing water and/or wetted feed in a dish on the cage floor to eliminate the need for a rodent to reach for its water.

Effective: 10-01-01

Rev.: 04-02-02

Rev.: 05-15-07

Table 3 Recommended Dosages of Analgesics by Species

Species	Drug	Dose (mg/kg)
Nonhuman Primate	Buprenorphine	0.01-0.03 BID SC
	Acetaminophen	5-10 PO TID
	Carprofen	2 PO or SC once daily
	Meloxicam	Initially 0.2 PO or SC once then 0.1 PO or SC once daily for up to one week
Dogs	Buprenorphine	0.01-0.02 BID SC
	OR Ketoprofen	1 IM BID
	OR Fentanyl patch	<10kg 25µg/hr; 11-20kg 50µg/hr; 20-30kg 75µg/hr; >30kg 100µg/hr
	Meloxicam	Initially 0.2 PO or SC once then 0.1 PO or SC once daily for up to one week
	Banamine	1mg/kg IM do not repeat
Cats	Buprenorphine	0.005-0.01 SC BID
Rabbits	Buprenorphine	0.02-0.1 SC BID
	Ketoprofen or Carprofen	2 SC once daily
	Meloxicam	Initially 0.2 PO or SC once then 0.1 PO or SC once daily for up to one week
	Banamine	1.1mg/kg IM BID
Rodents	Buprenorphine	Mice 0.1-0.2 SC BID Rat 0.2-0.5 SC BID Guinea pig and Hamster 0.05 SC BID
	Ketoprofen or Carprofen	2-5 SC once daily
	Meloxicam	Initially 0.2 PO or SC once then 0.1 PO or SC once daily for up to one week
Sheep and Goats	Buprenorphine	0.005 SC BID

	Fentanyl patch	<10kg 25µg/hr, 11-20kg 50µg/hr, 20-30kg 75µg/hr, >30kg 100µg/hr
	Banamine	0.5mg/kg BID IM
	Meloxicam	Initially 0.2 PO or SC once then 0.1 PO or SC once daily for up to one week
Swine	Buprenorphine	0.005-0.05 SC BID
	Ketoprofen	1 IM BID
	Carprofen	2 SC once daily
	Fentanyl patch	<10kg 25µg/hr, 11-20kg 50µg/hr, 20-30kg 75µg/hr, >30kg 100µg/hr
	Meloxicam	Initially 0.2 PO or SC once then 0.1 PO or SC once daily for up to one week
Birds	Buprenorphine	0.05 SC BID
Amphibians and Reptiles	Depends on species	

The decision to use anxiolytic drugs is one that requires subjective judgment. There are many occasions where animals will show behaviors that are interpreted as having their origin in the perception of pain but are not responsive to opioid analgesia. These same animals at times do respond to anxiolytics or tranquilizers. Anxiolytics should not be used as a substitute for analgesia, but rather as an adjunct to supplement analgesia. Table 4 lists recommended dosages of commonly used anxiolytics and tranquilizers.

Table 4 Recommended Dosages of Commonly Used Anxiolytics and Tranquilizers

Species	Drug	Dose (mg/kg)
Nonhuman Primate	Acetylpromazine OR Diazepam	0.2 BID SC IM IV 1.0 BID IM IV
Dogs	Acetylpromazine OR Diazepam	0.03-0.05 BID SC IM IV 1.0 BID IM IV
Cats	Acetylpromazine OR Diazepam	0.03-0.05 BID SC IM IV 1.0 BID IM IV
Rabbits	Acetylpromazine OR Diazepam	1.0 BID SC IM IV 2.0 BID IM IV
Rodents	Acetylpromazine OR Diazepam	Mice 2-5 BID SC IM IP 5.0 BID IP

	Acetylpromazine OR Diazepam Acetylpromazine OR Diazepam	Rat 1.0 BID SC IM IP 2-4 BID IM IP Guinea pig / Hamster 0.5-1.0 BID SC IM IP 5.0 IM IP
Sheep and Goats	Acetylpromazine OR Diazepam	0.04-0.06 BID SC IM IV 0.5-1.5 BID IM IV
Swine	Acetylpromazine OR Diazepam	1.1-2.2 BID IM IV 0.5-1.5 BID IV
Birds	Diazepam	1.0-1.5 BID IM IV

IM = intramuscular
SC = subcutaneous

IV = intravenous
BID = every 12 hours

IP = intraperitoneal
TID = every 8 hours

As a rule of thumb, all animals that receive an incision of any type should receive an analgesic post-procedurally. For minor skin incisions that do not invade a body cavity or cause more than minor trauma to musculoskeletal tissues, a long acting local anesthetic should be infiltrated subcutaneously (bupivacaine = Marcaine 0.25%). The dose used should not exceed 0.5 to 1 cc/kg. If larger volumes are required, Marcaine can be diluted to 0.125% in sterile saline and the volume administered doubled. In the case of thoracotomies, rib blocks with bupivacaine are preferred. If pain duration is anticipated to be less than 2 hours, lidocaine 2% with epinephrine can be substituted for bupivacaine (with less risk of toxicity). Bupivacaine will last 8-12 hours.

In almost all other surgical manipulations, post-operative analgesia with or without adjunctive anxiolytic should be administered. Analgesics are most effective, often requiring a diminished dose, when administered prior to creation of a surgical wound. Pre-emptive analgesia should be given prior to, or at the time of, induction of anesthesia. A decreased dose of analgesic may be possible when combined with use of Marcaine.

The duration of analgesic administration should be based upon the amount of tissue trauma associated with the procedure and the behavioral signs demonstrated by the animal. For most thoracic, abdominal and orthopedic procedures, analgesia should be given for a minimum of three days, longer if behavioral signs demonstrate the presence of chronic pain.

If you have questions regarding the necessity or use of analgesics or anxiolytic agents in laboratory animals, call the Center for Comparative Medicine at 924-2741 and speak with one of the University veterinarians.