Mice: Analgesia and Anesthesia Formulary

The appropriate use of pain medications (analgesics) and anesthetics is a critical aspect of the proper care and use of animals in research. Not only are they required by both the ethical conduct of research and regulatory agencies when an animal experiences more than momentary pain or discomfort, but minimization of pain and stress typically results in better, more reproducible results. (Resources to Aid in Recognition of Pain and Distress; Pain Relief In Animals)

The following is a listing of dosages for many of the more commonly employed analgesics and anesthetics, and is meant as a guide during protocol preparation. In all cases, animals may only be utilized with a currently IACUC approved protocol and any changes in the analgesics or anesthetics must be accompanied by an amendment to the protocol even if the medication is listed in this formulary.

The formulary is **not** meant to be an all-inclusive listing. If you would like to use a drug not included in this listing, please contact a DLAM veterinarian to discuss its use in your protocol.

Variability amongst models

The doses listed in the formulary were collected from the comparative medicine literature, but these articles typically evaluate rodent drug doses using the *most common* strains or stocks and *healthy* animals in the case of large animal trials. Moreover, it is well recognized there can be considerable variation in the effect of drugs across individuals, strains and stocks, as well as between sexes. Thus, it is critical to evaluate all animals, including strains or models that you have created, to determine if the doses and/or drugs chosen are appropriate in your study.

If your research focuses on a particular body system, it is also important to consider the effect of the drug on that system. We encourage you to work with the Division of Laboratory Animal Medicine (DLAM) veterinarians and/or review the literature for this information. There have been a considerable number of articles in the comparative medicine literature focusing on these considerations.

Selecting an appropriate analgesic or anesthetic

In most cases, the formulary includes information regarding the time of onset and duration of effect. In general, the opiates are shorter-acting than Non-Steroidal Anti-inflammatory Drugs (NSAIDs) and can be effectively used at the time of the procedure to dampen the induction of the pain pathways. The pain and discomfort which occurs later is typically attributed to inflammation, therefore, NSAIDs are used in many post-operative regimens. When using multiple drugs, it is also critical to consider their potential interactions. For example, certain opiates can actually antagonize each other's actions, thus cancelling their beneficial effect.

Additional resources

Currently there are a number of excellent textbooks about laboratory animal anesthesia and pain management available online through the UNC Library system. A select few are as follows:

1) http://search.lib.unc.edu/search?R=UNCb6247400 Laboratory animal anaesthesia, Flecknell, P. A. Elsevier/Academic Press, Amsterdam, Boston, 2009.
2) http://search.lib.unc.edu/search?R=UNCb6554539 Handbook of laboratory animal science.Volume 1, Essential principles and practices, CRC Press, Boca Raton, FL, 2011.

Mouse Anesthetics						
Drug	**Dose (mg/kg)**	**Route**	**Effect**	**Potential side effects**	**Notes**	**Preparation/ Use**
Ketamine/ Acepromazine	100/5.0 or 100/2.5	IP, IM	immobilization/ anesthesia for minor procedures; 20 - 30 min			if animal becomes "light", administer an additional half-dose of ketamine only- not the combination
Ketamine/Diazepam	100/5.0	IP	immobilization/ anesthesia; 20 - 30 min			do not mix in same syringe, drugs will precipitate if animal becomes "light", administer an additional half-dose of ketamine only- not the combination
Ketamine/Midazolam	100/5.0	IP	light anesthesia only - not surgical; 20 - 30 min	respiratory depression		if animal becomes "light", administer an additional half-dose of ketamine only- not the combination
Ketamine/ Dexmedetomidine	75/1.0 females	IP	surgical plane of anesthesia in most strains ~20 - 30 min	hypothermia, depression of cardiovascular / respiratory function	excellent muscle relaxation and analgesia	dexmedetomidine reversed with atipamezole (1.0 mg/kg IM, IP, SC, IV) to speed recovery, if animal becomes "light", administer an additional half-dose of ketamine only- not the combination
	40/1.0 males	IP				
	50/1.0 to 100/1.0	IP				
Ketamine/Xylazine	100/10	IP	depth of anesthesia can highly variable amongst strains, sexes, and individual animals; ~20-30 min	reduction of cardiac output		if animal becomes "light", administer an additional half-dose of ketamine only- not the combination
Ketamine/Xylazine/ Acepromazine	100/2.5 - 10/2.5-3.0	IP	addition of acepromazine increases depth and duration of anesthesia		literature recommends titrating the mixture with each strain	multiple other dose combinations have been published, consult with DLAM vets if this dose does not seem to be effective in strain of interest, if animal becomes "light", administer an additional half- dose of ketamine only- not the combination

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Drug	Dose (mg/kg)	Route	Effect	Potential side effects	Notes	Preparation/ Use
Pentobarbital (Nembutal)	40 - 50	IP	surgical plane of anesthesia ~15 - 60 min	severe respiratory and/or cardiovascular depression	very narrow safety margin; with widely variable responses	should be diluted to a 6.0 mg/ml solution
Propofol	26	IV	typically used for induction; 2 - 3 min of surgical anesthesia	apnea, hypotension	must be delivered IV due to pain /tissue damage if delivered extravascular	
Thiopental	30	IV	short-term (10 - 12 min) anesthesia	IV use only; hypothermia, respiratory and cardiovascular depression	marked accumulation in tissues	
Tribromoethanol	125 - 250 using a 1.25% solution	IP	15 - 30 min duration	single use only	peritonitis has been reported, particularly with repeated dosing and/or incorrectly formulated solutions	refer to TBE preparation instructions
Isoflurane	3.5 - 4.5% induction / 1.5 - 3.0% mainten-ance	inhaled			low risk, rapid recovery	Requires inhalational anesthetic training; Isoflurane Drop Method
Agents to reverse or antagonize anesthetics or anesthetic effects						
Drug	**Dose (mg/kg)**	**Route**	**Agent Antagonized**		**Notes**	
Atipamizole	0.1 - 1.0	IM, IP, SC, IV	xylazine or dexmedetomidine		highly specific alpha-2 adrenoreceptor antagonist; dose required is dependent on anesthetic dose given	
Doxapram	5.0 - 10	IM, IV			to increase respiratory effort post-anesthesia	
Atropine	0.04	SC, IM, IP			reduces salivary and bronchial secretions;	increases heart rate to counter anesthesia - induced bradycardia

Mouse Analgesics

NOTE: There is considerable strain and individual animal variation in response to medications. With some exceptions, female mice have been found to be more sensitive to pain than males and analgesics may show a stronger effect in males. All rodents should be assessed for analgesic effect after analgesic administration. Keep in mind that mice are nocturnal. Thus, it is believed their pain levels may be best evaluated at night. Administration of analgesics in food or water may lead to inadequate dosing due to lack of palatability, degradation by hydrolysis over time (in water), diurnal patterns of food consumption, pain induced anorexia (in rodents, eating and drinking are paired), or reduction of drinking. Animals should be acclimatized to the medicated water prior to the procedure and consumption measured to verify adequate fluid intake.

Opioids - *can be associated with pica and/or inappetence (dose and strain related effect). Consider potential adverse effects: respiratory depression, GI stasis, excitement (typically only at higher doses) and/or sedation.*

Drug	Dose (mg/kg)	Route	Interval (hours)	Effect	Notes
Buprenorphine	0.05 - 0.1 0.1 - 0.25 *Buprenorphine SR (sustained release) is available for use at 0.5- 1.0 mg/kg.	SC, IV PO SC	6 - 8 6 –8 48-72	postoperative pain relief	maximum analgesic effect reached 30 min post injection; however, if using injectable anesthesia, it is recommended not to use buprenorphine until the mouse has recovered to the sternal position*
Buprenorphine Extended Release (ER/XR)	3.25 mg/kg	SC	48-72	Postoperative pain relief	Animalgesiclabs.com
Butorphanol	1.0 - 2.0	SC, IM	4	mild to moderate pain	best used only preoperative or intraoperative due to short duration
Morphine	2.0 – 5.0	SC	hourly		very effective analgesic
	10	SC	2 - 4		

NSAIDS - *adverse effects may include blood dyscrasias, interference with platelet function and the targeting of GI, hepatic and renal tissues during prolonged administration. These effects are rarely of significance when treating for 2-3 days. Contraindicated in pregnant animals.*

Drug	Dose (mg/kg)	Route		Effect	Notes
Acetaminophen	200	PO		mild pain, little anti-inflammatory action	
Carprofen	5.0 5.0	SC PO	12 - 24 12 - 24	post-operative pain	commonly used, wide safety margin; works well when combined with an opiate
Ketoprofen	5.0	SC		moderate pain	commonly used
Meloxicam	5.0	SC, PO	12 - 24	post-operative pain	
Ibuprofen	15 - 30	PO	24		
Naproxen	57 - 350	PO	24		

Local anesthetics - *stop nerve transmission by blocking sodium channels; can reduce need for systemic postoperative analgesics and allow reduced dose of intraoperative anesthesia; epinephrine (vasoconstrictor) can be added (except in extremities) to reduce risk of systemic absorption*					
Drug	**Dose (mg/kg)**	**Route**	**Interval**	**Effect**	**Note**
Lidocaine	max dose: 4.0			duration of effect: 60 - 90 min	if epinephrine included at a 1:200,000 concentration, duration will be increased by 50%
Bupivacaine	max dose: 1.0 - 2.0 (less than 100ul of 0.25% solution)				

References:

Handbook of laboratory animal science. Hau, Jann; Schapiro, Steven Jay. 3rd ed. Boca Raton: CRC Press/Taylor & Francis.Group, 2011.

Laboratory animal anaesthesia .Flecknell, P. A. Elsevier/Academic Press: Amsterdam ,Boston; 2009.