Anesthesia and Analgesia in Laboratory Animals at UCSF

I. Overview:

Standard of care in animal pain management

Animal anesthesia, analgesia and pain management are crucial components of the animal use protocol. The standard of care at UCSF is to prevent animal pain whenever possible and to treat animal pain whenever diagnosed. Exceptions to these principles are permitted only in the minority of protocols approved by the Institutional Animal Care and Use Committee as USDA Category E (currently UCSF IACUC Category C).

Multi-modal anesthetic and analgesic regimens combine drugs from a variety of classes. They are designed to maximize the desired effects while minimizing those unhealthy side effects that occur with over-reliance on a single agent.

The ideal anesthetic/analgesic regimen

The ideal anesthetic/analgesic regimen must balance several goals:

1. It should provide pre-emptive analgesia so that animal pain is already being treated as the general anesthetic is wearing off, to prevent sensitization ("ramp-up") of pain sensory mechanisms, and to lower the overall amount of general anesthetic required for the procedure.
2. It should be precisely titratable to assure that animals receive adequate anesthesia to block pain sensation, to produce unconsciousness, and to produce immobility without experiencing hemodynamic instability or life-threatening anesthetic overdoses.
3. It should not interfere with the study that the animals are on.
4. It should not result in unhealthy post-operative side-effects.
5. It should not cause pain or distress on induction or recovery
6. It should be compatible with available equipment and available medications

To meet the first goal, LARC and IACUC advocate pre-emptive analgesia, using some combination of four drug classes 30 minutes or more prior to the start of surgery. The four classes of injectable drugs are:

- opioid analgesics (such as buprenorphine);
- non-steroidal anti-inflammatory drugs (such as carprofen, meloxicam, ibuprofen);
- dissociative anesthetic/sedatives (ketamine, tiletamine)
- local/regional anesthetics (lidocaine, bupivicaine, proparacaine)

The disadvantages of this approach are that they add pre-anesthetic injection that may be distressful to the animals, that some drugs may slow anesthesia recovery, and that some are Controlled Substances requiring special storage and records keeping.

Volatile anesthetics (isoflurane, halothane, sevoflurane) delivered via a precision vaporizer best meet the second goal. Adjusting the inhaled percentage of anesthetic gas to deepen anesthesia is far safer than repeated redosing of injected drugs. Volatile anesthetics are easier to decrease as well, even compared to drugs for which there is an injectable antagonist or reversal agent. A major shortcoming of the inhalant anesthetic agents is the lack of residual analgesia once the vaporizer has been turned off.

The very best anesthetic plans are only as good as the skill and care with which they are applied. Training is available from the IACUC training and compliance staff [link to Training info]. Veterinary consultation is encouraged when planning any potentially painful study (and is required by law for USDA-covered species).

Drug dosages and frequencies of administration

Drugs should be listed in the protocol with approximate dose ranges. These are starting points which must be titrated up or down for the individual animal, or for the particular application (procedures conducted, animal age and strain differences). When laboratory experience finds that recommended dose ranges are consistently too high or too low for the particular application, the veterinarian should be informed, and a protocol modification submitted to the Institutional Animal Care and Use Committee.

Anesthetics are always titrated to effect. It is not acceptable to conduct surgical procedures unless the animal is fully anesthetized.

Analgesic doses and frequencies are more difficult to gauge. Caution is required for overnight pain management. Most analgesics administered at 5 pm will not still be effective at 8 am the next morning. Newer, longer-lasting non-steroidal anti-inflammatory analgesics may have longer durations of action than available opioids; they are frequently co-administered with an opioid to combine potency of effect with duration of action.

Safe and effective animal anesthesia

General guidelines on use of anesthetics and analgesics are posted [http://www.research.ucsf.edu/aw/Policies/awGlAnes.asp]. Plans for intra- and post-operative monitoring must be included in the IACUC protocol application, and then practiced as written.

Animals should be acclimated to their surroundings for several days prior to major procedures. Supplemental administration of warmed fluids (lactated ringers solution or isotonic saline) and maintenance of body temperature will improve anesthetic safety for the animals.

II. Species-specific considerations

In general, smaller animals have higher metabolic rates and frequently require higher doses at more frequent intervals to achieve the desired effect. Species, strain and age differences often overshadow this general principle however. It is always best to start with a drug regimen developed in the species, age and strain with which the Principal Investigator is working, rather than extrapolate from one species to another.

Mice

Isoflurane is encouraged as the first choice anesthetic in mice. It should be delivered as a known percentage (1-3% for maintenance; up to 5% for induction) in oxygen from a precision vaporizer. [link to *Inhalant anesthetics* later in document]

Anesthetic monitoring of small rodents includes testing of rear foot reflexes *before* any incision is made, and continual observation of respiratory pattern, mucous membrane color and responsiveness to manipulations throughout the procedure. Rectal

temperature and heart rate are monitored electronically during long or involved procedures.

Injectable anesthetics are typically administered by intraperitoneal route. Injectable analgesics and reversal agents are often administered by the subcutaneous or the intraperitoneal route. Intramuscular injections must generally be avoided because of the small muscle mass. Diluting drugs in sterile saline solution will make it easier to accurately measure volume for injection. It may also make some drugs less irritating when injected. Dilution may decrease shelf-life; the LARC standard is to discard drugs within one month of dilution. Vials containing sterle, diluted drugs must be labeled with the contents and the expiration date.

Ketamine-xylazine and ketamine-medetomidine combinations produce short-duration surgical anesthesia in larger species, but are frequently insufficient for major surgical procedures in many strains of mice. An excellent approach is to use a ketamine combination, but then titrate to effect with isoflurane from a precision vaporizer. Safety and efficacy should be demonstrated in a pilot group of animals before a large-scale study is initiated. Partial reversal of the xylazine or medetomidine using yohimbine or atipamezole is possible, and will restore cardiovascular staus more quickly. [link to *Dissociative anesthetics* later in document]

Mice are nocturnal animals, and are frequently housed in groups of nearly identical animals. These two factors make diagnosis of mild to moderate pain challenging. Weight loss is frequently monitored in animals at risk for ongoing pain. Pre-emptive treatment of pain before signs of pain are obvious is recommended.

Isoflurane provides no post-operative pain relief. If used for surgery, concurrent and follow-up use of ketamine and/or buprenorphine and/or a non-steroidal anti-inflammatory will be necessary. LARC veterinary staff recommend injecting the analgesic 30 minutes prior to the *start* of surgery.
[link to *formulary* at end of document]

Rats

Rat anesthesia and analgesia considerations are similar to mouse anesthesia considerations, though some doses vary. In rats, ketamine combinations are more likely to provide adequate surgical anesthesia than in mice, and so may not require supplemental isoflurane. [link to *Dissociative anesthetics* later in document]
[link to *Inhalant anesthetics* later in document]
[link to *formulary* at end of document]

Hamsters

Hamster anesthesia is similar to rat and mouse anesthesia, though some anesthetic doses differ. Peripheral veins are extremely difficult to access in hamsters, limiting some of the anesthetic options.

Rabbits

UCSF works only with *Pasteurella*-negative rabbits, greatly reducing the risk of respiratory disease under anesthesia. Long procedures are best performed using inhalant anesthesia with an endotracheal tube in place. IACUC staff are available to train researchers in this technique. [link to *formulary* at end of document]

Guinea Pigs

Guinea pigs can be difficult to anesthetize, especially on a survival basis. Intravenous injection is difficult. Intramuscular injection is acceptable for non-survival procedures, though animals may self-mutilate at injection sites if they have recovered from anesthesia. Intraperitoneal (IP) administration works well, if the large cecum can be avoided. Guinea pigs may be anesthetized by face mask with volatile anesthetics; endotracheal intubation requires specialized training.

Cats

Cats are readily anesthetized using a variety of injectable or inhalant methods.

Initial restraint of a fractious or frightened cat can be a challenge for the researcher's safety and for the animal's welfare; choice of technique will depend on the skill level of the researchers as well as the individual cat's temperament. Intravenous injection of a fractious cat requires a very high level of skill. Chamber induction with isoflurane can be stressful to the cat, and poses occupational exposure risk to the workers. Intramuscular or subcutaneous injection of sedatives requires a moderate level of skill, and carries some risk of cat bites and scratches. Training is available through the IACUC staff [link], and LARC veterinarians and veterinary technicians can provide direct assistance when necessary.

Non-steroidal anti-inflammatory drugs are useful, but must be used with caution in cats. Do not exceed recommended doses or frequencies of administration. Acetaminophen is never used with cats. [link to *formulary* at end of document]

Dogs

Dogs are easily anesthetized with a variety of techniques. Intramuscular injection of ketamine or ketamine combinations are to be avoided, because of the incidence of behavioral disturbances. [link to *formulary* at end of document]

Nonhuman Primates

Nonhuman primates require specialized handling and restraint to deliver anesthetics without compromising human safety. Ketamine or ketamine-midazolam are typically used by intramuscular injection for initial sedation. Once sedated, primates are easily anesthetized with a variety of techniques. Use of palatable oral medications decreases the need for restraint for medication. [link to *formulary* at end of document]

Swine

Swine are easily anesthetized with a variety of techniques. Ketamine-xylazine is a common intramuscular sedative, but requires a large volume of injection. Use of Telazol® or Telazol® combinations can significantly reduce the volume of injection for larger animals. [link to *formulary* at end of document]

Frogs

Immersion anesthetic (tricaine methanesulfonate, or MS-222) is common, especially for fully aquatic species like *Xenopus*. Once a surgical plane of anesthesia has been reached, anesthesia may be supplemented, but not eliminated, by maintaining the

animal at 4° C. Post-operative pain management can include local infiltration of bupivicaine or with systemic xylazine. [link to *Local anesthetics* later in document]

Sheep

Sheep anesthesia is challenging because of the animals' large size and the unusual ruminant digestive physiology and anatomy. Adult sheep should have food withheld for 24-48 hours prior to general anesthesia, though they should be allowed access to water. Assessing anesthetic depth during constant-infusion ketamine anesthesia requires specialized training and, at UCSF, specialized certification by LARC veterinarians.

Fish

Immersion anesthetic (Tricaine methanesulfonate, or MS-222) is the most common anesthetic in use with fish

Birds

Small birds may be anesthetized by inhalation anesthetics (such as isoflurane) or injectable. Fasting is not generally required in advance. It is vital to maintain adequate warmth during the anesthetic period.

III. Commonly used anesthetics and analgesics

Inhalant agents

Isoflurane and Halothane

The standard inhalant anesthetics for laboratory animal use are either isoflurane or halothane, delivered to effect in concentrations of 1-3% in oxygen (up to 5% for initial induction), using a precision vaporizer.

Advantages: Advantages of inhalant agents include rapid induction and recovery, with the ability to precisely titrate the level of anesthesia.

Disadvantages: Disadvantages include the cost and logistics of using precision vaporizers, occupational exposure concerns, the risk of fatal overdosage if an open system is used instead of a precision vaporizer, and depressed respiratory rate and decreased blood pressure. In addition, once animals awaken from gas anesthesia, there is no residual analgesic activity.

Concurrent use of ketamine combinations and/or opioid and/or non-steroidal anti-inflammatory analgesics is strongly encouraged if the procedure is likely to result in any residual pain.

Several individual laboratories have their own isoflurane vaporizers, and the Laboratory Animal Resource Center maintains several vaporizers for laboratory use both within and outside of rodent barrier facilities [link to info on LARC website? I can't find it!].

Occupational safety is a serious concern. Inhalants must be directly vented out of the room, or (less reliable), adsorbed in a charcoal canister filter. Filters must be weighed and replaced before they reach target weight (usually an increase of 50 gm). Departmental Safety Advisors can provide isoflurane badges to monitor anesthetic exposure. [http://www.ehs.ucsf.edu/]

Nitrous Oxide (N_2O)

May be used 50:50 or 60:40 with oxygen as carrier gas for inhalant anesthetics such as Isoflurane. Nitrous oxide is not acceptable as sole anesthetic agent for surgery, but it may lower the required dose of inhalant.

Other inhalant agents

Other agents and techniques may be used for inhalant anesthesia, only when specifically approved by the IACUC in the animal use protocol.

Methoxyflurane is useful for open-system use in rodents (inside an appropriate fume hood). It is not currently readily available in the United States.

"Open-drop" inhalant anesthesia is acceptable with rodents only for some very short procedures. Diluting halothane in oil may make this option safer for the animals.

Ether is an irritant and a fire hazard, and its use is discouraged.

Carbon dioxide is a potent anesthetic, but concentrations are difficult to control, making the margin of safety unacceptably low

Nitrous oxide is a less potent anesthetic/analgesic gas in most animals than it is in people. It can be used up to 50% in oxygen as a carrier gas for inhalant agents such as isoflurane and halothane, and may thereby reduce the required concentration of the other agent required. Occupational exposure is potentially dangerous so direct venting is required (charcoal filters do not absorb nitrous oxide).

Dissociative anesthetics

Ketamine & Tiletamine

Ketamine is a widely used anesthetic in a variety of species. In low doses, ketamine provides chemical restraint with some analgesia. In higher doses, it may provide short-term surgical anesthesia in some species. In most instances, ketamine is used in combination with other injectable agents.

Tiletamine is similar to ketamine; it is primarily used in combination with zolazepam as the drug Telazol.

Advantages of ketamine: Advantages of ketamine are its wide margin of safety in most species and its analgesic action. In combination with other drugs, it can provide surgical plane of anesthesia for about one half hour.

Disadvantages of ketamine: Disadvantages of ketamine include some irritancy due to low pH, and insufficient anesthesia in some species and strains (especially mice) for some procedures. Ketamine is a Class III controlled substance [link to http://www.ehs.ucsf.edu/PROGRAM%20&%20SERVICES/control%20sub.htm]

Advantages of Telazol: A low volume of injection is required. Like ketamine combinations, it can occasionally produce short-term anesthesia, though rarely of sufficient depth for surgery. It is more useful as an induction agent prior to general inhalant anesthesia, or for chemical restraint for short non-surgical procedures.

Disadvantages of Telazol: Telazol must be stored under refrigeration once reconstituted. It is not safe for use in rabbits (kidney disease). Telazol is a Class III controlled substance [link to http://www.ehs.ucsf.edu/PROGRAM%20&%20SERVICES/control%20sub.htm]

Ketamine combinations

Ketamine-α2-agonists (Xylazine or Medetomidine)

Ketamine may be combined with the α2-agonists Xylazine or Medetomidine [link to *α2-agonists* later in document] in the same syringe to produce a deep level of sedation. In some situations in some species and strains an adequate depth of anesthesia for surgery may be attained. In other cases, this sedation may require an inhalant agent to achieve surgical anesthesia. It is generally safer to titrate to effect with inhalant anesthetic from a precision vaporizer than with supplemental injections of ketamine.

Advantages: Advantages of ketamine-α2-agonist combinations are that they may be combined in one syringe, that they may produce short-term surgical anesthesia with good analgesia, and that recovery can be hastened by reversing the α2-agonist with Atipamezole or Yohimbine.

Disadvantages: Disadvantages of ketamine-α2-agonist combinations are that they will not reliably reach surgical anesthesia in all cases, and that they can cause profound cardiac depression. Xylazine may cause vomiting, especially in cats. Ketamine is a Class III controlled substance [link to http://www.ehs.ucsf.edu/PROGRAM%20&%20SERVICES/control%20sub.htm]

Caution for use: if a ketamine α2-agonist combination is used for surgery longer than 20 minutes, animals will likely require additional anesthetic. Redosing with ketamine rather than the combination is usually safer, as the cardiovascular depression of α2-agonists is often longer-lasting than the sedation or analgesia produced.

Adding acepromazine to the ketamine-α2-agonist combination may result in deeper and/or longer plane of anesthesia in small rodents, especially rats, and possibly some strains of mouse as well.

Ketamine-benzodiazepines (Midazolam or Diazepam)

Ketamine may be combined with the benzodiazepines Midazolam or Diazepam in the same syringe to produce a deep level of sedation. In most cases, this sedation will require an inhalant agent or other anesthetic to achieve surgical anesthesia. In most applications, Midazolam is preferred, as it can be injected intramuscularly; intramuscular injection of propylene glycol (the carrier in injectable diazepam) can cause painful, sterile abscesses and is discouraged.

Advantages: Advantages of ketamine-benzodiazepine combinations are that they may be combined in one syringe and will produce deep sedation with moderate analgesia as well as amnesia. Recovery from ketamine-midazolam is often smoother than recovery from ketamine alone.

Disadvantages: Disadvantages of ketamine- benzodiazepine combinations are that they will not reliably reach surgical anesthesia in most cases. Diazepam should be restricted to intravenous or intraperitoneal use. Ketamine is a Class III controlled substance while the benzodiazepines are in Class IV [link to http://www.ehs.ucsf.edu/PROGRAM%20&%20SERVICES/control%20sub.htm]

Pharmacologically, Telazol is a dissociate-benzodiazepine combination.

Barbiturates

Though superseded in most applications by newer anesthetics, barbiturates still have their place in the animal laboratory. They are most frequently used in terminal or acute studies, as recovery can be prolonged and unpleasant, especially in larger animals. Barbiturates are often the anesthetic of choice when neurophysiological recordings are being conducted, such as visual or auditory evoked responses. Concurrent use of an analgesic (opioid or non-steroidal anti-inflammatory drug) is encouraged as it may improve pain relief with barbiturate use, and lower the required dose of barbiturate.

Sodium pentobarbital (Nembutal) and sodium thiopental (Pentothal) are currently the two most commonly used barbiturates. The duration of action of pentobarbital is considerably longer than that of thiopental.

Advantages: Barbiturates do not depress cortical evoked responses to the extent that other anesthetics might. Animals do not feel pain when they are at a surgical plane of anesthesia. Once stable anesthesia has been achieved, it may be longer lasting than with most other injectable agents. Barbiturates are the most common of the injected euthanasia solutions, as they reliably produce unconsciousness before respiratory depression and death.

Disadvantages: Disadvantages of barbiturates include a narrow margin of safety, primarily associated with respiratory depression. Pain sensation is only decreased at surgical planes of unconsciousness, and may even be heightened (hyperalgesia) at subanesthetic doses. Larger animals may experience a distressful anesthetic recovery. Outside of the vein (perivascular, or intraperitoneal) barbiturates can be irritating; barbiturates for IP injection should be diluted to a strength of 6 mg/kg. Barbiturates are Class II controlled substances, except for some Class III euthanasia solutions [link to http://www.ehs.ucsf.edu/PROGRAM%20&%20SERVICES/control%20sub.htm]

α2-agonists (Xylazine or Medetomidine)

The α2-agonists (Xylazine or Medetomidine) are hypnotic analgesics with significant pain relief. Used as sole agents, they do not produce sufficient depth of anesthesia for even minor surgical procedures. Combined with ketamine [link to *ketamine* earlier in document], and possibly supplemented with inhalants or local or topical analgesics [link to *local anesthetics* later in document], they may be useful during surgery. In some species, medetomidine appears to lead to greater anesthetic depth than does xylazine, and it is more reliably antagonized by atipamezole.

Advantages: α2-agonists are that they produce profound analgesia of short duration, can be combined with ketamine (and in rodents, acepromazine) to produce deeper anesthesia, they are not controlled substances, and they are reversible with IP or subcutaneous atipamezole (yohimbine is sometimes used for xylazine reversal). They are not irritant when injected via intramuscular or intraperitoneal routes.

Disadvantages: Disadvantages in most species include cardiovascular depression (decreased heart rate, decreased cardiac output, and hypotension), which is somewhat controlled by use of atropine or glycopyrrolate. α2-agonists cause a transient hyperglycemia which may have research implications. Xylazine often causes transient nausea and vomiting, especially in cats. Rapid IV administration of reversal agent has produced seizures in some species.

Caution for use: If a ketamine α2-agonist combination is used for surgery longer than 20 minutes, animals will likely require additional anesthetic. Redosing with

ketamine rather than the combination is usually safer, as the cardiovascular depression of α2-agonists is often longer-lasting than the sedation or analgesia produced.

Propofol

Propofol can produce general anesthesia in animals, as a sole agent with continuous infusion for surgery, or as a pre-anesthetic for endotracheal intubation. It is valued for its fast recovery time, even after prolonged administration.

Advantages: Animals recover from propofol in minutes, even after prolonged administration.

Disadvantages: Propofol has minimal analgesia at sub-anesthetic doses. It can be a profound respiratory depression, and may also cause hypotension. Because of its rapid elimination, it must be administered IV, and so is of limited use in small rodents. Unused propofol from an opened ampule should be discarded after use and not stored for future use.

Tribromoethanol (Avertin)

Avertin has been the standard anesthetic in much mouse transgenic work. It produces short-term (15-20 minutes) surgical anesthesia with good muscle relaxation and moderate respiratory depression. It does not produce significant residual post-procedural analgesia. Unless strongly justified in the UCSF animal care and use protocol, use of avertin is restricted to mice only, for a single survival anesthesia plus terminal/acute use.

Advantages: Advantages of avertin are that it is easily administered via the intraperitoneal route, produces good short-term surgical anesthesia, and is not a controlled substance.

Disadvantages: Avertin is not commercially available as a pharmaceutical drug, and must be made in the laboratory from the reagents tribromoethanol and tertiary amyl alcohol. Avertin can cause peritonitis in mice, and the risk of peritonitis, including fatal peritonitis, increases with each time it is used. Post-procedural analgesia has not been demonstrated, so use of another analgesic is generally required. Though surgical anesthesia is short (15-20 minutes), anesthetic recovery can take 40 minutes, during which time the animal must be continually attended and kept warm.

Cautions for use: Avertin must be carefully prepared in the laboratory under aseptic conditions (see recipe below). Stock solution must be kept no longer than one year. Working dilution of 1.25% is recommended -- this is best prepared fresh for use, or stored for no more than one week. Avertin is used only for mice. It is not to be used twice in one animal on a survival basis (if used a second time, that use should be terminal/acute). Where possible, UCSF veterinarians recommend that inhalants replace avertin.

Opioids

Opioid drugs are important components of many surgical anesthesia regimens, and are the most potent available post-procedural analgesics. Drugs in this group vary in their potency as well as their duration of action. Fentanyl, oxymorphone, buprenorphine and butorphanol are the most commonly used opioids in laboratory animal care, though others may be used on occasion. Fentanyl is the most potent of the three, but also the shortest acting. Buprenorphine is longer-acting and is good for most post-operative

applications. Butorphanol may be more efficacious than buprenorphine for birds and for cats. Buprenorphine and butorphanol are mixed agonist/antagonists at different opioid receptors; they produce a less profound respiratory depression than full agonists, but also have a "ceiling effect" in the degree of analgesia produced with increasing doses.

Opioids are most often administered by injection. Oral use is effective, but requires much higher doses because of "first-pass" liver metabolism when absorbed from the gut.

Pre-emptive analgesic use is strongly recommended -- buprenorphine may be administered when the general anesthetic is administered, or at any time during surgery. Respiratory depression is minimal, though sleep time may be lengthened. Pre-emptive use enhances pain management during the immediate post-surgical period. Though it increases animal handling (a stressor), administration of the analgesic 30 minutes prior to the initial surgical incision maximizes the analgesic efficacy in most situations.

Advantages: Opioids are potent analgesics. Concurrent use with inhalant or barbiturate general anesthesia will lower the required dose f the anesthetic.

Disadvantages: Opioids can suppress respiration (more marked effect in fentanyl than in buprenorphine). Opioids may increase locomotor activity, and may cause pica (abnormal ingestion of non-food items such as bedding) in rats. Alternatively, they may sometimes cause sleepiness and slower recovery from general anesthesia. Fentanyl has a very short duration of action in most animal species. Opioids are controlled substances [link to http://www.ehs.ucsf.edu/PROGRAM%20&%20SERVICES/control%20sub.htm]

Cautions for use: Buprenorphine has found favor as the longest-acting opioid analgesic. However, this duration of action is closer to 6 hours in most situations than it is to 12 hours. 12 hours is the absolute maximum dosing interval for use of buprenorphine for post-procedural pain.

Non-steroidal anti-inflammatory drugs (NSAIDs)

The advent of newer, more potent, more specific anti-inflammatory agents has increased their usefulness in laboratory animal use. Most reduce fever, reduce inflammation, and provide varying degrees of analgesia (acetaminophen does not significantly reduce inflammation).

Advantages: Carprofen, ketoprofen, ketorolac, and meloxicam may have duration of analgesic action up to 24 hours. They may be used concurrently with anesthetics, with opioid analgesics, and with local anesthetic/analgesics. Injectable NSAIDs are useful for accurate dosage and administration to small rodents. Oral flavored analgesics are useful for mild pain in nonhuman primates. They are not controlled substances (some are by veterinary prescription only, and must be obtained through Laboratory Animal Resource Center
http://www.larc.ucsf.edu/Purchasing/Purch.cfm#Purchasing%20Veterinary%20Supplies%20and%20Equipment)

Disadvantages: NSAIDs may decrease clotting ability, of possible concern following surgery. Gastric upset and even ulceration may occur, especially with prolonged use. Prolonged use carries the risk of kidney or liver disease.

Cautions for use: Cats are particularly susceptible to toxic effects of NSAIDs. Acetaminophen is never administered to cats; other NSAIDs should be used only at the dose and frequency recommended.

Undesired side effects are more likely with increasing length of usage -- for most situations, limit use of NSAIDs to 3-4 days per animal, except under veterinary supervision. Do not use in dehydrated animals, or in animals with kidney or liver dysfunction.

Local anesthetic/analgesic drugs (lidocaine and bupivicaine)

Local anesthetic/analgesic drugs (lidocaine and bupivicaine) may be useful both during surgery, and post-operatively. They block nerve conduction when applied locally at sufficient concentration. Lidocaine has a fast onset of action, and provides a couple of hours of analgesia. Bupivicaine has a slower onset of action (up to 30 minutes) but provides up to 12 hours of residual analgesia. Both are infiltrated subcutaneously at the surgical site, or (especially in larger animals) may be used regionally (epidural, intrathecal, intercostal).

Lidocaine cream (EMLA or ELAMax) is used topically on shaved, intact skin prior to venipuncture, though it requires 30-60 minutes or more of contact with skin to reach full effect. Tricaine methanesulfonate (MS-222) is a related compound used as a general anesthetic for fish and frogs.

Advantages: Intra-operative use can augment the pain relief of general anesthetics, and reduce the need for frequent redosing. Bupivicaine can augment the post-operative analgesic action of opioids and/or NSAIDs. They are not controlled substances. At appropriate doses, they have minimal cardiovascular effect.

Disadvantages: Intramuscular and intravenous injection should both be avoided. Systemic toxicity (including seizures and death) can result from overdosage (more likely to occur with smaller subjects) and with accidental intravenous injection. Lidocaine may sting when first injected.

Miscellaneous agents

Urethane, choral hydrate, equithesin, sodium thiamylal, α-chloralose have some specialized use in laboratory animal anesthesia. Their use should be discussed with a LARC veterinarian.

IV: Species-specific anesthesia-analgesia formularies:

Links to:
Mouse
Rat
Hamster
Guinea Pig
Rabbit
Cat
Dog
Nonhuman primates
Frog
Fish