Guidelines on Anesthesia and Analgesia in Nonhuman Primates

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1. Purpose
   1. This document has been designed by ULAM veterinary personnel as a guideline for sedation, anesthesia, and analgesia of laboratory nonhuman primates. This is not intended to be an all-inclusive tutorial on drug combinations that can be used in nonhuman primates. The following guidelines are also general recommendations and consequently do not include reference to specific research-associated concerns. If you have questions or comments about this document, contact ULAM Veterinary Personnel (ULAM-vets@umich.edu or 734-936-1696). The ULAM Training Core (ULAM-trainingcore@umich.edu or 734-763-8039) can be contacted to provide training in techniques at no charge.
   2. All surgical procedures, anesthetics, analgesics, antibiotics or other medications used on animals must be approved by the IACUC, described in the animal use protocol and performed by personnel listed on the protocol and appropriately trained for the surgical procedure.
   3. Any techniques or drug protocols deviating from this document must be justified and approved in the IACUC protocol prior to application.
   4. More information on appropriate injection techniques and volumes can be found in Guidelines on Administration of Substances to Laboratory Animals.
   5. More specific information regarding monitoring procedures can be found in Anesthesia and Sedation Monitoring Guidelines.
   6. More specific information regarding anesthetic, sedation and analgesic drug classes can be found in Anesthesia and Analgesia Drug Descriptions.
   7. For any concerns regarding animal health after work hours or on holidays/weekends, contact DPS (3-1131) who will contact the on-call veterinarian.

2. Responsibility
   1. Principal Investigator: Responsible to ensure appropriate anesthesia and/or analgesia is provided for all nonhuman primates undergoing potentially painful procedures, including survival surgery, unless otherwise indicated in the relevant approved protocol.

3. Definitions
   1. Anesthesia: Temporarily induces loss of sensation with or without loss of consciousness.
   3. IM: Intramuscular route of administration.
   4. IV: Intravenous route of administration.
   5. SC: Subcutaneous route of administration.
   6. Sedation: A mild degree of central depression in which the patient is awake but calm.

4. Procedures
   1. Prior to Anesthetic/Analgesic/Sedative Event
      1. Pre-Anesthetic Evaluation
         1. All subjects should be in good health prior to sedation or general anesthesia. If an animal has any pre-existing medical conditions or diseases (anemia, high blood pressure, diabetes, kidney problems, etc.), please consult the ULAM veterinarians prior to the administration of any drugs.
         2. Animals on food or water restriction should preferably have the restriction discontinued for 1-2 days prior to anesthesia.
      2. Handling & Restraint
         1. Nonhuman primates, regardless of origin, are still wild animals and will resist restraint. Direct contact with nonhuman primates without the use of chemical restraint is not recommended.
2. Personal protective equipment should always be worn when handling nonhuman primates to help prevent the transmission of zoonotic diseases (such as herpes B) to the handler or the spread of tuberculosis (TB) to the nonhuman primate.

3. The amount of restraint (generally chemical) and its duration should be kept to the minimum necessary to complete the procedure.

4. For some procedures, positive reinforcement training (PRT) to facilitate cooperation and acclimation to procedural techniques may provide an alternative to general anesthesia.

5. All necessary equipment and reagents for the procedure should be ready prior to restraint.

6. The use of pre-anesthetic sedatives/tranquilizers will help reduce anxiety and the subsequent doses of other agents.

3. Fasting

1. Nonhuman primates can vomit and aspirate stomach contents while under general anesthesia. To help prevent this, animals should be fasted for 12 hours prior to general anesthesia.

2. Juveniles or small species such as marmosets, squirrel monkeys and tamarins should only be fasted 4-6 hours to help avoid hypoglycemia.

3. Do not withhold water prior to anesthesia.

4. In the event of an emergency, when pre-anesthetic fasting is not an option, the primate should be intubated and placed in lateral recumbency (with its body and head lying on its side). The antiemetic metoclopramide may be given 30-60 minutes beforehand to help reduce the likelihood of vomiting and increase gastric emptying. Famotidine may also be given to decrease acid secretion. Suction is also helpful to clear the oral cavity if the animal does vomit.

4. Ocular lubrication such as Paralube® must be used to prevent corneal drying during anesthesia or sedation.

2. Normal Monitoring Parameters

1. More information on anesthetic/sedation monitoring requirements can be found in Anesthesia and Sedation Monitoring Guidelines.

2. The goal of monitoring should be to maintain normal cardiac function, respiratory function, and body temperature. Understanding the basic physiologic effects of the anesthetics used is paramount to correctly interpreting monitoring parameters. More information on anesthetic and sedative effects on physiologic parameters can be found in Anesthesia and Analgesia Drug Descriptions.

3. Under anesthesia, systolic blood pressure should remain above 90 mmHg. Mean blood pressure should remain above 60 mmHg.

4. Table 1: Physiologic Data of Nonhuman Primates

<table>
<thead>
<tr>
<th>Species</th>
<th>Rectal Temp a (°F)</th>
<th>Respiratory Rate b (Breaths per minute)</th>
<th>Heart Rate c (beats per minute)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cynomolgus macaque (Macaca fascicularis)</td>
<td>97-100.4</td>
<td>32-44</td>
<td>107-215</td>
</tr>
<tr>
<td>Rhesus macaque (Macaca mulatta)</td>
<td>98-102</td>
<td>10-25</td>
<td>150-220</td>
</tr>
<tr>
<td>Baboon (Papio spp.)</td>
<td>98-102</td>
<td>29</td>
<td>80-200</td>
</tr>
</tbody>
</table>

a 99.6-99.8°F is acceptable for anesthetized patients
b 10-20% reduction in rates for anesthetized patients is acceptable
c low end of range is acceptable for anesthetized patients

3. Physiologic Support

1. Hypothermia

   1. An external heat source should be provided during the entire anesthetic and recovery period to prevent hypothermia. For examples of approved external heat supplementation products, refer to Anesthesia and Sedation Monitoring Guidelines.

2. Endotracheal Intubation

   1. Airway control via endotracheal intubation is highly desirable during anesthesia and required in some situations where controlled ventilation is mandatory (e.g. thoracotomies).

   2. Administration of inhalation anesthetics is best accomplished via an endotracheal tube.

   3. Intubation of nonhuman primates requires some skill and practice and is best accomplished using a laryngoscope.

   4. Prior to attempting endotracheal intubation, training should be obtained through ULAM.

   5. Contact the ULAM training core (ULAM-trainingcore@umich.edu or 734-763-8039) to set up a time to learn how to correctly and safely perform endotracheal intubation in the nonhuman primate.

3. Vascular access and Fluid Support

   1. The placement of indwelling catheter(s) is advised. The cephalic vein of the forelimb or the saphenous vein of the hind limb are common sites for IV catheter placement. For more invasive catheterization with multilumen central lines, the femoral vein can be used.

   2. Intravenous fluids (e.g. Normosol or Lactated Ringers) should be supplied at a rate of 5-10 ml/kg/hr for procedures of 30 minutes or more. More information on appropriate fluid rates can be found in Guidelines on the Performance of Surgery in Non-Rodent Mammals.

4. Recovery

   1. More information on required monitoring parameters during post-operative recovery can be found in Guidelines on the Performance of Surgery in Non-Rodent Mammals and Anesthesia and Sedation Monitoring Guidelines.
2. Propofol or dexmedetomidine sedation can be used during recovery so animals can be allowed to return to consciousness in a controlled, safe manner.
3. Recover animals in their housing location or cage under supervision. Animals should be directly monitored until able to maintain a parent airway (swallow and cough) and sit up.
4. Food and water should be withheld until the animal is fully recovered and ambulating normally.
5. The use of cameras to enable remote monitoring will eliminate the stress associated with direct observation and may improve the quality and reliability of observations.
6. Pair-housed animals should be reintroduced to their social group as soon as possible to avoid fighting upon reintroduction. Animals should be able to eat, drink, ambulate well, and respond to stimulation before reintroduction. This time is usually 6-24 hours after the animal sits up postoperatively.

5. Sedatives

1. Detailed information on all approved anesthetics and sedatives can be found in Anesthesia and Analgesia Drug Descriptions.
2. Extrapolation of doses from primate to primate should be avoided. The recommended dosages for all of the recommended agents are listed according to species in Appendix A.
3. Generally, New World primates (i.e. marmosets, squirrel monkeys) require higher doses of anesthetics per kilogram body weight compared to Old World monkeys (i.e. macaques, baboons). Examples include ketamine and Telazol®.
4. All sedatives should be administered prior to the intended procedure based on the time to effect, which is generally 15-20 minutes for IM administration. Duration of action for sedative-analgesic combinations for use in minor procedures is generally 15-60 minutes depending upon combination used.
5. Contact ULAM Veterinary Personnel (ULAM-vets@umich.edu or 734-936-1696) with questions regarding specific applications, drugs or medications.

6. Table 2: Sedation Dosage Information

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage and Routea</th>
<th>Duration</th>
<th>Notesa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acepromazine</td>
<td>0.1-0.3 mg/kg SC, IM, IV</td>
<td>– Mild-moderate sedative (alone).&lt;br&gt;– Often used with other injectables (ketamine) to prolong deep sedation.&lt;br&gt;– Can cause profound hypotension, has no useful analgesic properties, and lowers seizure threshold.</td>
<td></td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>0.001-0.032 mg/kg SC, IM 0.5-1 mcg/kg bolus for emergence delirium</td>
<td>– Reduces fear, anxiety, and stress.&lt;br&gt;– Same dosage as medetomidine at 50% of medetomidine dosage guidelines.</td>
<td></td>
</tr>
<tr>
<td>Ketamine</td>
<td>5-15 mg/kg IM (4-10 times IM dose if given PO)&lt;br&gt;Smaller species 15-25 mg/kg&lt;br&gt;Larger species 5-15 mg/kg</td>
<td>30 min</td>
<td>– Moderate sedation, immobilization, some analgesia. No muscle relaxation.&lt;br&gt;– If salivation excessive, can give atropine.&lt;br&gt;– Bite reflex is lost but swallowing and laryngeal reflexes retained.&lt;br&gt;– Neurotoxic in neonatal rhesus macaques.&lt;br&gt;– Caution if risk of cerebral edema. Associated with muscle damage in marmosets.</td>
</tr>
</tbody>
</table>

a Intramuscular (IM), Intravenous (IV), Subcutaneous (SC)

7. Table 3: Sedation Dosage Information (Combination Agents)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Multiple Species Dosea</th>
<th>Duration</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketamine/Dexmedetomidine</td>
<td>5-10 mg/kg ketamine IM 10-30 mcg/kg dexmedetomidine IM</td>
<td>30-40 min anesthesia 60-120 min sleep</td>
<td>Sedation to light surgical anesthesia</td>
</tr>
<tr>
<td>Ketamine/Xylazine</td>
<td>10 mg/kg ketamine IM 0.15-0.25 mg/kg xylazine IM</td>
<td>30-40 min anesthesia 60-120 min sleep</td>
<td>Sedation to light surgical anesthesia. Can prolong anesthesia with repeat doses.</td>
</tr>
<tr>
<td>Ketamine/Diazepamid</td>
<td>15 mg/kg ketamine IM 0.3-1 mg/kg diazepam IM</td>
<td>30-40 min anesthesia 60-90 min sleep</td>
<td>Light surgical anesthesia</td>
</tr>
<tr>
<td>Anesthetic Combination</td>
<td>Dosage</td>
<td>Route</td>
<td>Notes</td>
</tr>
<tr>
<td>------------------------</td>
<td>--------</td>
<td>-------</td>
<td>-------</td>
</tr>
<tr>
<td>Ketamine/Midazolam</td>
<td>5-15 mg/kg ketamine IM 0.05-0.3 mg/kg midazolam IM</td>
<td>Immobilization, light to moderate sedation</td>
<td></td>
</tr>
<tr>
<td>Midazolam/Dexmedetomidine</td>
<td>3 mg/kg ketamine IM 0.015 mcg/kg dexmedetomidine IM</td>
<td>75 +/- 40 min</td>
<td>Deep sedation to light anesthesia</td>
</tr>
<tr>
<td>Butorphanol/Dexmedetomidine</td>
<td>0.3 mg/kg butorphanol IM 0.05 mg/kg medetomidine IM</td>
<td>Adequate for intubation. Maintain with isoflurane for longer procedures.</td>
<td></td>
</tr>
<tr>
<td>Tiletamine/Zolazepam (Telazol®)</td>
<td>1-3 mg/kg IM 4-6 mg/kg IM</td>
<td>15 min in smaller primates. Up to 60 min in macaques and baboons.</td>
<td>Immobilization to deep sedation. Minimal cardiovascular depression, lower drug volumes. Caution if risk of cerebral edema.</td>
</tr>
<tr>
<td>Alphaxalone/Dexmedetomidine</td>
<td>5 mg/kg alphaxalone IM 10 mcg/kg dexmedetomidine IM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alphaxalone/Diazepam</td>
<td>5 mg/kg alphaxalone IM 0.5 mg/kg diazepam IM</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**6. Anesthetics**

1. **Anticholinergics**

   1. May be administered prior to or in conjunction with alpha-2 agonists (e.g., xylazine or dexmedetomidine) or opioids to counteract bradycardia and hyper salivation. Contact the ULAM Veterinary Personnel (ULAM-vets@umich.edu or 734-936-1696) for recommendations regarding appropriate use of these drugs.

2. **Table 4: Anticholinergics Dosage Information**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage and Route</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atropine</td>
<td>0.025-0.05 mg/kg IM, SC, IV</td>
<td>Half-life is 2 hours. Repeat doses at ½ calculated dose. May also prevent or be used to correct opioid-induced bradycardia. Crosses blood brain barrier so can be used for emergencies.</td>
</tr>
<tr>
<td>Glycopyrrolate</td>
<td>0.005-0.010 mg/kg IM, SC, IV</td>
<td>Half-life is 4 hours. Repeat doses at ½ calculated dose. May also prevent or be used to correct opioid-induced bradycardia. Does not cross the blood brain barrier.</td>
</tr>
</tbody>
</table>

**2. Injectable Anesthetics**

1. Consider intubation for any animals undergoing anesthesia to allow for airway control and administration of oxygen or inhalant anesthetic.

2. If, for minor procedures, isoflurane is not utilized, in combinations involving ketamine, anesthesia can be prolonged by supplementing with ketamine only.

3. **Table 5: Injectable Anesthetic Dosage Information**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage and Route</th>
<th>Notes</th>
</tr>
</thead>
</table>

**a** Intramuscular (IM), Intravenous (IV), Subcutaneous (SC)

**b** See Appendix A for species-specific doses

**c** Macaque dose

**d** does not allow intubation

**e** Marked hypothermia, lasts 45-60 minutes
Propofol | 2-8 mg/kg IV to effect CRI 18-24 mg/kg/h | 10-20 minute duration; use a lower dose with premedication. Avoid apnea with slow initial dosing over 60 seconds. To extend anesthesia, give incremental doses (10-20% original). Highly recommended to use with intubation.

Propofol/Fentanyl | 2.4-7.2 mg/kg/h Propofol 10-25 mcg/kg/h fentanyl CRI |

Alphaxalone (Alfaxan®) | 1.0-3.0 mg/kg IV bolus 0.01-0.13 mg/kg/min CRI |

Used for induction and maintenance of general anesthesia. Premed with diazepam (0.5-1.25 mg/kg), ketamine, or midazolam IM. 10 mg/kg IM in marmosets to immobilize (ketamine alternative). May cause apnea.

Pentobarbital | 20 mg/kg IV alone 6.5-10 mg/kg with ketamine |

Replaced by inhalants for the most part. Useful for neurosurgical procedures, imaging studies, or non-survival procedures.

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**3. Inhalation Anesthetics**

**1. Table 6: Inhalation Anesthetic Dosage Information**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage and Route</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoflurane</td>
<td>3-5% Induction 0.5-3% Maintenance</td>
<td>Recovery is fast and reversal of circulatory and respiratory depression is rapid when the inhaled concentration is reduced. Mask or chamber induction may cause airway irritation and distress. Ataxia can be seen in recovery.</td>
</tr>
<tr>
<td>Sevoflurane</td>
<td>4-8% Induction 1.25-4% Maintenance</td>
<td>Excellent for mask induction because of the non-pungent smell. Not irritating to the respiratory tract. Because of the rapid recovery, use caution (and appropriate sedation) during the recovery phase.</td>
</tr>
</tbody>
</table>

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**7. Neuromuscular Blocking Agents (NMBA)**

**1.** Extreme care must be taken to ensure that a proper level of anesthesia and analgesia is achieved prior to administering a neuromuscular blocking agent.

**2.** Neuromuscular blocking agents require special monitoring procedures which are detailed in *Anesthesia and Sedation Monitoring Guidelines*.

**3.** These drugs require additional IACUC approval.

**4.** Concurrent positive pressure ventilation is required. Reversal of NMBAs with neostigmine and glycopyrrolate is possible under specific conditions. Consult the ULAM veterinarians for instructions on NMB reversal.

**5.** See *Anesthesia and Analgesia Drug Descriptions* for additional details.

**6. Table 7: Neuromuscular Blocking Agent Dosage Information**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage and Route</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atracurium</td>
<td>0.25-0.3 mf/kg IV 1.5 mcg/kg/min</td>
<td>Continuous intravenous infusion can be used to maintain and repeated doses are not cumulative.</td>
</tr>
</tbody>
</table>
Vecuronium 0.04-0.06 mg/kg IV Does not induce tachycardia or histamine release.

Pancuronium 0.08-0.1 mg/kg IV Lasts longer than vecuronium and produces mild increases in blood pressure and heart rate.

a Intravenous (IV)

8. Local Anesthetics

1. Appropriate as a supplement to sedation, anesthesia, and analgesia.

2. Table 7: Local Anesthetic Dosage Information

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage and Routea</th>
<th>Onset and Duration</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lidocaine 1-2%</td>
<td>1-4 mg/kg tissue infiltration (toxic dose &gt; 10 mg/kg other species)</td>
<td>Onset: 1-2 min Duration: 1.5-2 h</td>
<td>Can be diluted 1 in 2 to increase accuracy of dosing in smaller primates.</td>
</tr>
<tr>
<td>Bupivacaine 0.25-0.5%</td>
<td>1-2 mg/kg tissue infiltration (toxic dose &gt; 4 mg/kg other species)</td>
<td>Onset: 5-10 min Duration: 4-12 h</td>
<td>Cardio-toxic: aspirate prior to injection, do not give IV. Can be diluted 1 in 2 to increase accuracy of dosing in smaller primates.</td>
</tr>
</tbody>
</table>

a Subcutaneous (SC)

9. Analgesics

1. Signs of Pain in Nonhuman Primates
   May include, but not limited to, the following:
   1. Persistent vocalizations
   2. Restlessness
   3. Lethargy
   4. Inappetance
   5. Ungroomed hair and coat
   6. Crouched posture
   7. Glassy eyes
   8. Social isolation
   9. Abnormal aggression
   10. Increased respiratory rate or effort
   11. Increased resting heart rate
   12. Reluctance to move

2. Any procedure known to produce pain in humans or other species should be assumed to cause pain in nonhuman primates. In these instances, analgesic drugs are indicated to decrease discomfort and to reduce pain associated morbidity and mortality

3. Prevention and Management of Pain
   Prevention of pain by administering analgesics prior to anesthetic recovery is more effective than treatment after signs have developed. Several analgesics are available. Several analgesics are available. Several analgesics are available.
   1. Very low doses of propofol or dexmedetomidine, optionally with an opioid, are very useful for treating post-operative agitation or dysphoria. Please contact the ULAM veterinarians for these recommendations.
   2. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) - appropriate for treating mild to moderate pain or can be used in combination with opioids. Long-term use of NSAIDS has been associated with gastric ulcers and kidney disease. Consult with a ULAM veterinarian concerning repeated administration of these agents.
   3. Opioids - For moderately to very painful procedures (thoracic, abdominal or orthopedic procedures), opioids are the analgesics of choice.
   4. Please contact the ULAM veterinarians for additional analgesia therapy options such as local anesthesia blocks, epidurals, or intra-articular injections.

4. Preemptive Analgesia
   1. Particularly opiates like buprenorphine, can reduce the dose of anesthetics required for surgical anesthesia and increase the respiratory depression associated with anesthetics.
   2. When pre-emptive analgesia is used, consider reducing the dose of anesthetic (whether inhalant or injectable) to the low end of the recommended range.
   3. Anesthetic depth must be carefully monitored and drug doses may need to be titrated to maintain appropriate levels.
   4. With new projects, sexes, or anesthetic analgesic combinations, assess a subset of animals before expanding to use in a larger cohort.
   5. Please see the U-M Policy on Analgesia in Animals Undergoing Surgery for guidance on analgesics used in various surgical procedures.

5. Table 9: NSAID and Opioid Dosage Information

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage and Routea</th>
<th>Duration of Effect</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Ketoprofen

| 2-5 mg/kg IM, IV, SC | 6-8 h | Moderate analgesia. Only give to animals with normal renal function. May can an increased risk of stomach ulcers. Oral forms available. |

### Carprofen (Rimady®)

| 2-4 mg/kg PO, SC, IM | 24 h | Mild to moderate analgesia. Dosing frequency can be increased for 2-3 dosages if required. May can an increased risk of stomach ulcers. |

### Meloxicam

| Loading dose 0.2 mg/kg PO, SC once followed by 0.1 mg/kg once a day for 2-3 days | 24 h | Moderate analgesia. Only COX-2 selective for primates. May be given for up to 4-5 days if needed. Dosing frequency can be increased for 2-3 dosages if required. |

### Meloxicam SR (Sustained Release)

| 0.6 mg/kg SC | 2-3 d | Minimum of 6 weeks between dosing. Contact ULAM to acquire. |

### Opioids

#### Buprenorphine (Buprenex)

| 0.005-0.03 mg/kg SC, IM, IV | 6-12 h | Mild to moderate analgesia. Absorbed slowly (30 minutes to effect). Higher doses may lead to sedation and/or respiratory depression. Almost no sedation at lower doses. Cannot be effectively reversed. Useful to reverse mu agonist opioids while retaining analgesia. |

#### Fentanyl

| 5-10 mcg/kg IV bolus followed by 2-5 mcg/kg/h CRI | Taper at end of surgery. Causes dose-dependent respiratory depression. |

#### Butorphanol

| 0.1-0.2 mg/kg IM, IV | 3-4 h | Mild to moderate analgesia, no sedation or muscle relaxation. Can reverse the sedative and respiratory depressant effects of mu agonist opioids. More respiratory depressant effects in primates than other species. Can work synergistically with other injectables to prolong recovery. |

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**Intramuscular (IM), Intravenous (IV), Subcutaneous (SC)**

### Emergency Resuscitation

1. In the event of an anesthetic crisis, turn anesthetic gases off and contact a ULAM veterinarian at 734-936-1696 immediately.
2. Have emergency drugs and instruments in the surgery suite ready for use.
3. Reverse anesthetic agents, if appropriate.
4. Use the following guidelines to support the animal until the veterinarian arrives:
   - **A** - Ensure a patent **Airway**: Place a cuffed endotracheal tube or confirm patency of tube already in place. If an endotracheal tube is not available, use a face mask to ventilate.
   - **B** - Assist in **Breathing** if necessary: Turn anesthetic gases off and ventilate with pure oxygen. A rapid ventilation rate (> 20 breaths per minute) is recommended to remove carbon dioxide, prevent acidosis, and decrease cerebral pressure.
   - **C** - Provide **Cardiovascular Support** as indicated: This can include rapid chest compressions (30-40% of lateral dimension; 80-120/minute) with the animal in lateral recumbency, and rapid infusion of intravenous crystalloid fluids (50-60 ml/kg bolus) to support perfusion.
   - If no heartbeat can be heard or no pulses felt, then epinephrine should be given IV (see chart below). Reversal drugs should be given if opioids or xylazine have been used.

### Reversal Agents

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**Intramuscular (IM), Intravenous (IV), Subcutaneous (SC)**
Reversal agents are not required with sedation or anesthetic protocols, but can be useful to reduce prolonged recovery times or in the event of anesthetic complications. Analgesic effects are also reversed with the use of reversal agents, and pain management should be modified accordingly.

1. **Atipamezole (Antisedan®):** Can be used to reverse dexmedetomidine and xylazine.
   - Severe hypotension and tachycardia can occur following rapid IV injection. This can be prevented by giving the agent IM or very slowly IV.
   - The dose volume of atipamezole is the same as the preceding dose volume of dexmedetomidine, given IM.

2. **Yohimbine:** Can be used to reverse xylazine.
   - Dose is 0.1 mg/kg IV or IM.

3. **Naloxone:** Is used extra-label for opioid reversal in the event of respiratory depression or bradycardia.
   - Naloxone can be given IV or IM.
   - Half-life is 12-40 minutes.
   - Naloxone will also eliminate the analgesic effects of opioids and its duration of action may be shorter than the opioid it is being used to reverse. Careful monitoring and redosing may be needed if the animal begins to relapse as a result of this difference in duration of action.
   - Dose is 0.1-0.2 mg/kg as needed.
   - Partially reverse opioid effects by titrating naloxone IV ¼ - ½ dose mixed with and diluted in 6-10 mL saline, given to effect.

4. **Flumazenil:** A benzodiazepine receptor antagonist that can be used to reverse diazepam and zolazepam.
   - In general, only one dose of flumazenil is necessary to reverse benzodiazepine related problems.
   - Dose is 0.02 mg/kg IV.

5. **Related Documents**
   1. Anesthesia and Analgesia Drug Descriptions
   2. Anesthesia and Sedation Monitoring Guidelines
   3. Guidelines on Medical Records for Investigative Personnel
   5. Guidelines on Administration of Substances to Laboratory Animals
   6. UM Policy on Analgesia in Animals Undergoing Surgery
   7. EHS Anesthetic Gases in Animal Research

6. **References**
   1. APV Primate Formulary [https://www.primatevets.org/Content/files/Public/education/Nonhuman%20Primate%20Formulary.xls](https://www.primatevets.org/Content/files/Public/education/Nonhuman%20Primate%20Formulary.xls)
   11. Primate Medicine Department, California National Primate Research Center, University of California, Davis.