Non-Human Primate-Specific Anesthesia

I. Purpose:

This document has been designed by the ARC veterinary staff as a guideline for Non-human primate (NHP) anesthesia. This is not intended to be an inclusive list of all possible drug combinations that can be used in NHPs. Instead, these guidelines are general recommendations. Consequently, they do not include reference to specific research-associated concerns. If you have questions about the use of anesthetics for your particular situation, please work with your area veterinarian to develop the most effective anesthetic plan.

Anesthesia is the loss of feeling in all or part of the body, with or without loss of consciousness. Animals may be anesthetized for surgery, for non-surgical procedures that may be painful, or for non-painful procedures that require immobilization. Steps must be taken before, during, and after anesthesia to ensure the safety of the animal and efficacy of anesthesia. These are listed in the General Guidelines section below.

Anesthetic drugs can be administered parenterally or by inhalation. Commonly used anesthetic agents are described below. The choice of anesthetic agent will depend on the procedure to be performed, research aims, and other factors. Consult your area veterinarian with questions about drug selection.

II. General considerations:

- Prior to anesthesia, NHPs should be fasted for at least 4 hours (ideally overnight). Water should not be restricted.

- Most anesthetic drugs cause hypotension and hyperthermia. Provide supplemental heat under anesthesia. Regardless of the heat source used, do not place animals directly on the heat.

- Following sedation, place an indwelling catheter for administration of anesthetic drugs, emergency drugs, and intravenous fluid support. The most common sites for catheter placement are the saphenous and cephalic veins.

- It is important to provide supplemental fluid support in animals that will be under anesthesia for longer than 30 minutes. Appropriate fluid rates range from 5-10 mls/kg/hour, and may vary based on the anesthetic combination used.
• Standard mammalian monitoring techniques are applicable to NHPs. The goal of monitoring should be to maintain cardiovascular homeostasis and core body temperature. Understanding the basic physiologic effects of the anesthetics used is paramount to correctly interpreting monitoring parameters (see “Description of anesthesia agents” document for details).

• Parameters to be monitored in anesthetized NHPs include: Anesthetic depth, heart rate, respiratory rate, oxygen saturation, expired CO2 (EtCO2), temperature, blood pressure, mucous membrane color.
  
  o Normal ranges (without anesthesia)
    
    ▪ Temperature = 98.0 - 102.5 F
    ▪ Heart Rate (beats/min) = 150-220*
    ▪ Respiratory Rate (breaths/min) = 10-40 resting*
    ▪ Blood pressure: Systolic blood pressure >90 mm Hg and mean >60 mm Hg
    ▪ Oxygen saturation= >95%
    ▪ EtCO2: 35-45**
    ▪ Mucous membranes= pink not pale, white, gray, or blue
  
  o Normal ranges (with anesthesia)
    
    ▪ A 10-20% decrease is acceptable during anesthesia
    ▪ A CO2 up to 55 is acceptable during general anesthesia

• For more involved procedures, EKG, invasive pressure monitoring and blood gas analysis may be indicated. For long procedures, mechanical ventilation is recommended.

III. Stages of Anesthesia:

1. NHP anesthesia is generally broken into premedication (sedation), anesthetic induction, and anesthetic maintenance. As with other species, anesthesia (maintenance) can be accomplished via inhalation or parenteral methods.

   A. Sedation: Drugs administered to decrease excitement, and cause relaxation to allow for placement of indwelling catheters (for IV drug and fluid administration), or allow for intubation (for inhalation anesthesia). Often induction (see below) is required in addition to sedation to provide a level of sedation/anesthesia sufficient for intubation.

   i. Ketamine (5-10 mg/kg) is the most common agent used for chemical restraint of nonhuman primates. It has a wide margin of safety and is generally used in combination with drugs that provide a component of muscle relaxation. See chart below for suggested drug combinations.
ii. The anticholinergics glycopyrrolate (0.004-0.01 mg/kg IM) or atropine (0.04 mg/kg IM) may be used as a premedication to dry oral and respiratory secretions and for its vagolytic (ability to block vagal nerve stimulation and consequent bradycardia) effects during endotracheal intubation.

<table>
<thead>
<tr>
<th>Anesthetic:</th>
<th>Route:</th>
<th>Dose:</th>
<th>Notes:</th>
</tr>
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<tbody>
<tr>
<td>Ketamine + Dexmedetomidine</td>
<td>IM</td>
<td>5 mg/kg K 0.005 - 0.0075 mg/kg D</td>
<td>Dexmedetomidine can be reversed with the same volume of Atipamezole as the volume of Dexmedetomidine used.*</td>
</tr>
<tr>
<td>Ketamine + Diazepam</td>
<td>IM</td>
<td>5-10 mg/kg K 0.5 mg/kg D</td>
<td>Yohimbine can be used for xylazine reversal: 0.1-1.0 mg/kg IV. Atipamezole may also be used IM for reversal using an equal volume as the volume of Xylazine used.*</td>
</tr>
<tr>
<td>Ketamine + Xylazine</td>
<td>IM</td>
<td>7 mg/kg K 0.6 mg/kg X</td>
<td></td>
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* Atipamazole (5 mg/ml) is 10X the concentration of Dexmedetomidine (0.5 mg/ml). You need 4-6X as many mg of Atipamazole (5 mg/ml) to reverse Dexmedetomidine. However, it also has a very high safety margin, so giving an equal volume of Atipamazole to Dexmedetomidine gives you 10 X as many mg of Atipamazole, it is safe, and it allows for reversal without calculating a dose if reversal is urgent. Equal volumes of Atipamazole (5 mg/ml) to reverse small animal Xylazine (20 mg/ml) also works because even though Xylazine has a stronger concentration (20 mg/ml), Atipamazole (5 mg/ml) is cleaner and binds more tightly to the alpha 2 receptor, so equal volumes allows for reversal of xylazine (20 mg/ml) as well.

B. **Induction**: Anesthetic administered to place animal in an unconscious state and allow for tracheal intubation.

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<tr>
<td>Propofol</td>
<td>IV</td>
<td>2-5 mg/kg bolus</td>
<td>Should be given slowly to effect. Propofol causes respiratory depression- any animal receiving propofol should be intubated following administration. Propofol given as a</td>
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C. **Maintenance:** Drugs administered to keep animals unconscious and allow for surgical (or other) procedures to be performed.

i. Inhalation anesthesia may be delivered by a facemask, but is generally delivered via endotracheal intubation.
   a. NHPs can be intubated with the use of a laryngoscope.
   b. Endotracheal tube sizes vary depending on the size of the animal, but generally range from 3 to 5 mm. It is important to have several sizes available and ready with appropriate ties when attempting intubation. It is best to use the largest size that can be passed through the larynx without causing trauma.
   c. Application of sterile surgical lubricant to the tip of the endotracheal tube will help facilitate intubation.
   d. The ET tube should extend approximately from outside of the mouth to the thoracic inlet. This can be used as a guide for how far the tube should be inserted upon intubation.
   e. Verify proper placement of the ET tube by ausculting all lung fields for strong breath sounds. If no breath sounds are heard, back the tube out until sounds are heard in all lung fields.
   f. Inflate the cuff just enough to stop gas leakage. Over-inflation of the endotracheal tube cuff can damage the trachea.

ii. Facemasks and intubation require a gas anesthesia machine with an oxygen source and a precision vaporizer. For most macaque species (> 5 Kg), use a rebreathing system.

iii. When using inhalant anesthesia, use an anesthetic system equipped with a gas scavenging system to minimize occupational exposure to exiting gases.

iv. For anesthetic events lasting greater than 5 minutes and whenever facemasks are used, use an ophthalmic ointment (e.g., Paralube® or Lacrilube®) to the eyes to prevent corneal drying and trauma.

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<tr>
<td>Isoflurane</td>
<td>Inhalation</td>
<td>2-4% by facemask</td>
<td>bolus can cause hypotension.</td>
</tr>
<tr>
<td>Propofol</td>
<td>IV</td>
<td>0.3-0.4 mg/kg/min</td>
<td>Propofol causes respiratory depression-</td>
</tr>
</tbody>
</table>
any animal receiving proprofol should be intubated following administration.

| Isoflurane | Inhalation | 1-2% by endotracheal tube |

V. Post-operative considerations

1. Animals must be monitored continually during recovery (with entry into the surgical/post-op record every 15 minutes).

2. Animals should be recovered in the surgical suite as long as possible to continue monitoring vitals, and providing heat support. In the immediate postoperative period, thermal support is vital for rapid recovery. Keep animals on external heat support until they are nearly fully recovered.

2. Provision of stimulation and frequent switching of position will encourage recovery.

3. If animals are intubated, do not extubate until animals is observed swallowing.

4. Animals should not be returned to the housing room until they have been extubated and begin to regained muscle tone and purposeful movement.

5. Post-anesthetic animals are often less interested in eating. Provision of appealing supplements will aid in post-operative caloric consumption.

6. Once animals are returned to the housing room, they should be monitored for an additional 90 minutes. This should be continual monitoring (with entry into the post op record every 15 minutes) until animals are sitting up, and attempting to ambulate in the cage. Once they are upright and ambulatory, monitoring should continue with checks and post-operative record entries every 15-30 minutes until the 90-minute post-operative period is complete. If the animals is not upright and ambulating within this 90 minute window, the veterinary staff should be contacted, and the monitoring period extended per veterinary advisement. It is best practice to also do a final check of the post-operative animal as the last action prior to leaving for the day. If any concerns about the recovery are noted during the post-operative period, or at any time following surgery, the ARC veterinary staff should be contacted.
References:


4. ULAM Nonhuman Primate Anesthesia and Analgesia Guidelines

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