Anesthesia in Wild Small Mammals

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Overview

The **purpose** of this guide is to provide information and serve as a refresher for veterinarians and wildlife biologists *who have prior experience with anesthesia* and as a training tool for those learning anesthesia under supervision. **Anesthesia** is loss of sensation, with or without loss of consciousness. **General anesthesia** is a drug-induced state of total unconsciousness. Anesthesia is used for humane restraint, in order to prevent the perception of pain, to protect both animal and handler, and for humane euthanasia. The three components of anesthesia are *analgesia* (pain relief), *amnesia* (loss of memory) and *immobilization* (loss of mobility). Some drugs do not possess all three components and must be used in combinations to achieve full anesthesia. Balanced anesthesia refers to use of one or several drugs in order to accomplish anesthesia that: 1) minimizes side effects that would occur with higher doses of any of the component drugs if used alone and 2) results in unconsciousness, pain relief, and immobilization with smooth induction and recovery from anesthesia that is safer and more pleasant for the animal. All administered drugs should be used in consultation with a licensed veterinarian, although certain drugs are controlled by the United States Drug Enforcement Agency, and therefore are more difficult to acquire. Controlled drugs also have stricter reporting and storage requirements because of their abuse potential.

Provision of Anesthesia

In general, animals should be dosed at the low end of the effective range of a drug and given more as needed. Animals that are too lightly anesthetized can experience pain and may move during the procedure. Animals that are too deep run the risk of cardiopulmonary and respiratory arrest. If an animal is too lightly anesthetized, more drugs can be given; however it is more difficult to manage an animal that is too deep. Further, drugs should not be mixed in the syringe until it is determined that they are compatible.

Some anesthetic drugs can be "reversed", i.e. another drug given that partially or completely reverses and/or blocks the effects of the anesthetic. Reversal agents are injectable drugs used to quickly discontinue anesthesia and/or control anesthetic depth by countering the initial drug's effects. Care should be taken with reversal because sometimes only one durg in a combination can be reversed or the duration of reversal may be shorter than the duration of effect of the original anesthetic (and thus the animal may become anesthetized again once the reversal wears off).

Anesthetic drugs are delivered via cutaneous/mucous membranes (topical application), circulatory system (injectables), gastro-intestinal tract (oral), and respiratory system (inhalants). **Local anesthetics** can provide anesthesia to circumscribed areas of the body and avoid many

of the undesirable side effects of general anesthesia, such as unconsciousness, recumbency, regurgitation, and aspiration. It is important to avoid injecting local anesthetics into blood vessels to avoid systemic toxicity. **Injectable anesthesia** is often practical for animals in the field and can be adjusted to provide balanced, humane anesthesia. In general, injectable anesthetics are metabolized by the liver and excreted by the kidneys. Therefore, animals with liver or kidney disease should not be anesthetized with these agents (some wildlife considerations include leptospirosis, renal tuberculosis, environmental contaminant exposure, parasitic tapeworms/ flukes, etc.). **Inhalant anesthesia** can be a quick choice that can be discontinued rapidly if an animal does poorly. Major disadvantages are the requirement for specialized equipment, the lack of balanced anesthesia without use of other (e.g. sedative) drugs, and that the animal may not stay anesthetized at a safe level (i.e. either awake or too deeply anesthetized). If the anesthetic is an inhalant gas, the volume of gas delivered can be reduced (or discontinued), otherwise respiratory and cardiovascular support must be administered until the anesthetic is metabolized and the animal begins to lighten on its own.

Anesthetic depth and monitoring

Anesthetic depth is the concept that anesthetic agents cause progressive depression of central nervous system (CNS) function. There is a considerable range of variation in response to a drug and its dose under different conditions (i.e. in different species, stimuli, procedures, etc.). Also, an animal's anesthetic "needs" often change continuously (i.e., anesthesia should be reduced near the end of a procedure so that the animal can begin to regain consciousness). Historically different schemes have been used to describe and monitor the signs and stages of general anesthesia. In 1847 Plomley noted early intoxication, conscious and unconscious excitement, and deeper planes of narcosis. In 1920 Guedel developed the **classical description** for human patients consisting of four stages each with one or more planes. The first stage or Stage of Analgesia (a.k.a. Induction stage) is the period from beginning of induction to loss of consciousness. Plane 1 – Preanalgesia/preamnesia; Plane 2 - Partial analgesia, total amnesia; Plane 3 – Partial analgesia, total amnesia, with increased respiratory and heart rates, possibility of urination and defecation, and progressive mental depression until consciousness is lost. The second stage or Stage of Delirium (a.k.a. Stage of Involuntary Excitement) is the dream stage of anesthesia in humans and is from loss of consciousness to onset of "automatic respiration". This stage represents abolishment of higher cerebral centers and nervous response to stimulation is exaggerated. The third stage or Surgical Stage is characterized by progressive depression of circulatory and respiratory function, muscle relaxation and protective reflexes (onset of "automatic" respiration to respiratory arrest). Plane 1 – "light" surgical Anesthesia; Plane 2 – "moderate" surgical Anesthesia, Plane 3 – "deep" surgical anesthesia, Plane 4 – "excessive" surgical anesthesia. The fourth stage or Stage of Respiratory Paralysis (overdose) is the interval between respiratory arrest and eventual cardiovascular collapse. This classical approach is deficient because of the introduction of many new drugs and technological advances that have led to advances in patient monitoring.

The **contemporary description** consists of presurgical anesthesia (combination of Guedel's Stage I and II); Light, adequate, deep surgical anesthesia (Stage III); and anesthetic overdose (Stage IV). Signs of presurgical anesthesia variably consist of increased or decreased heart rate, irregular heart rhythms, arterial hypertension, pupillary dilation, production of tears, ocular

globe rotation, breath holding, deep breathing, reduced partial pressure of carbon dioxide gas (P_aCO_2) in the alveolar dead space and arterial blood, limb/body movement, salivation, vomiting, swallowing, laryngeal spasm, and/or making vocal sounds. Signs of deep surgical anesthesia include increased or decreased heart rate, pupillary dilation, dry cornea, centrally fixed eye, shallow breathing, elevated alveolar/arterial P_aCO_2, and/or muscle flaccidity. Signs of overdose include arrhythmia, cardiac arrest, arterial hypotension, and respiratory arrest (not breath hold).

Animals under anesthesia must be carefully monitored. Monitoring various physiological parameters frequently will allow you to detect and respond to changes in vital signs quickly and thereby avert anesthetic emergencies. It is best to make changes earlier on to avoid having to be in an emergency situation (for example, don't wait until the animal's temperature reaches 106ºF or until the animal stops breathing if you have been observing the respiratory rate get slower and slower). However, no single sign of anesthesia is infallible and multiple signs should be considered to make best judgments regarding anesthetic depth. If in doubt, reduce the level of anesthesia.

The following assessments can be used in order to determine an animal's depth of anesthesia:

Palpebral reflex- touching the eyelids causes blinking. The animal is lightly or not anesthetized if it is blinking.

Toe pinch- pinching the toe or foot web will cause a pain response. If the animal withdraws the toe, it is lightly or not anesthetized. If it doesn't withdraw, usually it is not sensing pain.

Corneal reflex- touching the cornea of the eye with a tuft of cotton results in a blink. Once the animal has lost its corneal reflex, it is very or too deeply anesthetized.

Eye position- The position of the eyeball usually is central in an unanesthetized animal, rotates ventrally during surgical anesthesia, and then return to a central position as an animal becomes over-anesthetized.

Pupil size-Dilation occurs as a response to anesthesia. There may be some dilation during the excitement of early anesthesia, then return to normal, then slight dilation at surgical anesthesia, and finally moderate to wide dilation as the animal becomes overanesthetized.

Pupil response to light- this response remains normal until surgical anesthesia during which it is sluggish, and absent response to light suggests very or overly deep anesthesia.

Muscle tone decreases as the depth of anesthesia increases, unless the animal is receiving a cataleptic drug like ketamine in the absence of a sedative. Test muscle tone by pulling on the lower jaw or a limb. Rigid tone indicates inadequate depth of anesthesia.

Cardiopulmonary function and body temperature- As an animal becomes very deeply anesthetized, respiration and cardiac output decrease, causing a decrease in respiratory and heart rates, which results in poor blood oxygenation and tissue perfusion and reduced blood pressure and temperature. Elevations in heart rate and blood pressure may be indications that an animal may be feeling pain and is anesthetized too lightly.

Circulation – Many anesthetics have effects on the heart or blood vessels, decreasing cardiac output and blood pressure. Monitor circulation to ensure that blood flow to the tissues is adequate. Practical field methods include assessing heart rate and rhythm (using a stethoscope), palpation of pulses, determining capillary refill time (time it takes for mucous membranes to regain normal color after gentle pressure is applied), and blood pressure monitoring. If the animal has pale mucous membranes, the capillary refill time is greater than 2 seconds, or if the other cardiovascular parameters are out of the species' normal range there may be a cardiovascular emergency. Injecting fluids will improve cardiac output temporarily; however, anesthetic depth will need to be reduced if possible.

Ventilation - monitor to ensure that the animal is breathing regularly and easily, and that there is adequate oxygen concentration in the animal's blood. Methods include measurement of respiratory rate and depth, observation of movement of chest wall or breathing bag, listening to breath sounds, and observation of mucous membrane color and pulse oximetry. A pulse oximeter is a non-invasive device that determines the oxygen in the blood by comparing changes in light transmission through tissues (e.g., tongue, skin, ear). Pulse oximeters are notoriously fussy (double counting, mis-counting, do not work across relatively dark colored tissue, etc.). Therefore, one should never rely on pulse oximiters alone, but really LOOK at the animal and monitor the basics such as membrane color. Mucous membranes (gums, nasal and oral cavities, conjunctiva (outermost layer of the eye and the inner surface of the eyelids**)**, body orifices, vulvar mucosa, etc.) are normally pink to red, but in some animals the mucus membranes may be heavily pigmented (monitoring color in this case is not very useful). As anasthsia alteraters the animal's circulatory perfusion pinkish membranes will turn pale in color. A blueish membrane indicates lack of oxygen supply. Reddish foam in the airway along with dyspnea (difficulty breathing) may indicate pulmonary edema. This can result from overventilation or overhydration. A diuretic like furosemide can be administered, but the prognosis is poor.

Anticipating and managing adverse events

Unforeseen complications may arise. Therefore, it is important to be able to detect the early warning signs via monitoring, and know how to aptly respond to different situations. Further, many problems can be minimized by shortening the duration of time the animal is under anesthesia.

Thermoregulation care- Hypothermia (low body temperature) is common with general anesthesia (hyperthermia less common), especially with small and older animals. Animals become hypothermic because of inhalation of cold gases, body cavity exposure to room air, and loss of normal thermoregulatory mechanisms and behaviors. Hypothermia depresses all physiologic functions (including respiration and cardiac function), slows the metabolism of anesthetics, and results in prolonged recoveries. Hypothermia also reduces the animal's anesthetic requirement, and therefore one must compensate by reducing anesthetic dose if possible. Hypothermia may be prevented by warming the animal's immediate environment (warm water bottles, heating pads, etc.). Also, careful monitoring of body temperature can alert you to early signs of hyperthermia (unfortunately, this is not easily done for rodents).

Hydration status- Animals exist in a state of fluid balance: take fluids in through food, water, moisture and loose fluids through urination, defecation, perspiration and respiration. Normal fluid balance can be disrupted during anesthesia by inhalant anesthesia (dry, cold oxygen increases respiratory fluid loss), fasting (reduces normal fluid intake); and bleeding or exposure of body tissues to air. Therefore, anesthetized animals often require increased fluids. Monitoring hydration is very important before, during, and after anesthesia. For example, animals stuck in a hot trap often become dehydrated, so it is important to cool the animal before processing and always look for signs of dehydration. Underhydration results in sticky mucous membranes, loss of skin elasticity, the eyes sinking into the orbit, decrease in blood pressure and increase in heart rate. In order to avoid underhydration, fluids can be provided. Fluids are crystalloid (e.g. saline, lactated Ringer's, and D5W) or colloid (e.g. plasma). In general, fluid should be supplemented at the rate of 5-10 ml/kg/hour during anesthesia. To replace blood loss with saline or lactated ringers, administer 3X the volume of blood lost: this can be done subcutaneously or intra-peritoneally. In severe circumstances, whole blood replacement may be necessary. Equally important, but less common, overhydration results in frequent urination and pulmonary edema.

Respiratory care- May involve tracheal intubation to ensure the airway is open, modification of anesthetic dose, respiratory stimulants such as doxapram, or mechanical ventilation. Adjusting head position may also help improve ventilation, as animals may crunch up with their necks bent (especially in the field) inihibiting their ability to breathe.

APPENDIX I. Drugs for the provision of anesthesia in selected small mammals

I. Sedatives and Hypnotics

A **sedative** or tranquilizer is a substance that reduces irritability or excitement. **Sedatives** help calm the animal, but do not provide analgesia (pain relief). They typically have a long duration of effect, lasting into the post-anesthetic phase. The major disadvantage of tranquilizers is that if used alone, animals are easily aroused and may have a defensive/aggressive response.

Hypnotic (also called **soporific**) drugs are a class of psychoactives (cross the blood–brain barrier and act on the central nervous system) whose primary function is to induce and maintain unconsciousness (sleep). Hypnotics do not provide analgesia, but can produce general anesthesia depending on the dose.

Alpha-2 adrenergic agonists:

These drugs cause CNS depression resulting in profound sedation, vomiting, and mild analgesia. However, animals may arouse from their sedative state, especially at low doses. The **thiazine derivatives** include Xylazine and Medetomidine (now dexmedetomidine). Xylazine is a commonly used, inexpensive drug for small mammals but can cause transient increased blood pressure followed by low blood pressure. Medetomidine has 10 times greater affinity for the alpha-2 receptors than xylazine (i.e. provides better sedative effects) and has fewer adverse effects). Their disadvantages include heart block, reduced heart rate, increased blood pressure (usually shortly after injection) followed within minutes by reduced blood pressure, vomiting, hyperglycemia, hypothermia, urine production, and decreased oxygen in blood. However, they are very useful in combination with other drugs, like ketamine, for anesthesia. Sedation caused by thiazine derivatives can be reversed by the administration of the specific alpha2 antagonists (yohimbine for xylazine or atipamazole for medetomidine and dexmedetomidine).

Phenothiazine and Buterophenone Sedatives:

Sedative, muscle relaxation, antiemetic (vomiting and nausea) and anti-arrhythmogenic properties. Disadvantages of these sedatives are that they cause peripheral vasodilation which can lead to hypothermia. Due to the risk of reduced blood pressure, they must be used with care (or not at all) in geriatric or debilitated animals, babies, or animals with liver dysfunction. These sedatives include acepromazine, chlorpromazine, droperidol (Innovar-Vet) and azaperone (Stresnil). Acepromazine is the most commonly used and is long acting. It is recommended as a sole sedative in dogs and as a pre-anesthetic agent in many species. Acepromazine improves induction/recovery and helps decrease the dose of general anesthetic required. Acepromazine also has no analgesic effect.

Barbiturates are chemical derivatives of barbituric acid and may have hypnotic properties, some are class III but most are class IV scheduled substances. Barbiturates provide poor analgesia but can help prevent seizures. Barbiturates induce cardiopulmonary depression, apnea (breath-holding), and hypotension. Because barbiturates upregulate some enzymes in the liver, they may alter the rate of metabolism of other drugs. A common problem in administering barbiturates is overdosing. Prolonged recovery can be a problem when barbiturates are used in older animals or animals with liver or kidney disease. Phenobarbital, pentobarbital, methohexital, and thiamylal are common intravenous short acting anesthetics. Phenobarbital is the longest-acting of the

barbiturates and usually is used for sedation or as an anticonvulsant. Pentobarbital is a short-acting oxybarbiturate and anesthesia can last 45-120 min. Ultra-short acting barbiturates (up to 10 min for Methohexital, up to 15-20 min with Thiopental or Thiamylal) are usually used IV to induce anesthesia agents to allow for an endotracheal tube to be placed prior to inhalant anesthesia. When low doses are given IV, there may only be several minutes of anesthesia. In rodents, longer anesthesia may be seen when these drugs are used intra-peritoneally (IP) but they are acidic and may be irritating when administered IP). Barbiturates also run the risk of dependence and tolerance develops with repeated use, i.e. more drug becomes needed to get the same level of sedation. However, this is not a significant concern for animals undergoing a single procedure.

Non barbiturate hypnotics include Chloral hydrate, Propofol, and Etomidate. Chloral hydrate is a Federally Controlled Substance that is infrequently used and is highly irritating to tissue if injected outside the vein (IV is the only route recommended). Chloral hydrate does not tend to depress heart and respiratory function although high doses can cause severe respiratory depression. Propofol's method of action is poorly understood. It produces a rapid induction of anesthesia followed by rapid recovery and clearance from the body. The disadvantages are that it has a poor analgesic effect, must be given intravenously, may be painful, is expensive, can slow heart rate and reduce blood pressure, and may cause respiratory depression or suspension of breathing. The agent is a phenol in a hyperlipid emulsion and can quickly become contaminated with bacteria, so once a bottle is opened, it should be used within 6-8 hours. Etomidate is rapidly metabolized, and therefore rapidly induces anesthesia and has a short duration of action, with minimal impact on the cardiovascular system. Disadvantages include that it is expensive, reduces blood flow to the brain, and may produce some involuntary muscle twitching, transient failure to breathe, and seizures.

II. Benzodiazapines

Benzodiazapines such as diazepam, midazolam, and zolazepam are anxiolytic (anti-anxiety) and anticonvulsant Controlled Substances. Benzodiazepines act by enhancing the effects of gamma-aminobutyric acid (GABA), a neurotransmitter that inhibits brain activity. They provide good muscle relaxation with minimal cardiovascular and respiratory effects but are not sedative and do not produce unconsciousness. The primary use of these drugs is in combination with other drugs for induction of general anesthesia and short procedures. Zolazepam should NEVER used alone (it is only used in combination with tiletamine in Telazol). Diazepam, also known under the brand name of Valium, is incompatible with many agents and should not be mixed in a syringe with any agent other than Ketamine. Diazepam has a high margin of safety and is reversible with Flumazenil. Midazolam has superior absorbtion to Diazepam when given intramuscularly, but it is significantly more expensive.

III. Opioids

The opioids include Morphine, Hydromorphone, Buprenorphine, Butorphanol, Pentazocine, Nalbuphine, Fentanyl, Meperidine, Oxymorphone, Alfentanil, Sufentanil, Oxymorphone, Methadone, Cartentanil, and Etorphine. They bind specific opioid receptors to provide analgesia and in some species sedation. Opioids do not usually produce unconsciousness, even in large doses. Direct antagonists are available, and therefore their actions can be reversed. The disadvantages are that they are Federally Controlled Substances, have variable effects among different species, may cause slowed heart rate, may cause significant respiratory depression,

and do not produce general anesthesia without other accompanying drugs. Another significant disadvantage is that they are a human safety hazard if a person is accidentally exposed, so often advanced training is required to work with these drugs.

IV. Dissociatives

The dissociatives prevent the brain from correctly coupling sensation, motor function, memory, and emotion. Animals are mentally detached and anesthetized. Dissociative drugs are Federally Controlled Substances and due to high acidity may sting (subcutaneous route discouraged). Examples include Ketamine (Vetalar, Ketaset) and Tiletamine (Telazol). They are rapidly absorbed and produce sedation to general anesthesia with a wide margin of safety. Muscle relaxation and analgesia are very poor. The swallowing reflex is often preserved in animals. Also, the animal's eyes usually remain open and the corneas should be protected from drying with an eye lubricant. Animals recovering from dissociatives often twitch or show seizure-like activity. In high doses, dissociatives can depress the cardiovascular system, although they tend to increase heart rate and blood pressure, intracranial (brain) and intraocular (eye) pressures, and salivation. They depress respiratory function. Because they can cause excitement or convulsions, dissociatives are often used concurrently with a tranquilizing agent (diazepam, acepromazine, or xylazine). Tiletamine is sold only in combination with zolazepam (a benzodiazepine).

V. Parasympatholytics (anticholinergics)

Parasympatholytic drugs block the action of acetylcholine at the terminal ends of the parasympathetic nervous system and reverse parasympathetic effects, e.g. production of tears, saliva, urine, and feces. These drugs include Atropine and Glycopyrrolate (a synthetic Atropine derivative, with longer duration of effect). They can be useful where such production is problematic, but also have the risk of accelerated heart rate and dilation of bronchioles in the respiratory tract. Anticholinergics are mainly used to decrease the build up of secretions (hypersalivation) or to increase heart rate when an animal is bradycardic.

VI. Inhalation Anesthesia

Inhalation anesthetics are administered and largely eliminated via the respiratory system. They induce unconsciousness, amnesia, muscle relaxation, and immobility but do not induce *balanced* anesthesia. Inhalants have a narrow **therapeutic window**, which is the dosage between the effective dose and the amount that gives adverse effects (i.e., concentrations effective for surgery often cause substantial depression of circulatory and respiratory function). Examples of inhalation anesthetics include Enflurane, Halothane, Isoflurane, Methoxyflurane (no longer available), Nitrous oxide, Desflurane, Sevoflurane, and Diethyl ether. Inhalation anesthetics are either gases or vapors. Liquid anesthetic in the anesthetic machine is vaporized, mixed with oxygen and delivered to the patient by mask or endotracheal tube. Inhalation agents readily leave the circulation and enter the brain, inducing anesthesia. All drugs in this class can cause malignant hyperthermia. One major benefit to their use is that anesthesia can be discontinued rapidly if needed.

Special anesthetic delivery equipment should be used such as the Inhalation Anesthetic Delivery Apparatus (IADA), which can be difficult to use, costly, and of limited portability. Instead, many investigators deliver inhalants in a “jar”, i.e. a chamber containing a wick onto which the anesthetic agent can be applied. The method dates back to the use of ether and methoxyflorane,

both of which were difficult to overdose using this method. However, Isoflorane and Halothane are very easy to overdose in a chamber and therefore extreme care should be used with this method.

Isoflurane provides good muscle relaxation, but with little or no analgesia. It has the risk of dose-dependent hypotension and decreased cardiac output, mild respiratory depression, and depression of thermoregulatory centers (use care to avoid hypo-/hyperthermia). Halothane can cause potentially severe liver injury. Isoflurane or halothane-only induction can take several minutes and be quite stressful for the animal. Return to consciousness with either of these drugs may occur in as little as 1-2 minutes.

VII. Non-steroidal anti-inflammatory drugs (NSAID):

Ketoprofen inhibits inflammation and reduced fever and pain but generally is avoided for long-term use because it can cause GI problems. Other drugs in this class include Carprofen, Etodolac, and Meloxicam although these are not used for anesthesia.

VIII. Other Anesthetics

Tribromoethanol (not available commercially) is a short-acting anesthetic used in surgery for rodents that is given IP. Urethane is a long-acting (8-10h) anesthetic used for long procedures in rodents. Urethane has minimal cardiopulmonary depression but is carcinogenic and should only be used with special justification for terminal procedures.