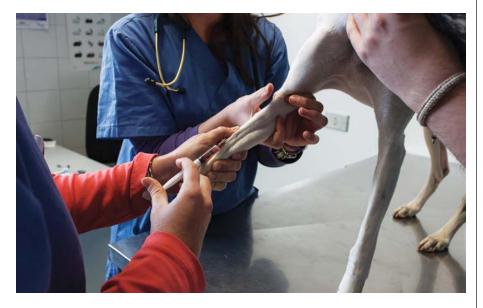
Injectable Anesthetics

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Indications

Injectable anesthetic agents are mostly employed in situations where rapid induction of anesthesia is indicated, and some agents are also suitable for maintenance of anesthesia. Important factors for the indication of these agents include onset of action, duration of anesthetic effect, routes of administration, and cardiorespiratory responses.¹

The author mainly uses products with rapid onset of action and brief duration of effect (eg, propofol, thiopental, or alfaxalone) for anesthetic induction. These agents are administered IV because of tissue irritation (thiopental) or poor bioavailability (propofol) when administered via other routes.

Alfaxalone can be administered IM to induce a light plane of anesthesia in sedated cats, but the large volume of the injection and the potential for a poor recovery are limiting factors for use by this route.²

Although these agents produce loss of consciousness and reasonable muscle relaxation, they do not provide analgesia. They should be injected slowly to effect because they can easily induce states of hypotension, respiratory depression, and post-induction apnea.

Injectable anesthetics are useful in situations where inhalational techniques are not readily available. They are also a suitable alternative when anesthesia must be provided outside of a hospital setting or for quick procedures, such as clinical examinations, diagnostic imaging, and minor surgical procedures.

Products with rapid onset of action and brief duration of effects (propofol, thiopental, alfaxalone) are mainly employed as induction agents.¹

MEDICATIONS

Agents with rapid metabolism and no cumulative effects, such as propofol and alfaxalone, are also suitable for maintenance of anesthesia via repeated boluses or through constant/variable rate infusions, depending on the case.^{3–6} Long or repeated infusions of propofol can accumulate in cats, because they cannot rapidly metabolize the drug.^{1.6} Thiopental is not suitable for anesthetic maintenance because it has cumulative effects and is metabolized slowly.

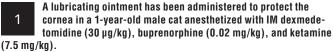
Orotracheal intubation should be performed to protect the patient's airway, as these agents will suppress protective reflexes; intubation will also help in management of apneic events. Oxygen supplementation is also recommended to prevent hypoxemia. These agents are rarely employed in settings with few technical capabilities, aside from providing anesthesia for very brief procedures (between 5–15 minutes).

Dissociative anesthetics (eg, ketamine, tiletamine) have a relatively rapid onset of action, a longer duration of effect (20–45 minutes), and are suitable for IV and IM administration.^{7,8,9} Dissociative anesthetics are preferred for shelter anesthesia protocols.

This type of anesthesia is characterized by catalepsy, amnesia, profound somatic analgesia, muscle rigidity (spontaneous movements and tremors are possible), the presence of active reflexes (ie, palpebral reflexes, gagging, swallowing), and salivation.

These agents cause minimal respiratory depression (irregular and apneustic breathing patterns may be observed) and moderate cardiovascular stimulation in healthy patients.^{1,7,8} Because of potential adverse effects, dissociative anesthetics should not be used alone. Ketamine is routinely employed in combination with sedatives (eg, benzodiazepines or α -2 agonists) and analgesics to improve muscle relaxation, surgical analgesia (antinociception), and quality of recovery.







The same cat intubated. A nebulization of lidocaine 2% has been sprayed onto the larynx to facilitate intubation.

Dissociative anesthetics (ketamine and tiletamine) have a relatively rapid onset of action, a longer duration of effects, and are suitable for IV and IM administration.



Two-year-old male dog admitted for suturing of lacerations. The patient was sedated with IM dexmedetomidine (7 μ g/kg)and methadone (0.2 mg/kg). After 10 minutes, ketamine (7.5 mg/kg) was administered IV, providing 20 minutes of surgical anesthesia.



External disturbances, such as intense light and noises, should be reduced during recovery from dissociative anesthesia.

Injectable Anesthesia: The Good & the Bad

Pros

- Less equipment compared with inhaled anesthesia
- No human exposure to waste gases
- Decreased cost

Cons

- Increased risk for overdose
- Rapid manipulation of anesthetic plane not possible
- For many of these agents, reversal is not possible once administered, even if severe complications occur
- Safety measures can easily be neglected

Tiletamine is closely related to ketamine but is more potent with a longer duration of effect.^{1,7} It is marketed in combination with zolazepam, a benzodiazepine, to reduce muscle rigidity. Because of its higher potency, small injection volumes of tiletamine-zolazepam are effective for achieving a rapid effect in fractious patients, even when administered IM.⁸

The quality of anesthesia with tiletamine-zolazepam can also be improved and its dose reduced by the inclusion of α -2 agonists and analgesics within the protocol. The persistence of cranial reflexes with dissociative agents does not guarantee adequate protection of the patient's airway. Therefore, tracheal intubation and oxygen supplementation are also recommended.

If the eyes remain open and centered in their orbit and the ocular reflexes are active, judgment of the adequacy of the anesthetic plane may be difficult under dissociative anesthesia. This eye position may also increase the risk of corneal drying and ulceration. The use of an eye lubricant is recommended in anesthetized patients to prevent corneal injuries.

Complete recovery from dissociative anesthesia is typically prolonged. Spontaneous movements, tonic-clonic spasms, and excitation are observed in cats and dogs if adjunctive drugs are not administered or if they are given at inadequate doses.^{7,9} These undesirable effects can be accentuated by an inadequate use of α -2 antagonists (atipamezole) to enhance the speed of recovery.

In the author's experience, reversal drugs can be safely administered 45-50 minutes after the administration of the dissociative agent. Premature reversal may result in a rough recovery, particularly in dogs.⁸ In these cases, the use of diazepam or midazolam at normal doses (0.2–0.4 mg/kg IM or IV) is useful to alleviate the excitatory effects of dissociative agents. During recovery, external disturbances such as intense light and loud noises, should be avoided.

Drug Interactions & Contraindications

Anesthesia is a complex state where unconsciousness, lack of perception or memory, and antinociception and proper muscle relaxation (the so-called "triad of general anesthesia") must be ensured. "Balanced" anesthesia can only be achieved by the use of several drugs.¹ Therefore, it is essential to provide the patient with a suitable preanesthetic medication (or adjuvant drug combination) that includes the use of sedatives and analgesics. It is particularly important to consider the use of analgesics, tailoring potency to the aggressiveness of the intended procedure.

continues

Table 1. Sedatives & Opioids for Pre-anesthetic Medication						
Drug	Dog	Cat	Comments			
Acepromazine	0.01–0.05 mg/kg IM	0.05–0.1 mg/kg IM	Mild sedative effect Onset of action: 20–40 min Prolonged effect: 4–8 hr Enhanced sedation with opioids Vasodilation			
Medetomidine	5–15 µg/kg IM	5–50 µg/kg IM	Potent sedative effect Onset of action: 10–15 min Duration of action: 40–140 min Reduced doses in combination with opioids Vomiting may occur Bradycardia, initial hypertension Can be antagonized with atipamezole to speed recovery (approximately same volume of medetomidine administered in dogs and half that volume in cats) Dexmedetomidine has similar effects with half the dose; can also be antagonized, but this is usually unnecessary			
Xylazine	0.2–1.0 mg/kg IM	0.2–2.0 mg/kg IM	Potent sedative effect Onset of action: 5–15 min Duration of action: 60 min Reduced doses in combination with opioids Vomiting, bradycardia, and hypertension followed by prolonged hypotension Can be antagonized with low doses of atipamezole (xylazine is not a highly selective α -2 agonist)			
Buprenorphine	0.01–0.02 mg/kg IM Half the dose IV	0.01–0.02 mg/kg IM Half the dose IV	Enhances sedation Slow onset of action: 20–40 min Prolonged effects 6–8 hr Good in postoperative phase to treat moderate pain Moderate analgesia (potent in cats) Unlikely to cause vomiting			
Butorphanol	0.1–0.5 mg/kg IM Half the dose IV	0.2–0.5 mg/kg IM Half the dose IV	Enhances sedation Suitable analgesia (1–2 hr) for minor to moderate procedures (eg, castration) Unlikely to cause vomiting or panting			
Hydromorphone	0.05–0.2 mg/kg IM	0.05–0.1 mg/kg IM	Similar to oxymorphone			
Morphine	0.1–0.5 mg/kg IM	0.1–0.2 mg/kg IM	Enhances sedation Onset of action: 10–20 min Effect: 2–6 hrs Potent analgesic Salivation, vomiting, defecation Bradycardia, dose-dependent respiratory depression Unlikely to cause panting			
Methadone	0.1–0.3 mg/kg IM	0.1–0.3 mg/kg IM	Enhance sedation Rapid onset of action: 5–10 min Effect: 2–6 hrs Potent analgesia Bradycardia, dose-dependent respiratory depression, panting effect Unlikely to cause vomiting			
Oxymorphone	0.05–0.2 mg/kg IM	0.05–0.1 mg/kg IM	Similar to morphine Less likely to cause vomiting, panting effect			

Table 2. Injectable General Anesthetics								
Drug	Induction dose	Maintenance	Comments					
Alfaxalone	Dogs: 2–3 mg/kg Cats: 5 mg/kg Lower doses may be required after sedation	Additional boluses as required (30%–50% of the initial dose) CRI studies conducted, but need to be better evaluated for clinical use	Inject slowly (over 1 min) to avoid respiratory depression Rapid effect (1–2 min) Rapid metabolism Minimally cumulative Minimal cardiovascular depression					
Propofol	Dogs & cats: 5–8 mg/kg in nonpremedicated patients Reduced doses after premedication	Additional boluses as required (30%–50% of the initial dose) CRI: 0.5–1.0 mg/kg reduced over time	Rapid effect (1–2 min) Recovery after 5–15 min Rapid metabolism Cardiovascular and respiratory depression Minimally cumulative (except in cats)					
Thiopental	Dogs & cats: 5–10 mg/kg after acepromazine-opioid premedication Half the dose after α-2/opioid premedication	Not recommended	Rapid effect (30–60 sec) Recovery after 5–15 min Cardiovascular and respiratory depression Irritant if given extravascularly Cumulative effects					

Table 3. Dissociative Anesthetics

Drug	Anesthetic dose	Comments	
Ketamine	Dogs: 2.5–10 mg/kg IM Cats: 5–10 mg/kg IM Use lower doses after α -2/opioid premedication Suitable doses for combination with 0.1–0.3 mg/kg of diazepam (IV) or midazolam (IM or IV) for noninvasive procedures; otherwise, analgesics should be added to this combination; half the doses for IV use	Additional boluses can be given as required to prolong anesthesia (30%–40% of the initial dose)	Effect in 5–10 min Duration 20–30 min Use in combination with sedatives (α-2 agonists) and opioids Excitement during recovery
Tiletamine- zolazepam	Dogs: 7–13 mg/kg IM Cats: 9–12 mg/kg IM Use lower doses after α-2/opioid premedication Reduce dose by 50%–60% for IV use	One or two additional boluses can be given to prolong anesthesia (25%–30% of the initial dose)	Effect in 5–10 min Duration: 40–45 min Better results in combination with sedatives (α-2 agonists) and opioids Excitement during recovery

MEDICATIONS

Good control of intraoperative nociception will produce a more stable plane of surgical anesthesia. Dissociative anesthetics are able to provide intense but brief analgesia, mainly for somatictype pain. Ketamine (and possibly other dissociative drugs) has an antihyperalgesic effect through the inhibitory action on *N*-methyl D-aspartate (NMDA) receptors. At subanesthetic doses, it can be effective for treatment of patients with chronic pain and central sensitization, and to reduce hyperalgesia following tissue trauma.^{1,6,7,10}

The inclusion of an NSAID in the anesthetic protocol is also recommended when opioids are not available or in combination with opioids for major procedures (eg, orthopedic surgery, major soft tissue procedures).¹⁰ The availability of veterinary licensed products with a cyclooxygenase-2 (COX-2) selective profile has improved the safety profile of these drugs. However, adverse effects may be induced if these drugs are used in anesthetized patients with hypovolemia, hypotension, or renal, gastrointestinal, or coagulation disorders.

Close monitoring of blood pressure and adequate intraoperative cardiovascular support (fluid therapy) should be performed when NSAIDs are administered preoperatively. The inclusion of locoregional analgesia techniques can be extremely useful to achieve balanced anesthesia and to control perioperative pain more efficiently.¹⁰

In the author's experience, the administration of the preanesthetic medication before anesthesia will decrease the necessary doses of anesthetic agents and will enhance the quality of the anesthesia and recovery. In healthy cats, for example, a suitable protocol may involve sedation with a combination of medetomidine (40 µg/kg) and butorphanol (0.3 mg/ kg) IM. Once sedation is established, anesthesia may be induced with ketamine 2.5–5.0 mg/kg IV or 5.0–7.5 mg/kg IM. The final dose of ketamine can be adjusted based on depth of sedation and duration of the scheduled procedure.

In fractious animals, simultaneous administration of sedative, analgesic, and dissociative agent could be a preferred technique to ensure quicker effect.

Every anesthetic event has risks, even in young, healthy patients. Injectable techniques should be employed with caution. The patient should be fasted to reduce the incidence of vomiting or regurgitation, particularly when tracheal intubation cannot be performed. Routine examinations and laboratory studies should be performed to determine the health status of the patient, as anesthesia may not be well tolerated in all patients. Body weight should also be accurately measured to avoid the risk of overdose. Every effort should be made to ensure that tracheal intubation, supplemental oxygen, and a form of respiratory support are readily available if necessary.

Pulse rate and rhythm, respiratory rate and breathing pattern, mucous membrane color, muscle tone, and eye position should be monitored at regular intervals, even if electronic monitoring devices are available. Hypothermia should be prevented, as it slows the metabolism of injectable agents and may cause unwanted consequences.

Cost

Injectable agents are not necessarily less expensive than inhalational agents, but the equipment required to administer the agents decreases the overall cost. Economic restrictions should not justify denying the patients rational anesthetic (and analgesic) protocols that can help ensure the basic safety principles required for an uneventful recovery from anesthesia. **Cb**

References

- Injectable anesthetic agents. Dugdale A. In Veterinary Anaesthesia principles to practice, 1st ed—Oxford: Blackwell Publishing, 2010, pp 45–54.
- 2. Cardiovascular and respiratory effects, and quality of anesthesia produced by alfaxalone administered intramuscularly to cats sedated with dexmedetomidine and hydromorphone. Grubb TL, Greene SA, and Perez TE. J Fel Med Surg 15:858–865, 2013.
- Comparison of alfaxalone and propofol administered as total intravenous anesthesia for ovariohysterectomy in dogs. Suarez MA, Dzikiti BT, Stegmann FG, et al. *Vet Anaesth Analg* 39:236–244, 2012.
- Alfaxalone for total intravenous anesthesia in dogs undergoing ovariohysterectomy: a comparison of premedication with acepromazine or dexmedetomidine. Herbert GL, Bowlt KL, Ford-Fennah V, et al. Vet Anaesth Analg 40:124–133, 2013.
- Minimum infusion rate of alfaxalone for total intravenous anesthesia after sedation with acepromazine or medetomidine in cats undergoing ovariohysterectomy. Schwarz A, Kalchofner K, Palm J, et al. Vet Anaesth Analg 41:480–490, 2014.
- Partial intravenous anesthesia in cats and dogs. Duke T. Can Vet J 54:276-282, 2013.
- Dissociative anesthetics. Lin HC. In Tranquilli WJ, Thurmon JC, Grimm KA (eds): Lumb & Jones' Veterinary Anesthesia and Analgesia, 4th ed—Oxford: Blackwell Publishing, 2007, pp 301–353.
- 8. Anesthesia in shelter medicine. Ko JC, Berman AG. *Top Companion* Anim Med 25:92–97, 2010.
- 9. Anesthetic and cardiorespiratory effects of romifidine/ketamine combinations in cats. Belda E, Laredo FG, Escobar M, et al. *Vet Anaesth Analg* 36:299–307, 2009.
- Guidelines for recognition, assessment and treatment of pain: WSAVA global pain council members and co-authors. Mathews K, Kronen PW, Lascelles D, et al. J Small Anim Pract 55:E10–68, 2014.