Chapter 12

Dissociative Anesthetics

Hui-Chu Lin

Introduction

The term *dissociative anesthesia* is used to describe an anesthetic state induced by drugs that interrupt ascending transmission from the parts of the brain responsible for unconscious and conscious functions, rather than by generalized depression of all brain centers as seen with most other general anesthetics.[1] Dissociative anesthesia is characterized by a cataleptoid state in which the eyes remain open with a slow nystagmic gaze.[2] Varying degrees of hypertonus and purposeful or reflexive skeletal muscle movements often occur unrelated to surgical stimulation. Although somatic analgesia may be intense, it is relatively brief.

Phencyclidine, ketamine, and tiletamine are dissociative anesthetics that have been used clinically for immobilization and anesthesia.[3,4] Phencyclidine was the first dissociative used in veterinary anesthesia, but it is no longer available for clinical use. Tiletamine is available for use only in combination with the benzodiazepine zolazepam. In a 1:1 ratio, this drug combination is marketed as Telazol in the United States and as Zoletil in Europe. In most respects, the pharmacodynamics of tiletamine are similar to those of ketamine (the most commonly used dissociative anesthetic), but tiletamine's potency and duration of action are intermediate between those of phencyclidine, the most potent, and ketamine, the least potent.

Pharmacology

Effects on the Nervous System

Dissociative anesthetics produce dose-related unconsciousness and analgesia. Because of their low molecular weight, a pK_a near physiological pH, and high lipid solubility, dissociative anesthetics have a rapid onset of action. Classically, the mechanism of action has been described as selective depression of neuronal function of the neocorticothalamic axis and the central nucleus of the thalamus with concurrent stimulation of selected parts of the limbic system, including the hippocampus.[5,6] More recently, antagonism of the *N*-methyl-D-aspartate (NMDA) receptor has been proposed as the most likely molecular mechanism responsible for most of the anesthetic, analgesic, psychotomimetic, and neuroprotective effects of the drug.[7] Alternatively, effects could be mediated in part by one or more of the following: (a) action on voltage-dependent sodium, potassium, and calcium channels; (b) depression of acetylcholine receptors; (c) enhancement and prolongation of γ-aminobutyric acid (GABA) receptors that link to chloride channels ($GABA_A$ receptors); and (d) depression of nociceptive cells in the medial medullary reticular formation and activity of cells in laminae I and V of the dorsal horn.[8–10]

Dissociative anesthetic administration to people with a history of seizures does not promote seizure activity despite the presence of thalamic and limbic epileptiform electroencephalogram patterns.[11,12] In fact, low doses of ketamine may have anticonvulsant properties through antagonism of NMDA receptors.[13–16] Nevertheless, ketamine-associated seizures have been reported in some animals, and use of ketamine, or any other dissociative anesthetic, in animals with a history of epilepsy or other seizure disorders should be avoided, if possible.[17–20]

Analgesia produced by dissociative anesthetics occurs at subanesthetic doses. Elevated pain thresholds correlate with plasma ketamine concentrations of 0.1 μg/mL or greater.[21] The degree of analgesia appears to be greater for somatic pain than for visceral pain.[22] In cats, visceral analgesia induced by ketamine (2, 4, and 8 mg/kg intravenously [IV]) is similar to that produced by butorphanol (0.1 mg/kg IV). With increasing doses of ketamine, or when ketamine and butorphanol are administered simultaneously, visceral analgesia is not increased.[23] At a high dose of ketamine (8 mg/kg), cats appear anesthetized but still respond to colonic nociceptor stimulation, suggesting limited visceral analgesia in cats and probably other species. Dissociative anesthetics appear to be more useful for anesthesia and postoperative analgesia related to integumentary and superficial musculoskeletal surgery.[23,24] Furthermore, NMDA receptors appear to be involved in hyperalgesic responses after peripheral tissue injury and inflammation, suggesting that ketamine (and possibly other dissociatives) would be effective at reducing hyperalgesia following tissue trauma.[25–29]

Local infiltration of ketamine may produce a brief period of local anesthetic effect.[30,31] When administered simultaneously with bupivacaine, ketamine doubles the duration of analgesic and local anesthetic effects of bupivacaine.[32] This peripheral analgesic effect of ketamine may be attributed to one or all of the following mechanisms: (a) blockade of sodium and potassium currents in peripheral nerves, (b) blockade of NMDA, α-amino-hydroxy-5-methyl-4-isoxazoleproprionic acid (AMPA), and kainite receptors on unmyelinated axons, and (c) blockade of glutamate effects on C-fiber free-nerve endings.[33–37]

Similar to systemic administration, epidural ketamine appears to produce profound somatic but poor visceral analgesia. Epidural administration produces a dose-dependent analgesic action.[38,39] In rats, a dose of 6 mg/kg induces motor blockade lasting 5 to 15 min, whereas sensory blockade alone occurs with lower doses (4 mg/kg).[40] In horses, the caudal epidural injection of lower doses of ketamine (0.5, 1.0, or 2.0 mg/kg) prevents nociceptive responses initiated by surgical incision and is associated with dose-dependent perineal analgesia.[41,42] In halothane-anesthetized ponies, epidural ketamine reduces the minimum alveolar concentration (MAC) of halothane between 14% (at a dose of 0.8 mg/kg) and 12% (at a dose of 1.2 mg/kg), which is similar to the reduction in MAC achieved with epidural morphine administration (14%).[43] When combined with epidural xylazine (0.5 mg/kg), ketamine (1 mg/kg) induces perineal analgesia lasting 20 min or longer. In some horses, analgesia is extended to the thigh and flank regions.[44] In another study, the subarachnoid administration of ketamine (1 to 2 mg/kg) at the L1-L2 intervertebral space of dogs produced analgesia of the hind limbs.[45]

Tissue trauma produces continuous nociceptive stimulation of C fibers that activates NMDA receptors in the central nervous system (CNS). This activation of NMDA receptors decreases the threshold to glutamate, making them more responsive to stimuli. As a result, *windup* may develop, which is clinically manifested as an exaggerated response to subthreshold noxious stimuli following a primary injury and amplification of postoperative pain.[46,47] These results have led to the concept of preemptively treating central sensitization as an important part of pain management. Consequently, the administration of ketamine at subanesthetic doses as a continuous-rate infusion in combination with other analgesics (e.g., opioids) has gained popularity in preventing or minimizing pain following surgery in both people and animals.[48–53]

Dissociative anesthetics induce significant increases in cerebral blood flow (CBF), intracranial pressure (ICP), and cerebrospinal fluid pressure as a result of cerebral vasodilation and elevated systemic blood pressure.[54–60] The mechanism of ketamine-induced elevated ICP remains controversial. Ketamine increases CBF and ICP in awake goats when arterial carbon dioxide partial pressure ($PaCO_2$) is allowed to rise but has no effect on CBF and ICP when $PaCO_2$ is maintained at a preketamine level, suggesting an indirect mechanism.[61–63] In piglets with preexisting intracranial hypertension, ketamine induced further increases in ICP, paralleling a rise in $PaCO_2$. When ventilation was controlled, no increase in ICP was observed in piglets with normal or elevated ICP.[62] These studies suggest that initiating controlled ventilation is prudent when dissociative anesthetics must be administered to patients with intracranial disease. Increased skeletal, thoracic, and abdominal muscle tone can also impede venous return from the head, increasing intracranial blood volume and pressure.[62,63]

Dissociative anesthetics may not be contraindicated in all patients at risk for intracranial hypertension, particularly when administered in the presence of another anesthetic and/or when controlled ventilation is instituted. It has been hypothesized that when ketamine is administered in the presence of another anesthetic, the second anesthetic may suppress ketamine's excitatory effect on the CNS. Nevertheless, administration of ketamine should be avoided in spontaneously breathing patients with suspected intracranial hypertension or disease until scientific evidence to the contrary emerges.

Abnormal behavior, which may progress to delirium, may occur during emergence from dissociative anesthesia. Depression of the inferior colliculus and medial geniculate nucleus leading to misperception of auditory and visual stimuli may be responsible for this reaction.[64] Emergence reactions are characterized by ataxia, increased motor activity, hyperreflexia, sensitivity to touch, and sometimes violent recovery.[16,65,66] These reactions usually disappear within several hours without recurrence. Premedication with or concurrent administration of α_2-adrenergic agonists, acetylpromazine, or a benzodiazepine (e.g., diazepam, midazolam, or zolazepam),decreases the incidence and/or severity of emergence reactions.[67–72]

Effects on the Cardiovascular System

The cardiovascular effects of dissociative anesthetics are characterized by indirect cardiovascular stimulation. Various effects on target organs include sympathomimetic effects mediated from within the CNS, inhibition of neuronal uptake of catecholamines by sympathetic nerve endings, direct vasodilation of vascular smooth muscle, and an inotropic effect on the myocardium.[73–76] Heart rate and arterial blood pressure usually increase as a result of increased sympathetic efferent activity.[77] Plasma concentrations of epinephrine and norepinephrine can increase within 2 min of intravenous administration of ketamine and return to control levels 15 min later.[78] In dogs and cats anesthetized with ketamine, mean arterial pressure, heart rate, and cardiac output increase while peripheral vascular resistance remains mostly unchanged.[22,79–84] Myocardial stimulation is associated with increased cardiac work and myocardial oxygen consumption. In healthy animals, increases in myocardial oxygen supply usually result from increased cardiac output and a decrease in coronary vascular resistance such that increases in coronary blood flow parallel the increase in oxygen consumption.[85,86] However, some studies indicate that ketamine-induced increases in coronary blood flow may be insufficient to meet myocardial oxygen demand, especially if cardiovascular disease is present.[87,88] The cardiovascular stimulating effects induced by dissociative anesthetics are blunted or prevented by prior administration of a benzodiazepine, droperidol, acetylpromazine, or α_2-adrenergic agonists, or the concomitant administration of inhalation anesthetics, including nitrous oxide.[89–93]

The direct effect of ketamine on the myocardium remains incompletely characterized. Positive inotropic effects have been demonstrated in patients whose heart rates were kept constant by atrial pacing and in isolated mammalian papillary muscle.[76,94–97] However, in denervated hearts, ketamine (and presumably other dissociative anesthetics) induces direct myocardial depression in vivo and in vitro.[97–102] Cook et al.[97] suggested that the predominant inotropic mechanism of ketamine is inhibition of catecholamine reuptake at the neuroeffector junction, leading to stimulation of β-adrenoceptors. The importance of an intact and normally functioning nervous system in stimulating cardiovascular function is underscored when ketamine is administered in the presence of other anesthetics. For example, when administered to dogs anesthetized with pentobarbital, ketamine induces a biphasic response in blood pressure, whereas in conscious dogs it induces only a pressor response.[79,100]

A direct dose-dependent negative inotropic effect of ketamine on failing and nonfailing human myocardium has been demonstrated. The negative inotropic effect of ketamine cannot be attributed primarily to the absence of sympathetic tone but rather to other direct negative inotropic mechanisms. Therefore, ketamine administration for induction of anesthesia may induce an unanticipated decrease in myocardial contractility in patients with end-stage heart disease.[103]

The survival rate of animals in shock is reportedly greater when they are anesthetized with ketamine versus halothane.[104] Ketamine has been shown to suppress activation of endotoxin-induced neuronal nuclear factor κB, which regulates the production of proinflammatory cytokines, including tumor necrosis factor α in human glioma cells in vitro and intact mouse brain cells in vivo. Therefore, in theory, ketamine may offer some neuroprotective effects during endotoxemia.[105] Furthermore, intravenous administration of ketamine (10 mg/kg/h) prior to injection of endotoxin to rats completely inhibits the hemodynamic effects (profound hypotension), metabolic acidosis, and the release of cytokines associated with endotoxin shock. However, the hemodynamic effect and the release of cytokine are only modestly suppressed when ketamine is administered after exposure to endotoxin. Thus, ketamine may have protective effect in patients with endotoxemia, but only when given preemptively.[106] Critically ill patients occasionally respond to ketamine with an unexpected decrease in blood pressure and cardiac output.[94] This likely results from depletion of catecholamine stores and an uncovering of ketamine's direct myocardial depressant effects.[107]

Effects on the Respiratory System

Dissociative anesthetics, when given alone, differ from most other anesthetics in that they do not depress ventilatory responses to hypoxia.[108] In dogs anesthetized with ketamine, respiratory rate and minute volume decrease initially, but both return to baseline values within 15 min.[109] In cats and sheep, ketamine induces a dose-dependent transient decrease in arterial oxygen partial pressure (PaO_2) in the presence of decreased or increased respiratory rate.[22,110–114] At higher doses, respiration is characterized by an apneustic, shallow, and irregular pattern.[3,19,84] Severe respiratory depression or arrest with an overdose of dissociative anesthetic has been reported in human patients and cats.[84,115–117]

Dissociatives often cause increased salivation and respiratory-tract secretions, which can be partially controlled by administration of an antimuscarinic (e.g., atropine). Laryngeal and pharyngeal reflexes usually are partially or fully maintained during dissociative anesthesia. Nevertheless, swallowing reflexes may be somewhat obtunded because most species can be intubated when anesthetized with ketamine. Careful airway management and/or endotracheal intubation should always be performed to prevent aspiration.

Effects on the Hepatic and Renal Systems

Hepatic dysfunction following clinical use of ketamine, and other dissociatives, is not evident in either people or dogs.[1,118] A significant increase in serum concentrations of liver enzymes has been observed in people anesthetized with a ketamine infusion and dogs given higher intramuscular doses (40 mg/kg daily for 6 weeks).[1,118] In rats, ketamine induces hepatic microsomal enzymes but to a lesser extent than that seen with phenobarbital.[119] The effect of ketamine-associated liver microsomal enzyme induction on drug interactions during anesthesia is largely uncharacterized.

Dissociative anesthetics generally undergo extensive hepatic biotransformation in dogs, horses, and people. Some hepatic metabolism occurs in cats, but normally the majority of drug is excreted via the kidney.[113,120] Rapid recovery following intravenous bolus ketamine administration is by rapid redistribution of ketamine from the CNS to other tissues, primarily fat, lung, liver, and kidney.[121] Clinically, animals with significant hepatic dysfunction do not metabolize ketamine as rapidly as do healthy animals. Animals with renal dysfunction or obstruction to urine flow also have prolonged sleep times when larger doses of ketamine are given.[112] Generally speaking, dissociative anesthetics should be given cautiously to animals that have significant hepatic or renal dysfunction.

Effects on Intraocular Pressure

In people, a slight increase in intraocular pressure (IOP) independent of changes in blood pressure has been observed during ketamine anesthesia.[122,123] However, conflicting results have been reported. Intravenous or intramuscular administration of ketamine alone (2 to 8 mg/kg) reportedly did not affect IOP significantly.[124,125] IOP increases during xylazine and ketamine anesthesia in dogs, whereas it tends to decrease in horses.[126,127] Increases in extraocular muscle tone induced by ketamine may be responsible for the IOP increase.[128] With this in mind, ketamine should be used with caution in patients with corneal injuries where increased IOP may result in expulsion of intraocular contents.

Clinical Use

Dogs

Dissociatives can increase muscle tone and can induce spontaneous movement and rough recoveries, and occasionally convul-

sions, in dogs (Tables 12.1 and 12.2).[66,109] To reduce these undesirable effects, dissociatives are often used in combination with adjunctive drugs. Benzodiazepines induce a central muscle relaxant effect that decreases the muscle hypertonus associated with ketamine.[129] In a comparative study, both midazolam-ketamine and diazepam-ketamine combinations induced minimal cardiovascular and respiratory effects. Time to intubation was significantly shorter with midazolam-ketamine, but recovery seemed to be smoother with diazepam-ketamine.[130] Zolazepam is combined with tiletamine in a fixed ratio in the proprietary mixture Telazol. This combination reduces the adverse effects of tiletamine when given alone, although the metabolism of zolazepam can vary among species and may result in a longer or shorter effect relative to tiletamine. Intravenous administration of acepromazine (0.11 mg/kg) and ketamine (11 mg/kg) induces anesthesia for 10 to 35 min, with good muscle relaxation and smooth recovery.[66]

Xylazine (1.1 mg/kg intramuscularly [IM]) or medetomidine (10 to 30 µg/kg [IM]) is often used with ketamine (5 to 10 mg/kg IM) for short-term anesthesia of 25 to 40 min. The ketamine dose can be adjusted, depending on the desired duration of surgery.[109,131] In high-strung small-breed dogs, small ketamine

Table 12.1. Use of ketamine alone or ketamine combinations in dogs.

Drug(s)	Dose(mg/kg) and Route	Duration (min)	Comment
Ketamine alone	10, IV	15±8	↑ Muscle tone Short duration Anesthesia inadequate for surgery
	1 or 2, intrathecally	—	Analgesia of the hind limbs
	10 µg/kg/min, CRI	—	↓ Isoflurane MAC by 25%
Ketamine Lidocaine Morphine	K 10 µg/kg/min; L 50 µg/kg/min; M 3.3 µg/kg/min, IV Simultaneously for CRI	—	↓ Isoflurane MAC by 45%
Acepromazine Ketamine Thiamylal	0.55, IM 11–22, IM To effect, IV	20–90	Occasional seizures
Acepromazine Ketamine	A 0.5, IV; K 10 IM	—	Good restraint
	A 0.2, IV; K 10 IV	39±8	Clinical anesthesia, less muscle rigidity
	A 0.22, IM; K 11–18 IM	—	Restraint, spastic movements, and prolonged recovery
Xylazine and Ketamine	X 0.55–1.1, IM; K 22, IV, to effect	—	Surgical anesthesia, muscle relaxation, and analgesia for abdominal surgery
	X 2.2, IM; K 11 IM	—	Occasional seizures
	X 2.2 IM; K 5.5 IM	—	Occasional seizures
	X 0.22, IM; K 10, IM	28–36	—
	X 1, IV; K 10, IM	32±6	Better muscle relaxation than ketamine alone
	X 1, IM; K15, IM	24.0±5.5	—
Xylazine Ketamine Thiamylal	1.1, IM 11–22, IM To effect, IV	25–60	Occasional seizures
Atropine Xylazine Ketamine	A 0.04, IV; X 1.1, IV; K 11, IV	—	—
	A 0.044, IM; X 1.1 IM; K 22 IM	17–35	↑ Risk in dogs with cardiopulmonary disease
Guaifenesin Xylazine Ketamine	G 50 mg/mL; X 0.25 mg/mL; K 1 mg/mL Induction, 0.55 mL/kg, IV Maintenance, 2.2 mL/kg/h, IV	120	Stable anesthesia
Medetomidine Ketamine	M 0.04, IM; K 2.5, IM	7.0±0.9	—
	M 0.04, IM; K 5, IM	30.0±4.9	Longer duration of muscle relaxation, and recovery than xylazine-ketamine, and prolonged recovery
	M 0.04, IM; K 7.5, IM	51±8	—
	M 0.04, IM; K 5, IM	>75	Significant cardiovascular changes
Diazepam Ketamine	D 0.28, IV; K 5.5, IV	—	Suitable induction for greyhound
Midazolam	M 0.5, IV; K 10, IV	13.3±3.1	↑ Heart rate, mild respiratory depression, and better muscle relaxation
Ketamine	M 0.28, IV; K 5.5, IV	—	More myoclonic movements, shorter time to intubation, and suitable induction for greyhound

CRI, continuous-rate infusion; IM, intramuscularly; IV, intravenously; MAC, minimum alveolar concentration.

Table 12.2. Use of Telazol alone or Telazol combinations in dogs.

Drug(s)	Dose and Route (mg/kg)	Duration (min)	Comment
Telazol alone	9.9, IM	21.0±10.9	Unsatisfactory recovery in two dogs
	9.9, IV	20.1±6.38	—
Telazol alone	6.6, IV	17.5±11.7	Smooth recovery
	13.2, IV	37.0±18.1	Rougher recovery
	19.8, IV	50.8±27.27	Rougher recovery
Telazol alone	6.6–9.9, IM	30	Diagnostic examinations Restraint
	2–4, IV	15–20	Diagnostic examinations Restraint
	9.9–13.2 IM	30–90	Minor surgical procedures (mild to moderate analgesia)
	4.0–9.9 IV	20–80	—
Telazol alone	2, IV	11.9±6.6	Minor procedures require no intubation Easy intubation
	4, IV	22.7±7.3	—
Telazol alone	15.4, IM	40	Anesthesia
	6.6, IV or IM	20–25	Light surgical anesthesia
Telazol alone	5.7, IM (4.0–8.6)	41.5 (15–77)	Satisfactory anesthesia
	9.7, IM (8.8–13.0)	56.6 (33–106)	Satisfactory anesthesia
	17.8, IM (13–22)	79.7 (37–124)	Satisfactory anesthesia
Telazol alone	4, IV	—	Satisfactory restraint for intradermal skin testing
Telazol alone	5, IV	38.5±23.0	Injection of flumazenil shortens recovery
Telazol alone	6–12, IM	—	—
Telazol alone	4–100, IM	—	—
Telazol Xylazine Butorphanol	8.8, IM 1.1, IM 0.22, IM	100	Anesthesia Good muscle relaxation Good analgesia
Telazol alone	19.7±3.3, IM	—	Unsatisfactory sedation in vicious dogs
Butorphanol Telazol	0.7, IM 10.6±1.3, IM	—	Unsatisfactory sedation in vicious dogs
Acepromazine Telazol	1.8±1.2, IM 19.3±1.8, IM	—	Adequate sedation in vicious dogs

IM, intramuscularly; IV, intravenously.

doses produce insufficient anesthesia and have a greater tendency to cause seizure. Dogs might salivate excessively during ketamine anesthesia, but this can be controlled with atropine or glycopyrrolate. α_2-Adrenergic agonist–induced bradycardia and second-degree atrioventricular block may be minimized by ketamine's sympathomimetic effect. However, atropine should be given if cardiac slowing is pronounced. An advantage of α_2-adrenergic agonist–ketamine combinations is the reversibility of CNS and cardiopulmonary depression. Antagonism should not be initiated for at least 20 min after ketamine administration unless required to treat severe adverse effects. Earlier antagonism may cause ketamine-induced hyperexcitability and seizures.[132]

In dogs, intravenous continuous-rate infusion of a low dose of ketamine (10 μg/kg/min) reduces the isoflurane MAC by 25%, whereas the continuous-rate infusion of a combination of morphine (3.3 μg/kg/min), lidocaine (50 μg/kg/min), and ketamine (10 μg/kg/min) has reduced the isoflurane requirement as much as 45%.[133] Concurrent administration of either morphine-lidocaine or morphine-ketamine combinations reportedly reduces CNS hypersensitivity in people suffering inflammatory or neuropathic pain.[134–137] Tables 12.1 and 12.2 further summarize the use of ketamine and Telazol either alone or in combination with various other classes of drugs when employed as anesthetics in dogs.

Cats

In cats, dissociatives have been used as primary anesthetic agents. Diazepam (0.3 mg/kg) is commonly mixed in the same syringe with ketamine (5.5 mg/kg) and given slowly IV for short-term anesthesia. This has proven to be a safe combination in cats with compromised cardiovascular function. Diazepam (0.22 mg/kg IV or 0.44 mg/kg IM) followed by ketamine (1 to 5 mg/kg IM) has also been used successfully in geriatric cats.[138] Administration of butorphanol prior to diazepam-ketamine may increase analgesia and enable diagnostic or surgical procedures to be performed when endotracheal intubation and delivery of an inhalant anesthetic are not feasible.[132] When various doses of midazolam (0.05, 0.5, 1.0, 2.0, or 5.0 mg/kg IV) are combined with ketamine (3 mg/kg IV), the duration of anesthesia increases slightly. However, increasing the intravenous midazolam dose (5

mg/kg) will often prolong objectionable behavioral signs (restlessness, vocalization, and changes in ability to approach and restrain).[139] Telazol has been used alone or in combination in cats. Zolazepam appears to be metabolized at a slower rate than tiletamine in this species, resulting in residual muscle relaxation and sedation, which often prolongs complete recovery. Xylazine and ketamine have been combined with Telazol to alter the dissociative anesthetic–benzodiazepine ratio, improving recovery characteristics, as well as facilitating possible antagonism with an α_2-adrenergic antagonist. This combination, which has been called *TKX* (Telazol-ketamine-xylazine), is made by reconstituting 500 mg of Telazol powder with 100 mg (1 mL of 100 mg/mL) of xylazine and 400 mg (4 mL) of ketamine. The resulting solution is very potent and, by using an insulin syringe, is more accurately dosed at 0.1 mL/5 kg of body weight.

Phenothiazine tranquilizers such as acepromazine have been combined with ketamine for better muscle relaxation and a smoother recovery. However, phenothiazine derivatives are α-adrenoceptor antagonists, and hypotension, prolonged recovery, and hypothermia may occur if they are used in higher doses.

α_2-Adrenergic agonist–ketamine combinations have often been used in cats. Xylazine (0.5 to 1.1 mg/kg IM), with or without atropine, is administered 20 min before ketamine (11 to 22 mg/kg IM).[68,140] Emesis is a common side effect of xylazine in cats, and it has been suggested that this should be allowed to occur prior to ketamine administration so as to prevent aspiration of stomach contents.[66] When compared with acepromazine (0.11 mg/kg IM)-ketamine (4.6 mg/kg IM), the simultaneous administration of xylazine (0.23 mg/kg IM)-ketamine (4.6 mg/kg IM) produces a longer anesthetic action. However, xylazine-ketamine anesthesia is also accompanied by longer-lasting cardiopulmonary depression.[141]

Medetomidine (10 to 80 μg/kg IM) has been combined with several different doses of ketamine (2.5, 5, 7.5, and 10 mg/kg IM) in cats undergoing ovariohysterectomy. The dose of ketamine is usually reduced as the medetomidine dose increases. Apnea may occur when the ketamine dose approaches 10 mg/kg. Good muscle relaxation and profound analgesia are comparable to that achieved with xylazine (1 mg/kg IM)-ketamine (10 mg/kg IM), and anesthesia lasts longer than it typically does with the acepromazine (1 mg/kg IM)-ketamine (10 mg/kg IM) combination.[142,143] Specific α_2-adrenergic antagonists such as atipamezole have been used to reverse medetomidine-ketamine anesthesia. Atipamezole dosed at two- to threefold the medetomidine dose is effective in antagonizing most of the anesthetic and analgesic effects of the medetomidine-ketamine combination.[144,145] Recovery to sternal recumbency usually occurs within 10 to 12 min after injection.[146] Bradycardia, vomiting, and excessive salivation, not unlike those seen with xylazine-ketamine, are the most common side effects following (2 to 5 min) medetomidine-ketamine administration.[147]

The use of oxymorphone, morphine, meperidine, and butorphanol has been assessed in combination with ketamine in cats.[148,149] When administered at oxymorphone's peak effect, the ketamine requirement is decreased by 2.5% to 10%.[148] Apparently, the administration of morphine or meperidine neither improves nor reduces the anesthetic effects of ketamine.[149] Adding butorphanol (0.1 mg/kg IV) to ketamine (8 mg/kg IV) appears to increase the intensity and duration of analgesia for a variety of procedures. The most effective dose of butorphanol ranges from 0.05 to 0.2 mg/kg IV. Some clinicians' experiences suggest that doses below and above this range provide less analgesia. It is important to realize that butorphanol is an opioid agonist-antagonist that has a *ceiling effect* on analgesia as well as undesirable opioid actions (e.g., respiratory depression). Doses above 0.2 mg/kg may cause CNS stimulation that is unaccompanied by an increased analgesic action. Tables 12.3 and 12.4 further summarize the use of ketamine and Telazol either alone or in combination with other drugs for use as anesthetics in cats.

Horses

Dissociatives should not be used as a monoanesthetics in horses because of the potential for dangerous and uncontrollable behavior and muscle incoordination. Preanesthetic sedation and tranquilization must be present before ketamine is administered. α_2-Adrenergic agonists (xylazine, detomidine, or romifidine) are most commonly used for this purpose. Xylazine (1.1 mg/kg IV), followed in 5 to 10 min by ketamine (2.2 to 3.0 mg/kg IV), induces a short period of anesthesia in horses. Higher doses of ketamine (2.75 to 3.0 mg/kg IV) are usually required for ponies, young "high-strung" Arabians, Hackneys, and thoroughbreds.[150] Ketamine should not be administered if xylazine fails to produce adequate sedation, and an alternative anesthetic technique (e.g., guaifenesin-thiobarbiturate mixture) should be considered.[150] It is not uncommon for heart and respiratory rates to decrease by one-third after xylazine administration.[151] After ketamine injection, heart rate may remain decreased while respiratory rate returns to prexylazine values.[151] Cardiac output and systemic arterial, pulmonary, and central venous pressures remain within normal ranges during xylazine-ketamine anesthesia.[151] Duration of anesthesia (15 to 20 min) is related to redistribution of ketamine to other body tissues and hepatic metabolism. In horses, approximately 60% of ketamine is metabolized by the liver, with the remainder excreted unchanged in the urine.[152] Anesthesia can be extended by administering one-third to one-half of the original dose of each drug.

In horses, the addition of butorphanol (0.01 or 0.02 mg/kg) enhances muscle relaxation and analgesia when using a xylazine-ketamine combination.[153] Behavioral changes caused by butorphanol may be breed dependent. CNS stimulation characterized by hyperresponsiveness and spasmodic lip movements has been reported in high-strung individuals after butorphanol intravenous administration, whereas deep sedation and ataxia were observed at the same dose when given to a Belgian stallion.[154] For extremely painful procedures, methadone with and without acepromazine has been administered to enhance analgesia during xylazine-ketamine anesthesia.[155,156]

Ketamine (1.5 to 2.0 mg/mL) can be added directly to a 5% solution of guaifenesin and the mixture administered as a rapid infusion, or ketamine can be administered as a bolus (1.5 to 2.2 mg/kg IV) after administration of enough guaifenesin to produce limb weakness (e.g., 1 to 2 mL/kg of a 5% solution). Less cardiovascular depression occurs with this combination, as compared

Table 12.3. Use of ketamine alone or ketamine combinations in cats.

Drug(s)	Dose and Route (mg/kg)	Duration (min)	Comment
Ketamine alone	2, 4, or 8, IV	105–115	Visceral analgesia
	4–30, IM	20–45	Incomplete immobilization and chemical restraint
		(11–40, IM)	Little analgesia, better muscle relaxation, and minor surgical procedures
	22–44, IM	—	Chemical restraint, cataleptoid anesthesia, and lack of muscle relaxation
	22, IM		Castration, onychectomy, and restraint
	33, IM	77	Ovariohysterectomy, cesarean section, laparotomy, orthopedic procedures; little analgesia, respiratory depression, and occasional apnea
Oxymorphone Triflupromazine Ketamine	0.16, SC, IM, IV 1.1, SC, IM, IV 1.1–2.2, SC, IM, IV	10–20	Light anesthesia
Xylazine Ketamine	X 1.1, IM; K 15.4–22, IM	25–40	Vomiting
	X 2.2, IM; K 11, IM	118	Vomiting
	X 0.23, IM; K 4.6, IM	85–135	Vomiting, and longer duration of anesthesia than acepromazine-ketamine
	X 2.2–4.4, IM; K 6.6, IM	60–100	—
	X 1, IM; K 10, IM	46.0±22.6	Satisfactory anesthesia, and depression of cardiovascular system
Atropine Xylazine Ketamine	0.3, IM 1.1, IM 22, IM	20	Satisfactory anesthesia
Guaifenesin Xylazine Ketamine	G 10 mg/mL; X 0.05 mg/mL; K 0.2 mg/mL Induction, 1.32±0.33 mL/kg, IV Maintenance, 10 mL/kg/h, IV	360	Easy administration, stable anesthesia, rapid recovery, and reversible with yohimbine or tolazoline
Acepromazine Ketamine	A 0.11, IM; K 4.6, IM	35–45	Better maintained heart rate than xylazine-ketamine
	A 1, IM; K 10, IM	20.0±14.8	Poor muscle relaxation and analgesia
	A 0.1, IV; K 2, IV	65	Visceral analgesia
	A 0.1, IV; K 4, IV	80	Visceral analgesia
	A 0.1, IV; K 8, IV	125±22	Visceral analgesia
Butorphanol Ketamine	B 0.1, IV; K 2, IV	280	Visceral analgesia
	B 0.1, IV; K 4, IV	325	Visceral analgesia
	B 0.1, IV; K 8, IV	360	Visceral analgesia
Medetomidine Ketamine	M 0.08, IM; K 2.5, IM	36.2±11.5	Better muscle relaxation and satisfactory anesthesia
	M 0.08, IM; K 5, IM	59.0±6.4	Better muscle relaxation and satisfactory anesthesia
	M 0.08, IM; K 7.5, IM	65.6±22.9	Better muscle relaxation and satisfactory anesthesia
	M 0.08, IM; K 10, IM	99.7±26.7	Better muscle relaxation, satisfactory anesthesia, and occasional apnea
	M 0.08, IM; K 7, IM	46±15	Vomiting, surgical anesthesia, and good muscle relaxation
	M 0.08, IM; K 5, IM	50.2	—
Detomidine Ketamine	D 0.5; K 10, oral	—	Greater sedation than oral xylazine-ketamine or medetomidine-ketamine
Diazepam Ketamine	D 0.2, IV; K 2, IV	20	Visceral analgesia
	D 0.2, IV; K 4, IV	60	Visceral analgesia
	D 0.2, IV; K 8, IV	100	Visceral analgesia
Midazolam Ketamine	M 0.5, IV; K 3, IV	—	↓ Muscle tone, dose-related behavioral signs, and suitable for clinical use
	M 0.5, IV; K 3, IV	5.0±1.1	Muscle relaxation and suitable for clinical use
	M 1, IV; K 3, IV	—	Suitable for clinical use
	M 2, IV; K 3, IV	—	—
	M 5, IV; K 5, IV	6.2±1.62	Prominent and long-lasting behavioral signs
Ketamine Propofol	K 23 or 46 µg/kg/min; P 0.025 mg/kg/min, IV Simultaneously	—	↓ Propofol dose requirement

IM, intramuscularly; IV, intravenously; SC, subcutaneously.

Table 12.4. Use of Telazol alone or Telazol combinations in cats.

Drug(s)	Dose and Route (mg/kg)	Duration (min)	Comment
Telazol alone	6–40, IM	—	—
Telazol alone	6–12, IM	—	Anesthesia
Telazol alone	12.8, IM	52.6±22.0	Salivation
			Apneustic breathing
	12.8, IV	52.8±17.3	Salivation
			Apneustic breathing
Telazol alone	7.5, IM	49.9±12.7	Surgical anesthesia
			Mild muscle relaxation
			Rough recovery
Telazol alone	9.7–11.9, IM	30	Diagnostic examinations
			Dentistry
	9.9, IV	25	Diagnostic examinations
			Dentistry
	10.6–12.5, IM	60	Minor procedure (mild to moderate analgesia)
	4.5, IM	30–60	Ovariohysterectomy
	4.5, IM	—	Onychectomy
	14.3–15.8, IM	60–135	—
Telazol alone	10.4, IM (6–16)	64.6 (32–135)	Satisfactory surgical anesthesia
			Salivation
Telazol alone	9.7, IV	60	—
	15.8, IV	>90	Respiratory depression
	23.7, IV	>90	Respiratory depression
Telazol alone	3.1±0.99, IM	—	Inadequate analgesia for castration
Acepromazine Telazol	A 0.1, IM; T, 3.4±1.09, IM or 2.7±0.97, IV	—	Adequate anesthesia for castration
Telazol alone	4.5±0.9, IM	—	Adequate anesthesia for castration
	4.5±0.9, IV	—	—
Telazol alone	5, IV	20.2±10.3	Injection of doxapram and flumazenil speed recovery
Telazol[a] Ketamine Xylazine	3.3, IM 2.64, IM 0.66, IM	43.4±9.1	Smooth induction and recovery Excellent muscle relaxation Good analgesia

IM, intramuscularly; IV, intravenously.
[a]Reconstitute with 4 mL of ketamine and 1 mL of 10% xylazine.

with thiopental-guaifenesin or thiamylal-guaifenesin anesthetic induction.[150,157] Bolus administration of ketamine plus guaifenesin in foals rapidly induces anesthesia with good muscle relaxation and analgesia followed by a smooth recovery.[158]

Continuous infusion of a guaifenesin-ketamine-xylazine combination is safe and effective for extending anesthesia in adult horses after xylazine (1.1 mg/kg IV) and ketamine (2.2 to 3.0 mg/kg IV) induction. This drug combination is prepared by adding 500 mg of xylazine and 2000 mg of ketamine to 1 L of 5% guaifenesin.[159–161] In ponies anesthetized for 2 h with this mixture, arterial blood pressure and left ventricular stroke work index were transiently decreased for the first 15 to 30 min after induction.[160] Cardiac index and arterial pH were also decreased for 15 min after induction. Hypoventilation with mild hypercapnia was noted throughout the study. These changes are transient and comparable to those reported for other injectable anesthetic drugs or drug combinations. In ponies and foals, anesthesia can be induced with a rapid intravenous injection of 1.1 mL/kg of the guaifenesin-ketamine-xylazine mixture. Anesthesia may be maintained by continuous intravenous infusion of 2 to 4 mL · kg^{-1} · h^{-1}, depending on anesthetic requirement. Standing recovery usually occurs within 25 to 45 min of discontinuation of the mixture.[150–162] An α_2-adrenergic antagonist such as tolazoline (2 to 4 mg/kg) can be administered IV to hasten recovery. When diazepam (0.1 mg/kg) is combined with xylazine (0.3 mg/kg) and ketamine (2 mg/kg), muscle relaxation is improved when compared with the administration of xylazine-ketamine alone. Diazepam provides practical advantages over guaifenesin in commercial preparation, small volume, and ease of administration.[163]

Detomidine is approved for use in horses in the United States as a sedative-analgesic for colic. Short-term anesthesia in horses can be achieved with detomidine (20 µg/kg IV) sedation followed in 6 to 8 min by ketamine (2.2 mg/kg IV). Mean arterial blood pressure increases after detomidine-ketamine injection.[164,165] When compared with xylazine, detomidine may induce better muscle relaxation when combined with ketamine. Recovery can be somewhat unpredictable. Occasionally, horses and ponies experience a rough recovery.[166] This may result from the longer sedation and muscle relaxation achieved with detomidine in some animals.[164–166]

Romifidine (100 µg/kg IV) has also been used in combination with ketamine (2.0 to 2.2 mg/kg IV) for short-term anesthesia or for induction prior to inhalation anesthesia in horses. The anesthesia duration produced by this combination is 10 to 25 min, similar to that of xylazine-ketamine.[167–169] Tables 12.5 and 12.6 further summarize ketamine and Telazol combination anesthesia in horses.

Ruminants

Xylazine (0.1 to 0.2 mg/kg IV) is commonly administered prior to, or concomitantly with, ketamine (2.2 to 3.0 mg/kg IV) for short-term anesthesia of ruminants. Tracheal intubation is easily achieved in cattle anesthetized with this combination.[170,171] Anesthesia may be safely prolonged by administering ketamine (1 to 2 mg/kg) slowly to effect. Alternatively, anesthesia can be

Table 12.5. Use of ketamine alone or ketamine combinations in horses.

Drug(s)	Dose and Route (mg/kg)	Duration (min)	Comment
Xylazine Ketamine	X 1.1, IV, wait 3–5 min; K 2.2, IV	16.1±7.3	Excellent analgesia and light anesthesia
	X 1.1, IV; K 2.2, IV Simultaneously	—	Excitement following induction
	X 1.1, IV, wait 3–5 min; K 6.6, IV	12.1±3.2	Muscle twitching, rapid nystagmus, and prolonged and rough recovery
	X 1.1, IV; K 2.2, IV	24	Inadequate muscle relaxation
	X 1.1, IV; K 2.2, IV	12–35	Smooth induction and recovery
Xylazine Butorphanol Ketamine	X 1.1, IV; B 0.1 or 0.2, IV; K 2.2, IV	Arabian, 18.25 Belgian, 52.5 Appaloosa: 56.5	Behavioral changes and enhanced muscle relaxation and analgesia
	X 1.1, IV; B 0.044, IV; K 2.2, IV	37	Adequate muscle relaxation and good analgesia
Xylazine Ketamine Methadone	X 1.1, IV; K 2.2, IV; M 0.1, IV	—	Satisfactory anesthesia
Methadone Acepromazine Xylazine Ketamine	M 0.1, IV; A 0.15, IV; X 1.1, IV; K 2.2, IV	—	Inadequate anesthesia
Acepromazine Methadone Ketamine	A 0.1, IV; M 0.1, IV; K 2.2, IV	—	—
	A 0.04, IV; M 0.04, IV; K 2.0–2.5, IV	10.2 (3–18)	Muscle tremor lasted < 1 min after induction
Guaifenesin Xylazine Ketamine	G 50 mg/mL; X 0.5 mg/mL; K 1 mg/mL Induction, 1.1 mL/kg, IV Maintenance, 2.75 mL/kg/h, IV	120	↓ Blood pressure initially and hypoventilation
	G 50 mg/mL; X 0.5 mg/mL; K 1 mg/mL Induction, 1.1 mL/kg, IV Maintenance, 4.5 mL/kg/h, IV	49±3	Surgical anesthesia
	G 50 mg/mL; X 0.5 mg/mL; K 2 mg/mL Induction, 1.1 mL/kg, IV Maintenance, 4.3 mL/kg/h, IV	44±2	Better muscle relaxation, analgesia, and surgical anesthesia
	G 100 mg/mL; X 1 mg/mL; K 2 mg/mL Maintenance, 1.1 mL/kg/h, IV	51–95	Presence of swallowing reflex, not suitable for laryngeal surgery, surgical anesthesia, and smooth recovery
	X 1.1, IV; G 100, IV; K 2, IV	—	Supplemental ketamine 200–1000 mg, maintain with halothane, and good muscle relaxation
Guaifenesin Ketamine	G 50 mg/mL; K 2 mg/mL at 1.5–2.2 mg/kg K, IV	—	Less cardiovascular depression than thiamylal-guaifenesin or thiopental-guaifenesin
	K 6 mg/mL in 150 mg/mL G; IV infusion of 7.8 µg/kg/min initially	—	↓ Halothane MAC by 50%
Xylazine Diazepam Ketamine	X 0.3, IV; D 0.05, IV; K 2, IV	—	Supplemental ketamine 200–500 mg, maintain with halothane
	X 1.1, IV; D 0.1, IV; K 2, IV	—	Supplemental ketamine 200–750 mg, maintain with halothane, good muscle relaxation

(*continued*)

Table 12.5. Use of ketamine alone or ketamine combinations in horses (*continued*).

Drug(s)	Dose and Route (mg/kg)	Duration (min)	Comment
Xylazine Temazepam Ketamine	X 1.1, IV; T 0.044, IV; K 2.2, IV	—	Longer recumbency
Romifidine Ketamine	R 0.1, IV; K 2.0–2.2, IV	10–25	Initial limb rigidity and mild muscle tremor
Romifidine Midazolam Ketamine	R 0.08, IV; M 0.06, IV; K 2.2, IV R 20 mg, M 15 mg, K 500 mg in 50 mL 0.9% NaCl; maintenance, 0.24 mL/kg/h, IV; one-third of induction MK, IV if spontaneous movements occur	25–40	May require additional dose of MK Smooth recovery
Ketamine alone	5–6 mg/100 kg in subarachnoid space	—	Effective spinal block
	10–12 mg/100 kg in subarachnoid space	—	Blockade of T13 to L3 Effective surgical analgesia
	0.5, 1, 2 mg/100 kg in caudal epidural space	10–15	Dose-dependent perineal analgesia
	5 mL of 1, 2, or 3% solution, infiltration at the base of the proximal sesamoid		↓ Halothane MAC by 14% and 12%, respectively Abaxial sesamoid nerve block
Xylazine Ketamine	X 0.5 mg/100 kg; K 1 mg/100 kg; simultaneously in caudal epidural space	>20	Perineal analgesia may extend to the thigh and flank region
Methotrimeprazine Midazolam Guaifenesin Ketamine	Me 0.5, IV; Mi 0.1, IV; G 100, IV; K 1.6, IV	—	Induction of anesthesia, smooth recovery
Detomidine Ketamine	D 0.02, IV; K 2.2, IV	—	Second dose of ketamine (1.4 mg/kg) given 15 min after first dose; improve anesthesia
	D 0.02, IV; K 2.2, IV	10–43	Required more time than xylazine-ketamine to assume recumbency, occasional poor recovery, and longer-lasting hypertension
	D 0.02 IV; K 2.2, IV	26.8 (14–42)	Smooth induction and occasional rough recovery
Guaifenesin Detomidine Ketamine	G 50 mg/mL; D 5 μg/mL; K 2 mg/mL Induction, 0.67–1.1 mL/kg, IV Maintenance, 2.2 mL/kg/h, IV	—	Good muscle relaxation and analgesia, and minimal cardiovascular effects
	G 100 mg/mL; D 0.04 mg/mL; K 4 mg/mL Maintenance, 0.67±0.17 mL/kg/h, IV	140	Surgical anesthesia but may require additional ketamine during surgery Good recovery
Detomidine Butorphanol Ketamine	0.02, IV 0.04, IV 2.2, IV	36.2 (18–67)	Smooth induction Smoother recovery Muscle relaxation

IM, intramuscularly; IV, intravenously; MAC, minimum alveolar concentration.

maintained in adult cattle with a continuous infusion of ketamine in saline or 5% dextrose solution (2 mg/mL) at a rate of 10 mL/min.[172] Clinical experience shows that guaifenesin-ketamine-xylazine mixture is an effective anesthetic combination in ruminants. The concentration of each drug in the mixture is 50 mg/mL, 2 mg/mL, and 0.1 mg/mL for guaifenesin, ketamine, and xylazine, respectively. Anesthesia can be induced with 0.55 to 1.1 mL/kg initially and maintained with adjustment for surgical stimulation with 2.2 mL $\cdot$ kg^{-1} $\cdot$ h^{-1} in adult cattle and 1.65 mL $\cdot$ kg^{-1} $\cdot$ h^{-1} in calves, kids, and lambs. Anesthesia onset is gradual but smooth. Muscle relaxation is excellent, easily enabling tracheal intubation. Supplementation with oxygen (5 to 10 L/min) during procedures may help prevent hypoxemia. Mild hypoventilation is induced by the anesthetic mixture. Surgical procedures that can be performed in cattle anesthetized with guaifenesin-ketamine-xylazine include femoral fracture plating and pinning, penile surgery, umbilical hernia repair, cesarean section, and celiotomy.[172] Tables 12.7 and 12.8 further summa-

Table 12.6. Use of Telazol alone or Telazol combinations in equids.

Species	Drug(s)	Dose and Route (mg/kg)	Duration (min)	Comment
Horses	Xylazine Telazol	1.1, IV 1.65, IV	—	Anesthesia Smooth recovery
		1.1, IV 0.5, IV	26.25	Adequate anesthesia Easy intubation Hyperresponsiveness during recovery
		1.1, IV 0.75, IV	29.25	Adequate anesthesia Easy intubation Hyperresponsiveness during recovery
		1.1, IV 2.2, IV	34.33	Adequate anesthesia Easy intubation Smooth recovery
		1.1, IV 1.65, IV	32.8±2.8	Good muscle relaxation Smooth recovery[b]
	Detomidine Telazol	0.02, IV 2, IV	38.5±9.0	Balanced anesthesia Smooth recovery[b]
		0.04, IV 2, IV	66.5±10.3	Balanced anesthesia Excellent recovery[a]
		0.06, IV 3, IV	91.5±18.0	Balanced anesthesia Prolonged duration Rough recovery[c]
		0.015, IV 2, IV	25.5±3.0	Satisfactory induction and recovery
	Xylazine Telazol	1.1, IV 1.1, IV	30.7 (24–35)	Good muscle relaxation Smooth recovery[b]
	Xylazine Butorphanol Telazol	1.1, IV 0.04, IV 1.1, IV	41.3 (33–66)	Good muscle relaxation Prolonged analgesia Smooth recovery[b]
	Detomidine Telazol	0.02, IV 1.1, IV	26±4	Good muscle relaxation Prolonged analgesia Hypoxemia
		0.04, IV 1.4, IV	39±11	Good muscle relaxation Prolonged analgesia Hypoxemia
	Detomidine Ketamine Telazol	0.013, IV 0.53, IV 0.67, IV	—	Poor recovery
	Telazol alone	0.5 and 1.0 in caudal epidural space	60–90	Perineal analgesia One horse had muscle fasciculation and central nervous system excitation after high dose Ataxia
Mules	Xylazine Telazol	1.1, IV 1.1, IV	21.1	Smooth recovery[b]
Donkeys	Xylazine Telazol	1.1, IV 1.1, IV	46	Satisfactory anesthesia Good muscle relaxation Smooth recovery[b]
Miniature donkeys	Xylazine Butorphanol Telazol	1.1, IV 0.044, IV 1.1, IV	33.8±6.3	Satisfactory anesthesia Good recovery IM, intramuscularly; IV, intravenously.

IM, intramuscularly; IV, intravenously.
[a]Animals stood at first attempt.
[b]Animals stood requiring less than three attempts.
[c]Animals stood requiring greater than five attempts.

Table 12.8. Use of Telazol alone or Telazol combinations in ruminants.

Species	Drug(s)	Dose and Route (mg/kg)	Duration (min)	Comment
Calves	Telazol alone	4, IV	50–60	Anesthesia
	Xylazine Telazol	0.1, IV 4, IV	66	Anesthesia
Cattle	Telazol alone	2–6	—	—
Sheep	Telazol Butorphanol	12, IV 0.5, IV	31 (25–45)	Adequate anesthesia
	Telazol alone	11.9±2.7, IV (8.1–16.8) Suppl,[a] 5.7, IV	150 (48–222) 210 (48–318)	Cataleptoid anesthesia Excellent muscle relaxation Muscle relaxation not as good as single dose
	Telazol alone	14.4, IV (12–22)	41.5 (25–65)	Satisfactory anesthesia for neurosurgical procedures
	Telazol alone	2.2–4.4, IM	—	Immobilization
	Telazol alone	8–22	—	—
	Telazol alone	12, IV	39±5	Smooth induction Gradual but unremarkable recovery Apneustic breathing
	Telazol alone	24, IV	40±14	Smooth induction Gradual but unremarkable recovery Apneustic breathing
	No atropine			
	Telazol	9, IM	14	Variable anesthetic response
	Telazol	12, IM	35	Surgical anesthesia
	Telazol	15, IM	51	Prolonged anesthetic duration
	With atropine	0.04, IM		
	Telazol	9, IM	13	—
	Telazol	12, IM	28	—
	Telazol	15, IM	42	—
	Atropine Telazol	0.03, IM 13.2, IV	41.6±15.0	—
	Xylazine Telazol	0.01, IM 13.2, IV	101.7±26.0	Better muscle relaxation Longer anesthetic duration Apnea
Llamas	Telazol alone	4.4, IM	25–50	Chemical restraint

IM, intramuscularly; IV, intravenously.
[a]Suppl, supplemental dose.

rize the use of ketamine combinations and Telazol for anesthesia in ruminants.

In llamas, xylazine (0.25 mg/kg IM) followed in 15 min by ketamine (5 mg/kg IM) induces 30 to 60 min of anesthesia and restraint sufficient for minor procedures such as suturing lacerations, abscess drainage, or cast application.[173] If tracheal intubation is desired, xylazine (0.25 mg/kg IV) with ketamine (2.5 mg/kg IV) can be used. Changes in heart rate and blood pressure are similar to those observed in other species. A recent study compared the anesthetic effects of two combinations of xylazine (0.4 and 0.8 mg/kg IM) and ketamine (4 and 8 mg/IM) in llamas. The low-dose combination induced sternal recumbency, but analgesia-anesthesia was observed in only two llamas. The high-dose combination produced longer recumbency (87 vs. 19 min) and analgesia (73 vs. 18 min). Severe hypoxemia was observed in llamas receiving the high-dose combination, as evidenced by low saturation of peripheral oxygen measured by pulse oximeter and low PaO_2 measured from arterial blood gas. Hypoxemia can be treated effectively with nasal insufflation of 100% oxygen.[174]

Swine

Ketamine has been used extensively in pigs premedicated with atropine (0.04 mg/kg IM) for minor surgical and diagnostic procedures. At intramuscular doses of 11 to 20 mg/kg, muscle relaxation is poor and analgesia is brief. Green et al.[175] reported that pigs react violently to intramuscular injections of ketamine and then exhibit muscle tremor, extensor rigidity, panting respiration, and erythema. These responses can be minimized by combining diazepam (1 mg/kg IM) or xylazine (2 mg/kg IM) with ketamine (10 to 20 mg/kg IM). Deep sedation and good muscle relaxation occur with these drug combinations, but pigs may still respond to noxious stimuli such as incision of the abdominal wall.[175,176] Alternatively, a combination of oxymorphone (0.075 mg/kg), xylazine (2 mg/kg), and ketamine (2 mg/kg) mixed in the same syringe and given IV induces surgical anesthesia. When given IM, satisfactory anesthesia can be achieved by doubling the dose of each drug.[171,177]

Short-term anesthesia in pigs can also be achieved with atropine (0.025 mg/kg IM)-butorphanol (0.2 mg/kg IM)-xylazine (2 mg/kg IM)-ketamine (10 mg/kg IM) (ABXK) or with atropine (0.025 mg/kg IM)-butorphanol (0.2 mg/kg IM)-medetomidine (80 µg/kg IM)-ketamine (10 mg/kg IM) (ABMK). Anesthesia is induced rapidly with both combinations, but ABMK appears to induce more effective anesthesia for major surgery, which is characterized by good muscle relaxation enabling endotracheal intubation for over 1.5 h. Atipamezole (240 µg/kg IV or IM) can be administered to shorten the anesthesia.[178] Medetomidine-ketamine appears to produce longer periods of muscle relaxation (43.6 vs. 12.7 min vs. 21.0 vs. 14 min) and anesthesia (49.4 vs. 13.5 min vs. 34.6 vs. 17.2 min) than does xylazine-ketamine in pigs. Slight cardiovascular stimulation with minimal respiratory effect occurs during medetomidine-ketamine anesthesia.[179] Tables 12.9 and 12.10 further summarize the use of ketamine combinations and the use of Telazol for anesthesia in swine.

Table 12.9. Use of ketamine alone or ketamine combinations in swine.

Drug(s)	Dose and Route (mg/kg)	Duration (min)	Comment
Atropine Ketamine	0.044, IM 20, IM	10–30	Poor muscle relaxation and analgesia
Xylazine Ketamine	2, IM 20, IM	—	Required supplemental dose for intubation
Innovar-Vet Ketamine	1 mL/13.6 kg, IM 11, IM	41.75	Good muscle relaxation
Acepromazine Ketamine	0.5, IM 15, IM	18.25	Strong, sharp muscle activity
Xylazine Ketamine	0.2, IM 11, IM	24.5	Strong, sharp muscle activity
Ketamine alone	10–20, IM	—	Violent reaction, muscle tremor, extensor rigidity, ↑ heart rate and respiratory rate, panting respiration, and erythema
Diazepam Ketamine	1, IM 10, IM	40	Deep sedation and response to incision Good muscle relaxation
Xylazine Ketamine	2, IM 15, IM	40	Deep sedation Good analgesia Excellent muscle relaxation
Xylazine Ketamine Oxymorphone	2, IV 2, IV 0.075, IV	20–30	Good analgesia and muscle relaxation Smooth recovery, which can be shortened by naloxone
Xylazine Ketamine	1, IV 10, IV	25	Good analgesia
Guaifenesin Xylazine Ketamine	50 mg/mL 1 mg/mL 1 mg/mL Induction, 0.67–1.1 mL/kg, IV Maintenance, 2.2 mL/kg/h, IV	120	Good muscle relaxation and analgesia Minimal cardiovascular changes
Atropine Butorphanol Xylazine Ketamine	0.025, IM 0.2, IM 2, IM 10, IM	—	Rapid induction of anesthesia

(continued)

Table 12.11. Use of ketamine alone or ketamine combinations in exotic and wildlife animals (*continued*).

Common Names (Genus and Species)	Drug(s)	Dose and Route (mg/kg)	Duration (min)	Comment	Reference
Fallow deer (*Dama dama*)	Medetomidine Ketamine	0.08–0.12, IM 1–2, IM	—	Complete immobilization	192
Red deer (*Cervus elaphus*)	Xylazine-ketamine mix (1:1) Xylazine, 125 mg/mL Ketamine, 100 mg/mL	Mature stags, 2 mL, IM[a] Yearlings, 1.5 mL, IM[a]	— —	—	194
	Xylazine Ketamine	1.2, IM 1, IM	—	—	195
Domestic reindeer	Medetomidine Ketamine	0.025, IM 0.5, IM	—	Complete immobilization	192
Forest reindeer (*Rangifer tarandus fennicus*)	Medetomidine Ketamine	0.059±0.013, IM (0.037–0.084 range) 0.9±0.3, IM (0.4–1.9 range)	—	Immobilization	196
	Medetomidine Ketamine	0.0487, IM 1.1, IM	—	Complete immobilization	193
White-tailed deer (*Odocoileus virginianus*)	Xylazine Ketamine	0.54–1.99, IM 3.78–14.77, IM	—	Immobilization	197
	Xylazine Ketamine	100 mg total, IM 300 mg total, IM	—	—	198
	Xylazine Ketamine	0.35, IM (0.1–0.62) 2.92, IM (1.65–6.2)	—	—	189
	Medetomidine Ketamine	0.06, IM 1.7, IM	—	Complete immobilization	192
	Medetomidine Ketamine	0.0593, IM 1.7, IM	—	Complete immobilization	193
Formosan sika deer (*Cervus nippon taiouanus*)	Medetomidine Ketamine	0.233±0.061, IM (0.169–0.363) 2.33±0.61, IM (1.69–3.63)	—	Immobilization	192
Elk (*Cervus canadensis*)	Xylazine Ketamine	600 mg total, IM 1200 mg, total, IM	—	Immobilization	199
Order Carnivora, family Canidae					
Coyote (*Canis latrans*)	Ketamine alone	12.3, IM	52	Immobilization Extensive salivation Rigidity	200
	Xylazine Ketamine	1.8–2.9, IM 9.2–14.7, IM	—	Chemical restraint	

(*continued*)

Table 12.11. Use of ketamine alone or ketamine combinations in exotic and wildlife animals (*continued*).

Common Names (Genus and Species)	Drug(s)	Dose and Route (mg/kg)	Duration (min)	Comment	Reference
Coyote (*Canis latrans*)	Xylazine Ketamine	2, IM 4, IM	—	—	201
Cape hunting dogs (*Lycaon pictus*)	Medetomidine Ketamine	0.043–0.121, IM 2.6–3.0, IM	—	Partial or complete immobilization Bradycardia ↓ Respiration rate	202
Arctic fox (*Alopex lagopus*)	Medetomidine Ketamine	0.05, IM 2.5, IM	—	Complete immobilization	192
Blue fox (*Alopex lagopus*)	Medetomidine Ketamine	0.05–2.5, IM 2.5, IM	—	Immobilization	203
Gray fox (*Urocyon cinereoargenteus*)	Xylazine Ketamine	6.6–11.0, IM 11.0–17.6, IM	—	Chemical restraint	200
Kit fox (*Vulpes macrotis*)	Xylazine Ketamine	6.6–11.0, IM 11.0–17.6, IM	—	Chemical restraint	200
Red fox (*Vulpes fulva*)	Xylazine Ketamine	6.6–11.0, IM 22–33, IM	—	Chemical restraint	200
Gray wolf (*Canis lupus*)	Xylazine Ketamine	2.2, IM 6.6, IM	—	Significant bradycardia	204
Wolf (*Canis lupus* L.)	Xylazine Ketamine	30 mg total, IM 400 mg total, IM	148.0±52.7	—	205
	Xylazine Ketamine	2–3, IM 5–6, IM	35–40	—	206
Order Carnivora, family Felidae					
Bobcat (*Lynx rufus*)	Acepromazine Ketamine	0.66–1.1, IM 17.6, IM (11.9–34.9)	—	Immobilization	200
	Ketamine alone	33.4, IM (22.4–60.3)	—	—	200
California bobcat (*Felis rufus californieus*)	Ketamine alone	5.5–17.0, IM	—	—	207
Fishing cat (*Felis viverrina*)	Ketamine alone	19–25, IM	—	—	208
Flat-headed cat (*Felis planiceps*)	Ketamine alone	8, IM	—	—	208
Jungle cat (*Felis chaus*)	Medetomidine Ketamine	0.1, IM 2.5, IM	—	Immobilization	192

(*continued*)

Table 12.11. Use of ketamine alone or ketamine combinations in exotic and wildlife animals (*continued*).

Common Names (Genus and Species)	Drug(s)	Dose and Route (mg/kg)	Duration (min)	Comment	Reference
Leopard cat (*Felis bengalensis*)	Ketamine alone	8–25, IM	—	—	209
Cheetah (*Acinonyx jubatus*)	Ketamine alone	8–12, IM	—	—	209
	Ketamine alone	10	—	—	208
	Medetomidine Ketamine	0.06–0.07, IM 2.5–3.0, IM	—	Immobilization	292
Jaguar (*Panthera onca*)	Ketamine alone	13–18, IM	—	—	209
	Medetomidine Ketamine	0.05, IM 1.5–2.0, IM	—	Immobilization	192
Leopard (*Panthera pardus*)	Medetomidine Ketamine	0.07–0.08,IM 2.5–3.0, IM	—	Immobilization	192
Black leopard (*Panthera pardus*)	Ketamine alone	15, IM	—	Occasional convulsion Inadequate muscle relaxation	209
	Ketamine alone	11 (5.5–17.0 range), IM	—	—	207
	Ketamine alone	7.5, IM	—	—	210
Chinese leopard (*Panthera pardus japonensis*)	Ketamine alone	15, IM	—	Occasional convulsion Inadequate muscle relaxation	209
Clouded leopard (*Neofelis nebulosa*)	Ketamine alone	8.6, IM	—	Occasional convulsion Inadequate muscle relaxation	209
		7, IM	—	—	208
Snow leopard (*Panthera uncia*)	Ketamine alone	10, IM	—	—	208
	Medetomidine Ketamine	0.06–0.08, IM 2.5–3.0, IM	—	Complete immobilization	192
	Medetomidine Ketamine	0.067±0.016, IM (0.038–0.107 range) 2.7±0.8, IM (1.3–5.7 range)	45	Complete immobilization Allowed tracheal intubation	193
	Xylazine Ketamine	2.2±0.2, IM (1.9–2.6 range) 10.9±1.0, IM (9.6–12.8 range)	30–45	Immobilization Moderate to good muscle relaxation	211

(*continued*)

Table 12.11. Use of ketamine alone or ketamine combinations in exotic and wildlife animals (*continued*).

Common Names (Genus and Species)	Drug(s)	Dose and Route (mg/kg)	Duration (min)	Comment	Reference
Snow leopard (*Panthera uncia*)	Medetomidine Ketamine	0.067±0.014, IM (0.038–0.109 range) 2.9±0.8, IM (1.6–5.7 range)	30–60	Immobilization Shorter recovery compared with xylazine-ketamine Good to excellent muscle relaxation	211
Lion (*Panthera leo*)	Medetomidine Ketamine	0.03, IM 1.0–1.5, IM	—	Immobilization	192
	Ketamine alone	10–20, IM	—	Rapid immobilization	209
		5–7, IM	—	—	212
		5.0–7.5, IM	—	—	210
	Xylazine Ketamine	110 total, IM 450 total, IM	240	Immobilization	190
	Xylazine Ketamine	3.2, IM 8, IM	—	—	213
Mountain lion, puma (*Felis concolor*)	Xylazine Ketamine	0.88–0.99, IM 7.3–7.7, IM Suppl,[b] 4.4–8.8, IM	—	Immobilization	200
	Ketamine alone	11–25, IM	—	—	209
	Xylazine Ketamine	1.8, IM 11, IM	—	—	214
Margay (*Felis wiedii*)	Ketamine alone	15, IM	—	Occasional convulsion Inadequate muscle relaxation	209
Tiger (*Panthera tigris*)	Ketamine alone	7–14, IM	—	—	209
	Medetomidine Ketamine	0.03, IM 1.0–1.5, IM	—	Immobilization	192
Order Carnivora, family Mustelidae					
Badger (*Taxidea taxus*)	Ketamine alone	11–33, IM	—	Immobilization	200
Beaver (*Castor canadensis*)	Ketamine alone	22, IM	—	Immobilization	215
	Acepromazine Ketamine	0.22, IM 11, IM	—	Immobilization	200
	Diazepam Ketamine	0.1, IM 25, IM	—	Smooth induction	216

(*continued*)

Table 12.11. Use of ketamine alone or ketamine combinations in exotic and wildlife animals (*continued*).

Common Names (Genus and Species)	Drug(s)	Dose and Route (mg/kg)	Duration (min)	Comment	Reference
Ferret (*Mustela putorius furo*)	Ketamine alone	20–25, IM	—	—	217
	Xylazine Ketamine	2, IM 25, IM	80.0±11.4	—	218
	Ketamine alone	60, IM	—	Muscle rigidity Incomplete analgesia	219
	Diazepam Ketamine	3, IM 35, IM	—	Muscle rigidity Incomplete analgesia	219
	Xylazine Ketamine	2, IM 25, IM	—	Acceptable analgesia Muscle relaxation	219
	Ketamine alone	25, IM	—	Excessive salivation Muscle tremor Paddling motions	220
	Xylazine Ketamine	2, IM 25, IM	—	Good muscle relaxation	220
Fisher (*Martes pennati*)	Ketamine or with acepromazine	7.5, IM (11.0–24.2) 1.1, IM	—	Immobilization	200
Mink (*Mustela vision*)	Ketamine alone	5–20, IM	—	—	217
		10–15, IM	—	Suitable for electroejaculation Surgical anesthesia	217
		100, IM	—	Immobilization	217
		15.4–22.0, IM	—		217
Pine marten (*Marten americana*)	Ketamine alone	11–22, IM	—	Immobilization	200
European otter (*Lutra lutra*)	Diazepam Ketamine	0.5, IM 18, IM	—	Good muscle relaxation Smooth recovery	221
Asian small-clawed otter (*Aonyx cinerea*)	Medetomidine Ketamine	0.1–0.12, IM 4–5, IM	—	Good muscle relaxation Immobilization	222
River otter (*Lutra canadensis*)	Ketamine alone	22, IM	—	—	200
Sea otter (*Enhydra lutris*)	Ketamine alone	1, IM	—	Immobilization	200

(*continued*)

Table 12.11. Use of ketamine alone or ketamine combinations in exotic and wildlife animals (*continued*).

Common Names (Genus and Species)	Drug(s)	Dose and Route (mg/kg)	Duration (min)	Comment	Reference
Australian skink and bobtail skink (*Tiliqua rugosa*)	Ketamine alone	170–230 mg total, IM	—	Good muscle relaxation	223
King's skink (*Egernia kingii*)	Ketamine alone	170–230 mg total, IM	—	Good muscle relaxation	223
Common skunk (*Mephitis mephitis nigra*)	Ketamine alone	10–20, IM	—	—	224
Spotted skunk (*Spilogale gracilis*)	Ketamine alone	30.1, IM	—	Immobilization	200
Striped skunk (*Mephitis mephitis*)	Ketamine alone	4.5–60.0, IM	—	Immobilization	225
		26.8, IM	44	Immobilization	200
Weasel (*Mustela frenata*)	Ketamine alone	15.4–22.0, IM	—	Immobilization	200
Order Carnivora, family Ursidae					
American black bear (*Ursus americana*)	Medetomidine Ketamine	0.03–0.04, IM 1.0–1.5, IM	—	Immobilization	192
	Xylazine Ketamine	2.0–4.5, IM 5–9, IM	—	Good chemical restraint	180
		1.9–9.25, IM 1.9–9.25, IM	45–100	—	181
		3.6–10.5, IM 3.6–10.5, IM	—	Immobilization	226
Brown bear (*Ursus arctos horribilis*)	Medetomidine Ketamine	Zoo: 0.02–0.03, IM Wild: 0.06–0.08, IM UK: 0.03–0.04, IM Zoo: 0.5–1.0, IM Wild: 1.0–1.6, IM UK: 1.0–1.5, IM	—	Immobilization	192
Grizzly bear (*Ursus arctos*)	Xylazine Ketamine	11.1, IM (6.3–14.0 range) 11.1, IM (6.3–14.0 range)	—	—	226
Himalayan bear (*Selnarctos thibetanus*)	Medetomidine Ketamine	0.03–0.04, IM 1.0–1.5, IM	—	—	192
Polar bear (*Ursus maritimus*)	Medetomidine Ketamine	0.03, IM 1.0–1.5, IM	—	Immobilization	192

(*continued*)

Table 12.11. Use of ketamine alone or ketamine combinations in exotic and wildlife animals (*continued*).

Common Names (Genus and Species)	Drug(s)	Dose and Route (mg/kg)	Duration (min)	Comment	Reference
Polar bear (*Ursus maritimus*)	Xylazine Ketamine	6.8, IM 6.8, IM	—	Immobilization Good muscle relaxation	182
Sloth bear (*Melursus ursinus*)	Xylazine Ketamine	1.4–2.44, IM 5.8–9.75, IM	—	Immobilization	227
Other species					
Camel (*Camelus bactrianus*)	Xylazine Ketamine	0.25, IM 5.5, IM	—	Good muscle relaxation Good analgesia	228
		0.15, IM 2.5, IM	—	Good muscle relaxation Good analgesia	228
African elephant (*Loxodonta africana*)	1st dose Xylazine Ketamine 2nd dose Xylazine Ketamine or Ketamine	1st dose 0.14±0.03, IM 1.14±0.21, IM 2nd dose 0.08±0.03, IM 0.61±0.19, IM 0.47, IV	11.6±6.9 (7–31) 27.0±8.9 (13–50)	Deep sedation to immobilization —	229
	Xylazine Ketamine	0.2, IM 1.0–1.5, IM	—	—	230
		0.1±0.04, IM 0.6±0.13, IM	—	Chemical restraint only	231
Spotted hyena (*Crocuta crocuta*)	Xylazine Ketamine	6.3, IM 13.2, IM	100	Immobilization	232
Collared peccaries (*Tayassu tajacu*)	Ketamine alone	14.71–24.61, IM	71.7	Smooth recovery	233
Rabbit (*Sylvilagus floridanus*)	Xylazine Ketamine	5, IM 70, IM	—	—	234
	Ketamine EMTU[c]	35, IM 25.0–45.5, IV	18.75 (15–60)	Lack of consistency in induction of surgical anesthesia	235
	Xylazine Acepromazine Ketamine	5, SC 0.75, IM 35, IM	95.25 (58–177)	Respiratory depression Hypothermia Surgical anesthesia	235
	Ketamine Chloral hydrate	20, IM 250, IV	15 (0–30)	Lack of consistency in induction of surgical anesthesia	235
	Xylazine Ketamine	5, IM 35, IM	46.5 (15–83)	Lack of consistency in induction of surgical anesthesia	235

(*continued*)

Table 12.11. Use of ketamine alone or ketamine combinations in exotic and wildlife animals (*continued*).

Common Names (Genus and Species)	Drug(s)	Dose and Route (mg/kg)	Duration (min)	Comment	Reference
Rabbit (*Sylvilagus floridanus*)	Xylazine Ketamine	5, IM 35, IM	—	—	236
	Xylazine Butorphanol Ketamine	5, IM 0.1, IM 35, IM	68±2	—	236
New Zealand white rabbit (*Oryctolagus cuniculus*)	Xylazine Ketamine	5, IM 35, IM	35±6	Surgical anesthesia	237
		5, IV 25, IV	—	—	238
		5, IM 35, IM	77±5	—	239
	Xylazine Acepromazine Ketamine	5, IM 0.75, IM 35, IM	99±20	—	239
	Guaifenesin Ketamine	200, IV 50, IM	30	Surgical anesthesia	240
Raccoon (*Procyon lotor*)	Ketamine alone	10–14, IM	—	Inadequate jaw muscle relaxation	241
		20–29, IM	180 (150–270 range)	Adequate jaw relaxation (30–100 min) Immobilization	241
	Ketamine alone	16.7, IM	—	Chemical restraint	200
	Xylazine Ketamine	2.2–3.3, IM 11.0–16.5, IM	—	Incomplete restraint with lower dose of ketamine	200
	Acepromazine Ketamine	1.25, IM 13.6, IM	—	—	200
Feral pig (*Sus scrofa*)	Xylazine Ketamine	9.8–19.6, IM 9.8–19.6, IM	47.9±12.7	Immobilization	242
Ringtail (*Bassariscus astutus*)	Ketamine alone	15, IM	—	Immobilization	200
Gopher snake (*Pituophis melanoleucus catenifer*)	Ketamine alone	75, IM	43.6±8.1 (11–63)	Sedation to surgical anesthesia	243

(*continued*)

Table 12.12. Use of ketamine alone or ketamine combinations in birds.

Common Names (Genus and Species)	Drug(s)	Dose and Route (mg/kg)	Duration (min)	Comment	Reference
Accipiters	Diazepam Ketamine	1, IM 30, IM	—	—	254
Bald eagle (*Haliaeetus leucocephalus*)	Diazepam Ketamine	1, IM 10–30, IM	—	—	254
Budgerigar (*Melopsittacus undulatus*)	Xylazine Ketamine	10, IM 40, IM	—	—	255
Double-wattled cassowary (*Casuarius casuarius*)	Etorphine Ketamine	10–12 total, IM 200–300 total, IM	—	Immobilization suitable for minor procedures	256
Chicken (*Gallus gallus*)	Ketamine alone	1–160, IM 14, IV	15	Muscle tremor LD_{50},[b] 67.5 mg/kg	257
Columbiformes and corvids	Diazepam Ketamine	2–5, IM 20–40, IM	—	—	254
Ducks and geese	Diazepam Ketamine	2–4 20–60	—	—	254
Pekin duck (*Anas platyrhyncos*)	Ketamine alone	20, IV	—	—	258
	Xylazine Ketamine	1, IV 20, IV	—	Respiratory depression	258
Emu (*Dromiceius novaehollandiae*)	Ketamine alone	25, IM initially 5–8, IV additionally	—	Anesthesia	259
		25 initially, IM 5, suppl[a] IV	—	Short-term immobilization	259
Leghorn (*Gallus domesticus*)	Xylazine Ketamine	2, IM 2, IM	—	—	260
Red-tailed hawk (*Buteo jamaicensis*)	Xylazine Ketamine	2.2, IV 4.4, IV	—	—	261
Herons	Diazepam Ketamine	1–2, IM 20, IM	—	—	254
Ostrich (*Struthio camelus*)	Diazepam Ketamine	0.22, IV 4.4, IV	—	Good induction and recovery	262
		0.33, IV 6.6, IV	—	Poor induction Good recovery	262
	Xylazine Diazepam Ketamine	0.44, IM 0.15, IV 2.8, IV	—	Poor induction Good recovery	262
	Xylazine	0.9, IM	—	Fair induction	262

Table 12.12. Use of ketamine alone or ketamine combinations in birds (*continued*).

Common Names (Genus and Species)	Drug(s)	Dose and Route (mg/kg)	Duration (min)	Comment	Reference
Ostrich (*Struthio camelus*)	Xylazine Ketamine	0.03, IV 4.8, IV		Poor recovery	262
Blue-necked ostrich (*Struthio camelus austrealis*)	Etorphine Ketamine	10–12 total, IM 200–300 total, IM	—	Immobilization suitable for minor procedure	256
Barred, long-eared, and short-eared owls	Diazepam Ketamine	1, IM 10, IM	—	—	254
Great horned (*Bubo virginianus*) and screech owls (*Otus asio*)	Diazepam Ketamine	1, IM 25, IM	—	—	254
Parakeets	Ketamine alone	1 total, IM 2 total, IM 3 total, IM	— — —	Sedation Surgical anesthesia Surgical anesthesia	263
Pigeon (*Columbia livia*)	Ketamine alone	1 total, IM 2 total, IM 3 total, IM	— — —	Respiratory depression — —	263
Cape vulture (*Gyps coprotheres*)	Ketamine	7.5–28.8, IM	—	Immobilization	264
Turkey vulture (*Cathartes aura*)	Xylazine Ketamine	1, IM 10, IM	19.8±25.4	Good muscle relaxation Consistent level of anesthesia	265

IM, intramuscularly; IV, intravenously.
[a]Suppl, supplemental dose.
[b]LD_{50}, median lethal dose.

Nondomestic Animals

Ketamine and Telazol have both been used extensively in various combinations for the immobilization of captured and wild animals. Ketamine usage has been somewhat limited because of its relatively low concentration, requiring a large volume be delivered to many larger species. Ketamine can be lypholized and reconstituted to a smaller volume to create a higher concentration when a larger dose is required via a remote delivery device (e.g., darts).[180–182] In contrast, Telazol has the advantage of being reconstituted to a small volume with potent sedatives or adjunctive analgesic drugs to increase overall potency. Both anesthetics have been used alone or in combination in many wild and exotic species.[183–186] Tables 12.11 through 12.15 further summarize the use of ketamine and Telazol, alone and in combination with other drugs, in nondomesticated species.

References

1. Corssen G, Miyasaka M, Domino EF. Changing concepts in pain control during surgery: Dissociative anesthesia with CI-581—A progress report. Anesth Analg 47:746, 1968.
2. Winters WD, Ferrer-Allado T, Guzman-Flores C. The cataleptic state induced by ketamine: A review of the neuropharmacology of anesthesia. Neuropharmacology 11:303, 1972.
3. Thurmon JC, Nelson DR, Christie GJ. Ketamine anesthesia in swine. J Am Vet Med Assoc 160:1325, 1972.
4. Chen G, Ensor C. 2-(Ethylamino)-2-(2-thienyl) cyclohexanone–HCl (CI-634): A taming, incapacitating, and anesthetic agent for the cat. Am J Vet Res 29:863, 1968.
5. Miyasaka M, Domino EF. Neuronal mechanisms of ketamine-induced anesthesia. Int J Neuropharmacol 7:557, 1968.
6. Massopust LC, Wolin LR, Albin MS. The effects of a new phencyclidine derivative and diazepinone derivative on the electroencephalographic and behavioral responses in the cat. TIT J Life Sci 3:1, 1973.
7. Kohrs R, Durieux ME. Ketamine: Teaching an old drug new tricks. Anesth Analg 87:1186, 1998.
8. Brockmeyer DM, Kendig JJ. Selective effects of ketamine on amino acid-mediated pathways in neonatal rat spinal cord. Br J Anaesth 74:79, 1995.
9. Ohtani M, Kikuchi H, Kitahata LM, Taub A, Toyooka H, Hannaoka K, Dohi S. Effects of ketamine on nociceptive cells in the medial medullary reticular formation of the cat. Anesthesiology 51:414, 1979.
10. Kitahata LM, Taub A, Kosaka Y. Lamina-specific suppression of dorsal-horn unit activity by ketamine hydrochloride. Anesthesiology 38:4, 1973.
11. Corssen G, Little SG, Tavakoli M. Ketamine and epilepsy. Anesth Analg 53:319, 1974.
12. Ferrer-Allado T, Brechner VL, Dymond A, Cozen H, Crandall P. Ketamine-induced electroconvulsive phenomena in the human limbic and thalamic regions. Anesthesiology 38:333, 1973.
13. Reder BS, Trapp LD, Troutman KG. Ketamine suppression of chemically induced convulsions in the two-day-old white leghorn cockerel. Anesth Analg 59:406, 1980.
14. Church J. The anticonvulsant activity of ketamine and other phencyclidine receptor ligands, with particular reference to *N*-methyl-D-aspartate receptor mediated events. In: Domino EF, ed. Status of Ketamine in Anesthesiology. Ann Arbor, MI: NPP, 1990:521.
15. Anis NA, Bery SC, Burton NR, Lodge D. The dissociative anesthetics, ketamine and phencyclidine, selectively reduce excitation of central mammalian neurons by N-methyl-D-aspartate. Br J Pharmacol 79:565, 1983.
16. Velisek L, Mares P. Anticonvulsant action of ketamine in laboratory animals. In: Domino EF, ed. Status of Ketamine in Anesthesiology. Ann Arbor, MI: NPP, 1990:541.
17. Kaplan B. Ketamine HCl anesthesia in dogs: Observation of 3 cases. Vet Med Small Anim Clin 67:631, 1972.
18. Humphrey WJ. Ketamine HCl as a general anesthetic in dogs. Mod Vet Pract 52:38, 1971.
19. Evans AT, Krahwinkel DJ, Sawyer DC. Dissociative anesthesia in the cat. J Am Vet Med Assoc 8:371, 1972.
20. Beck CC. Evaluation of Vetalar (ketamine HCl): A unique feline anesthetic. Vet Med Small Anim Clin 66:993, 1971.
21. Nimmo WS, Clements JA. Ketamine. In: Prys-Roberts C, Hug CC, eds. Pharmacokinetics of Anesthesia. Boston: Blackwell Scientific, 1984:235.
22. Haskins SC, Peiffer RL, Stowe CM. A clinical comparison of CT-1341, ketamine, and xylazine in cats. Am J Vet Res 36:1537, 1975.
23. Sawyer DC, Rech RH, Durham RA. Effects of ketamine and combination with acetylpromazine, diazepam, or butorphanol on visceral nociception in the cat. In: Domino EF, ed. Status of Ketamine in Anesthesiology. Ann Arbor, MI: NPP, 1990:247.
24. Sawyer DC, Rech RH, Durham RA. Does ketamine provide adequate visceral analgesia when used alone or in combination with acepromazine, diazepam, or butorphanol in cats? J Am Anim Hosp Assoc 29:257, 1993.
25. Castroman PJ, Ness TN. Ketamine, an *N*-methyl-D-aspartate receptor antagonist, inhibits the reflex responses to distension of the rat urinary bladder. Anesthesiology 96:1401, 2002.
26. Castroman PJ, Ness TN. Ketamine, an *N*-methyl-D-aspartate receptor antagonist, inhibits the spinal neuronal responses to distension of the rat urinary bladder. Anesthesiology 96:1410, 2002.
27. Olivar T, Laird JM. Differential effects of *N*-methyl-D-aspartate receptor blockade on nociceptive somatic and visceral reflexes. Pain 79:67, 1999.
28. Alams S, Saito Y, Kosaka Y. Antinociceptive effects of epidural and intravenous ketamine to somatic and visceral stimuli in rats. Can J Anaesth 43:408, 1996.
29. Iwasaki H, Collins JG, Namiki A, Yamasawa Y, Omote K, Omote T. Effects of ketamine on behavioral responses to somatic and visceral stimuli in rats. Masui 40:1691, 1991.
30. Pederson JL, Galle TS, Kehlet H. Peripheral analgesic effects of ketamine in acute inflammatory pain. Anesthesiology 89:58, 1998.
31. Warncke T, Jørum E, Stubhaug A. Local treatment with the *N*-methyl-D-aspartate receptor antagonist, ketamine, inhibits development of secondary hyperalgesia in man by a peripheral action. Neurosci Lett 227:1, 1997.
32. Tverskoy M, Oren M, Vaskovich M, Dashkovsky I, Kissin I. Ketamine enhances local anesthetic and analgesic effects of bupivacaine by peripheral mechanism: A study in postoperative patients. Neurosci Lett 215:5, 1996.
33. Brau ME, Sander F, Vogel W, Hemelmann G. Blocking mechanisms of ketamine and its enantiomers in enzymatically demyelinated peripheral nerves as revealed by single-channel experiments. Anesthesiology 86:394, 1997.
34. Orser BA, Pennefather PS, MacDonald JF. Multiple mechanisms of ketamine blockade of *N*-methyl-D-aspartate receptors. Anesthesiology 86:903, 1997.