Chemical Restraint of the Fisher

Matthew R. Dzialak, *Department of Forestry, University of Kentucky, Lexington, KY 40546*

Thomas L. Serfass, *Department of Biology, Frostburg State University, Frostburg, MD 21532*

Abstract: As fisher *(Martes pennanti)* populations recover throughout portions of their historic distribution in the southeastern United States, responsibilities and opportunities in their conservation research likely will become more prevalent. Chemical restraint often is a valuable tool in studying wildlife populations. We reviewed previous research on chemical restraint of fishers with the objective of providing a comparative assessment of field and clinical applications of specific chemical restraints or chemical restraint combinations. Chemical restraints that have been studied in fishers include ketamine, Telazol, and combinations of ketamine-xylazine, ketamine-medetomidine, and ketamine-acepromazine. Ketamine was safe and effective, but when used alone, its applications were limited to brief, non-invasive procedures because it generally provided shallow immobilization and rapid recovery. Telazol was more versatile than ketamine because it provided better myorelaxation, more efficient ventilation, and dose-dependent duration of anesthesia. Telazol would enable brief or prolonged procedures at doses of 5.0–11.0 mg/kg. We considered medetomidine-ketamine combinations and atipamezole to be a preferred alternative to other chemical restraints because these drugs combined broad clinical and field utility with reversibility. Medetomidine-ketamine at 0.07–0.08 mg/kg medetomidine combined with a 3.5–4.0 mg/kg ketamine, and atipamezole at approximately 0.35–0.40 mg/kg (administered upon completion of procedures) would be appropriate for most management and research objectives. Ketamine-xylazine, although generally effective, was the only drug or drug combination associated with clinical concerns (respiratory complication). Generally, physiologic responses of fishers were consistent with known drug pharmacologies. Fishers may be prone to hyperthermia and mild hyperventilation during immobilization with ketamine or ketamine-α_2-agonist combinations, respectively. Our recommendations and precautions can be a useful guide for restraining fishers. However, no chemical restraint or dose regimen should be perceived as a panacea, so managers and biologists must base selection of a chemical restraint and determination of an appropriate dose on specific objectives and attributes (e.g., physical condition of the fisher) of the restraint event. Further research on chemical restraint of fishers should focus on refining field immobilization protocols, clinical evaluation of cardiopulmonary regulatory mechanisms mediated by α_2 receptors, conditions associated with thermoregulatory disruption, and new chemical restraints (particularly ketamine-α_2-agonist combinations).

Proc. Annu. Conf. Southeast. Assoc. Fish and Wildl. Agencies 56:275–289

Table 1. Chemical restraints used on fishers (*Martes pennanti*) and their general pharmacologic classes.

Drug	Class
Acepromazine maleate	Phenothiazine
Atipamezole	Alpha$_2$-adrenergic antagonist
Atrophine[a]	
Chlordiazeproxide hydrochloride	Benzodiazepine
Diazepam	Benzodiazepine
Flumazenil	Benzodiazepine antagonist
Halothane[b]	Inhalent (halogenated alkane)
Ketamine hydrochloride	Cyclohexamine (cyclohexanone)
Medetomidine hydrochloride	Alpha$_2$-andrenergic agonist
Phencyclidine hydrochloride	Cyclohexamine (arylcycloalkylamine)
Promazine hydrochloride	Phenothiazine
Telazol	1:1 ratio by weight tiletamine HCL and zolazepam HCL
Tiletamine hydrochloride	Cyclohexamine (cyclohexanone)
Xylazine hydrochloride	Alpha$_2$-andrenergic agonist
Yohimbine hydrochloride[c]	Alpha$_2$-andrenergic antagonist
Zolazepam hydrochloride	Benzodiazepine

a. Alternate spelling of atropine, an alkaloid (anticholinergic agent) combined commonly with ketamine.

b. Use on fishers reported by Griffin and Gilbert (1993).

c. Has not been evaluated for use on fishers, but is mentioned in the text.

The historic distribution of the fisher in the eastern United States included mountainous regions as far south as North Carolina and Tennessee. However, fisher became extirpated throughout southern portions of its eastern distribution by the early 1900s because of extensive timber harvest and unregulated trapping (Powell 1993). In 1969, the fisher was reintroduced in West Virginia and, subsequently, the population expanded into portions of western Maryland (Cottrell 1978, Pack and Cromer 1981). Recently, 40 fishers were reintroduced in the Cumberland Plateau region of Tennessee (B. Anderson, pers. commun.). Although it would be premature to judge the outcome of fisher reintroduction in Tennessee, the population in the central Appalachian Mountains of West Virginia and Maryland seems to be well established and expanding into portions of western Virginia (R. Farrar, pers. commun.). Recovery of fisher populations throughout portions of their historic distribution in the southeastern United States has consequences for regional management and conservation planning (Carroll et al. 2001) and has implications for research examining carnivore recovery in the region. Often, efforts to manage or conduct research on fishers include chemical restraint (e.g., Arthur 1988).

Several chemical restraints have been used to immobilize fishers (Tables 1, 2). Irvine et al. (1964), Kelly (1977), Berg (1982), Jessup (1982), Arthur (1988), Roy (1991), Griffin and Gilbert (1993), and Frost et al. (1997) chemically restrained fishers to facilitate translocation, radio-tagging, or laboratory analyses. Formal research on safety and efficacy of chemical restraints for use on fishers was conducted by Belant (1991), Frost and Krohn (1994), Mitcheltree et al. (1999), Dzialak et al. (2001, 2002), Dzialak and Serfass (2002, in press). Many studies reported drug doses, route of administration, number of animals restrained, approximate or specific induction

Table 2. Chemical restraints[a] and associated dose ranges, sample sizes, and references, used to immobilize fishers *(Martes pennanti).*

Drug	Dose	*N*	Reference
Chlordiazeproxide		<61	Irvine et al. 1964
Phencyclidine-promazine	0.7–1.0 mg/kg phencyclidine and 0.5–2.0 mg/kg promazine	5	Seal et al. 1970
Ketamine-atrophine	11.1 mg/kg ketamine and 0.1mg/kg atrophine		Berg 1982
Ketamine-acepromazine	22.0 mg/kg ketamine and 2.5 mg/animal acepromazine	15	Kelly 1977
	2.3–5.0 mg/kg ketamine and 0.2 mg/kg acepromazine	21	Jessup 1982[b]
	6.7–22.5 mg/kg ketamine and 0.7–2.2 mg/kg acepromazine	96	Frost and Krohn 1994[c]
		72	Frost et al. 1997
Ketamine	20.0–60.0 mg/kg	40	Arthur 1988
	11.7–61.2 mg/kg	22	Frost and Krohn 1994[c]
	20.0–58.7 mg/kg	47	Mitcheltree et al. 1999[c]
	17.5–20.0 mg/kg	13	Dzialak et al. 2002[c]
Ketamine-xylazine	22.4–29.0 mg/kg ketamine and 4.1–6.6 mg/kg xylazine	5	Belant 1991[c]
	22.0 mg/kg ketamine and 2.0 mg/animal xylazine	31	Roy 1991
	21.5–41.9 mg/kg ketamine and 2.1–4.2 mg/kg xylazine	12	Mitcheltree et al. 1999[c]
Ketamine-diazepam-halothane		4	Griffin and Gilbert 1993
Telazol	5.0–8.5 mg/kg		Petrini 1992
	5.5–16.5 mg/kg	29	Mitcheltree et al. 1999[c]
	2.9–10.2 mg/kg	4–11	Dzialak and Serfass 2002[c]
Telazol/flumazenil	10.0–11.0 mg/kg Telazol and 0.02 mg/kg flumazenil	4	Dzialak and Serfass In press[c]
Medetomidine-ketamine	0.07 mg/kg medetomidine and 3.7 mg/kg ketamine	13	Dzialak et al. 2002[c]
Medetomidine-ketamine/ atipamezole	0.07–0.08 mg/kg medetomidine, 3.6–3.8 mg/kg ketamine and 0.36–0.38 mg/kg atipamezole	10	Dzialak et al. 2001[c]

a. Intramuscular drug administration was reported by all authors except Irvine et al. (1964), Berg (1982), Petrini (1992), and Griffin and Gilbert (1993). These authors did not specify a route of drug administration (halothane used by Griffin and Gilbert is an inhalant).

b. Authors provide a measure of central tendency.

c. Authors provide measures of central tendency and variability.

Table 3. Response of fishers *(Martes pennanti)* to chemical restraint including induction time, recovery time, body temperature, respiratory rate, and associated references.

Drug	Induction (minutes)	Recovery (minutes)	Temperature (C)	Respiration (breaths/minute)	Reference
Chlordiazeproxide					Irvine et al. 1964
Phencyclidine-promazine	5.0–20.0	45.0–60.0			Seal et al. 1970
Ketamine-atrophine					Berg 1982
Ketamine-acepromazine	<5.0	≤60.0			Kelly 1977 Jessup 1982
	5.0–7.0[b]		39.0–40.1[c]		Frost and Krohn 1994[a]
Ketamine	2.0–5.0	<20.0	>36.0		Arthur 1988
	5.0–7.0[b]		39.2–40.2[c]		Frost and Krohn 1994[a]
	3.2	61.6	39.6–40.3[c]	36.6–53.1[c]	Mitcheltree et al. 1999[a]
	4.5	81.1	39.0–40.3[c]	36.5–44.0[c]	Dzialak et al. 2002[a]
Ketamine-xylazine	3.3	119.4	38.6–39.8[c]	73.8	Belant 1991[a] Roy 1991
	2.3	128.9	38.5–40.2[c]	56.0–119.0[c]	Mitcheltree et al. 1999[a]
Ketamine-diazepam-halothane					Griffin and Gilbert 1993
Telazol					Petrini 1992
	2.4	238.6	38.6–40.3[c]	20.7–64.7[c]	Mitcheltree et al. 1999[a]
	4.0–6.3[b]	107.8–357.8[b]	38.5–39.9[c]	24.0–67.0[c]	Dzialak and Serfass 2002[a]
Telazol/flumazenil	4.0–5.6[b]	357.8–379.8[b,d]	37.5–39.3[c]	19.0–85.0[c]	Dzialak and Serfass In press[a]
Medetomidine-ketamine	4.7–7.6[b]	200.5–231.9[b]	38.7–40.1[c]	34.7–81.2[c]	Dzialak et al. 2001[a]
	4.6	199.4	39.0–40.3[c]	45.4–70.0[c]	Dzialak et al. 2002[a]
Medetomidine-ketamine/ atipamezole	4.6–5.3[b]	69.8–94.8[b,d]	39.0–40.3[c]	45.4–70.0[c]	Dzialak et al. 2001[a]

a. Authors provide measures of central tendency and variability.

b. Range of mean values among age, gender, or dose classes.

c. Range of mean values among different intervals through time.

d. Recovery was associated with a reversal agent; flumazenil was used to partially reverse Telazol and atipamezole was used to reverse medetomidine-ketamine.

time (generally, time from injection until the desired level of immobilization is attained), and recovery time (generally, time from injection until the animal recovers normal or near-normal function; Tables 2, 3). Additionally, several studies reported body temperature and respiratory rate of immobilized fishers for ≤48 minutes post-injection (Table 3). Our objective was to provide a comparative assessment of the safety and efficacy of chemical restraints used previously on fishers. We discuss practical application, field and clinical concerns, areas of future research, and provide recommendations associated with their use. To supplement physiologic comparisons among studies, we derived estimates of normal resting body temperature (38.0–40.0 C), respiratory rate (35.0–45.0 breaths/minute), and pulse rate (159 and 190 bpm for males and females, respectively) of fishers based on Stahl (1967), Tomson (1987), Roy (1991), and Mitcheltree (1996) to which we compare drug-affected values. Much of our discussion is based on first-hand experiences in handling and immobilizing fishers as part of the Pennsylvania Fisher Reintroduction Project (Serfass et al. 1994).

Techniques used to chemically restrain fishers and other medium-sized carnivores are presented in Nielsen et al. (1982), Arthur (1988), Clark and Jessup (1992), Frost and Krohn (1994), Mitcheltree et al. (1997), and Nielsen (1999). For detailed pharmacologic information pertaining to each drug, readers should consult Haigh (1982), Wright (1982), Amrein et al. (1987), Lheureux and Askenasi (1989), Jalanka (1989), Virtanen (1989), Jalanka and Roeken (1990), Lin et al. (1993), and Nielsen (1999).

Support for this project was provided by the Pennsylvania Game Commission, the Pennsylvania Wild Resource Conservation Fund, the Allegheny National Forest, and the National Forest Foundation. We thank E. Orff of the New Hampshire Fish and Game Department, T. Hardisky, J. Hassinger, and C. Dubrock of the Pennsylvania Game Commission, F. Felbaum of the Wild Resource Conservation Fund, and B. Nelson of the Allegheny National Forest.

Chemical Restraints

Irvine et al. (1964), Seal et al. (1970), and Berg (1982) reported using chlordiazeproxide, phencyclidine-promazine combinations, and ketamine-atrophine (atropine) combinations to restrain fishers (Tables 1, 2). No information was provided on their safety or efficacy. Clinical use of chlordiazeproxide is infrequent because it is less potent than the similar benzodiazepine derivative, diazepam, it is largely ineffective for many felids, and it may contribute to renal impairment. Likewise, use of phencyclidine is uncommon because it is largely unsuitable for herbivores and, moreover, it is no longer available in the United States because of its abuse by humans (phencyclidine also is known as PCP). Promazine is a phenothiazine derivative similar pharmacologically to acepromazine. Although promazine is available commercially, its use in chemical immobilization is uncommon. Ketamine, Telazol, and combinations of ketamine and α_2-andrenoreceptor agonists or phenothiazines (Table 1) were the focus of formal studies of chemical restraint in fishers.

Ketamine

Ketamine is used commonly to restrain carnivores, including the fisher (Tables 2, 3). Generally, ketamine effectively immobilized fishers, providing rapid mean induction (≤7.0 minutes) and calm, rapid mean recovery (<82.0 minutes; Table 3). Arthur (1988), Frost and Krohn (1994), and Mitcheltree et al. (1999) demonstrated that ketamine had a high therapeutic index (i.e., broad margin of safety) for use on fishers. Generally, therapeutic index is an indicator of drug safety and refers to the ratio of median lethal dose to median effective dose. The effects of ketamine (induction and recovery) have been reported to be dose-dependent in carnivores (Nielsen 1999). However, fishers restrained with ketamine at a broad range of doses generally exhibited rapid recovery. Arthur (1988) reported that in some instances, fishers appeared to exhibit individual variation (not related to dose) in induction. Mitcheltree et al. (1999) reported that 17% of fishers given ketamine at doses of 20.0–35.2 mg/kg were not immobilized sufficiently and required additional ketamine. Although many factors could influence response of a fisher to chemical immobilization, including sex, age, body composition and condition, degree of stress, and reproductive status (Nielsen 1999), Mitcheltree et al. (1999) speculated that incomplete injections or disparate degrees of tissue vascularization among injection sites resulted in apparent variability in response among fishers. Mitcheltree et al.'s (1999) speculation may be accurate because Dzialak et al. (2002) reported reliable immobilization of fishers with ketamine at a mean dose of approximately 19.0 mg/kg.

Physiologic responses of fishers to ketamine were remarkably uniform among studies (Frost and Krohn 1994, Mitcheltree et al. 1999, Dzialak et al. 2002; Table 3). In clinical settings, body temperature generally was 39.0–40.3 C. Arthur (1988) immobilized fishers with ketamine in the field and reported body temperatures >40 C on sunny days and ≥36.0 C on cold days (e.g., –12.0 C). Although Arthur (1988) did not provide precise information on body temperature of fishers or ambient temperatures, he cautioned that hyperthermia likely was of greater concern than hypothermia. Respiratory rates of fishers restrained with ketamine also approximated Mitcheltree's (1996) estimate of normal resting respiration rate (Table 3). In addition to body temperature and respiratory rate, Dzialak et al. (2002) examined pulse rate, blood-oxygen saturation, and blood pressure of fishers restrained with ketamine. The study demonstrated that the general physiologic response of fishers was consistent with known pharmacologic effects of ketamine (Wright 1982), and reported no instance of clinical concern. However, Dzialak et al. (2002) reported that ketamine induced considerable muscle rigidity, mildly apnic respiratory patterns, mild tachycardia in females compared to males, and characterized immobilization as shallow. Persistent muscle tension in fishers immobilized with ketamine was not conducive to palpation to detect injuries or pregnancy. Likewise, shallow immobilization provided by ketamine would not be conducive to prolonged invasive procedures such as surgery. Nonetheless, Mitcheltree et al. (1999) and Dzialak et al. (2002) considered ketamine to be appropriate for brief clinical or field procedures such as radio-tagging, ear-tagging, or veterinary evaluation associated with captive management.

Clinical concerns associated with using ketamine to restrain fishers were few. Ketamine lacks a specific antagonist, so when used in the field at these doses (Table 2) biologists should be prepared to monitor fishers for approximately 60.0–80.0 minutes after injection. Further, field biologists should evaluate ambient conditions and be prepared to recognize and ameliorate hyperthermia. Although ketamine is relatively well-studied in the fisher, additional carefully-regulated evaluations in field settings could advance our understanding of the conditions associated with ketamine-induced thermoregulatory disruption in carnivores.

Ketamine-acepromazine Combinations

Kelly (1977), Jessup (1982), and Frost and Krohn (1994) restrained fishers with ketamine-acepromazine combinations. Studies by Kelly (1977) and Jessup (1982) indicated that ketamine-acepromazine combinations generally were effective to mobilize fishers, but provided little quantitative information on their safety and efficacy. Kelly (1977) remarked that fishers could be handled approximately 5.0 minutes post-injection and remained anesthetized for 30.0–60.0 minutes. Jessup (1982) reported that 5 out of 23 fishers required multiple injections of ketamine-acepromazine to achieve adequate immobilization. However, doses administered by Jessup (1982) often were less than doses reported by Kelly (1977) and Frost and Krohn (1994; Table 2). Frost and Krohn (1994) reported that a 10:1 ratio by weight combination of ketamine-acepromazine immobilized fishers effectively. Positive qualities of ketamine-acepromazine at this ratio by weight included rapid mean induction ($\leq$7.0 minutes) and body temperatures generally within 38.0–40.0 C. Repeated immobilization of fishers with ketamine-acepromazine had no apparent adverse behavioral or physiologic effects. Frost and Krohn (1994) reported greater $\bar{x} \pm$ SD body temperature in adult than juvenile males at 15 minutes post-injection (39.4 $\pm$ 0.4 vs. 39.0 $\pm$ 0.7 C) but attributed the difference to larger body size and greater capacity to retain heat among adults. Unfortunately, no studies reporting use of ketamine-acepromazine combinations on fishers provided recovery times or additional physiologic responses. Acepromazine is a potent tranquilizing agent and its synergistic effects in combination with cyclohexamines such as ketamine are well documented (e.g., Haigh 1982). Compared to ketamine alone, ketamine-acepromazine may provide less muscle rigidity and better facilitate external examination of fishers. Nonetheless, acepromazine may be associated with seizures in bobcats *(Lynx rufus)* and other carnivores (B.D. Leopold, pers. commun.). Although occurrence of seizures in fishers restrained with acepromazine combinations has not been reported, caution would be advisable in future applications. Like ketamine, acepromazine has no specific antagonist. As with use of ketamine on fishers, field biologists using ketamine-acepromazine combinations should be prepared to address thermoregulatory response disturbance and to monitor fishers throughout recovery. Further research on recovery time and cardiopulmonary responses associated with ketamine-acepromazine combinations would be necessary to enable a more comprehensive comparison with other chemical restraints used on fishers. Although acepromazine remains in common use throughout the veterinary profession, its purposes as a synergist in combination with cyclo-

hexamines for use on wildlife have been largely replaced by newer, reversible α_2-agonists such as xylazine or medetomidine (Table 1).

Ketamine-xylazine Combinations

Roy (1991), Belant (1991), and Mitcheltree et al. (1999) restrained fishers with combinations of ketamine and xylazine. Belant (1991) and Mitcheltree et al. (1999) used comparably similar doses, but the dose of xylazine administered by Roy (1991) was considerably less than the doses of xylazine reported by Belant (1991) and Mitcheltree et al. (1999; Table 2). Unfortunately, Roy (1991) provided no information on safety or efficacy of ketamine-xylazine at the dose he used. Belant (1991) and Mitcheltree et al. (1999) reported rapid induction (<4.0 minutes), similar recovery times (119.0–129.0 minutes; Table 3), and considered ketamine-xylazine effective to immobilize fishers. Compared to ketamine, ketamine-xylazine combinations provided longer recovery times and less muscle rigidity. Consequently, Mitcheltree et al. (1999) considered ketamine-xylazine to be more appropriate than ketamine for prolonged clinical procedures such as minor surgery, extensive physical assessment, or collection of morphological data. Mean body temperature of fishers restrained with ketamine-xylazine generally was 38.0–40.0 C and was comparable to mean body temperatures in fishers restrained with ketamine and ketamine-acepromazine combinations (Frost and Krohn 1994, Mitcheltree et al. 1999, Dzialak et al. 2002; Table 3). Typically, α_2-agonists (i.e., xylazine; Table 1) induce mild bradypnea in carnivores (e.g., Jalanka 1989, Arnemo et al. 1994, Spelman et al. 1994). However, Belant (1991) and Mitcheltree et al. (1999) reported elevated respiratory rates (Table 3). Further, Belant (1991) reported that 1 fisher hyperventilated, and Mitcheltree et al. (1999) reported that respiratory arrest occurred in 2 fishers during ketamine-xylazine restraint. Emergency medical intervention was required to resuscitate the 2 fishers restrained by Mitcheltree et al. (1999). Both authors attributed ketamine-xylazine-induced respiratory complications to pre-existing compromised health conditions in fishers and reported that all fishers recovered normally. It is unclear why ketamine-xylazine combinations induced conflicting respiratory complications on these studies. Mammals that are stressed or agitated often produce high levels of norepinephrine which can competitively limit receptor-level binding of xylazine (Berne and Levy 1993). Perhaps compromised health condition of these fishers enabled competitive exclusion of xylazine by norepinephrine resulting in the emergence of residual cyclohexamine effects, which may produce conflicting cardiovascular responses (Wright 1982, Nielsen 1999). Regardless, occurrence of clinical complications in 2 independent studies is cause for concern and may suggest that ketamine-xylazine combinations are less appropriate to use on fishers than other chemical restraints, particularly under conditions of psychological or physical stress. This would have implications for reintroduction programs that often obtain wild-caught fishers that are unaccustomed to human contact, and may have sustained trapping or transport related injuries or other forms of capture myopathy. Although xylazine can be reversed with the α_2-antagonists atipamezole or yohimbine (Table 1), practical applications of ketamine-xylazine combinations in fishers may be limited given the develop-

ment of more reliable (e.g., specific and selective) α_2-agonists and antagonists (see below).

Medetomidine-ketamine Combinations and Atipamezole

Dzialak et al. (2001, 2002) restrained fishers with medetomidine-ketamine and evaluated atipamezole to reverse effects of medetomidine-ketamine. At a medetomidine:ketamine ratio by weight of 1:50, medetomidine-ketamine was an excellent chemical restraint for fishers because it provided rapid induction (<8.0 minutes), complete muscle relaxation, and prolonged recovery (199.0–240.0 minutes; Table 3). Dzialak et al. (2001) administered atipamezole at a dose by weight relative to medetomidine of 5:1 approximately 20 minutes post-medetomidine-ketamine injection and reported that atipamezole rapidly reversed anesthetic effects of medetomidine-ketamine and reduced recovery time considerably (Table 3). Dzialak et al. (2002) observed that medetomidine-ketamine induced mild bradycardia and hypertension compared to ketamine. Dzialak et al. (2002) reported that bradycardia was more profound in females than males and that both sexes exhibited transient hypotension upon administration of atipamezole. However, these responses were mild and generally consistent with known pharmacologic effects of medetomidine-ketamine and atipamezole (Dzialak et al. 2001, 2002). Like ketamine-xylazine combinations, medetomidine-ketamine induced elevated respiratory rates compared to ketamine alone and to Mitcheltree's (1996) estimate of normal respiration. This is contrary to bradyapnic responses typically associated with α_2-agonism in carnivores and may indicate a species-specific difference in pulmonary mechanisms mediated by α_2-receptors.

The effectiveness of medetomidine-ketamine and atipamezole combinations results from the specificity by which medetomidine and atipamezole function. Medetomidine functions similarly to the α_2-agonist xylazine, but has 200 times the affinity and 10 times the selectivity for α_2-adrenoreceptors than xylazine. Atipamezole has no significant receptor interactions other than with α_2-adrenoreceptors, enabling its specific, competitive reversal of medetomidine. Further, medetomidine-ketamine combinations enable reliable immobilization of fishers at lesser doses than other cyclohexamine-α_2-agonist combinations (e.g., ketamine-xylazine). For example, doses of ketamine and xylazine administered to fishers by Mitcheltree et al. (1999) were approximately 8 and 40 times greater than doses of ketamine and medetomidine administered to fishers by Dzialak et al. (2001, 2002), respectively. Low quantities of ketamine used in association with medetomidine are metabolized rapidly, reducing the potential for emergence of undesirable cyclohexamine side-effects upon reversal of medetomidine with atipamezole.

Medetomidine-ketamine was broad in its clinical and field applications (Dzialak et al. 2001). Prolonged recovery (Table 3) at the dose administered by Dzialak et al. (2001, 2002; Table 2) appeared suitable for invasive procedures such as surgery. Rapid reversal by atipamezole enhanced practical application of medetomidine-ketamine, conferring utility in conditions for which brief immobilization is desirable, such as in the field or for clinical procedures such as palpation to evaluate

physical condition. Medetomidine's high degree of receptor selectivity enables it to out-compete many post-ganglionic neurotransmitters, such as norepinephrine, for α_2-adrenoreceptors. Therefore, in animals that are physically or psychologically stressed and may be producing high levels of norepinephrine, receptor level exclusion of medetomidine by norepinephrine, and consequent expression of residual ketamine effects, would be unlikely. Thus, medetomidine-ketamine combinations may be more reliable and appropriate than other ketamine-α_2-agonist or ketamine-phenothiazine combinations for use on fishers under conditions of compromised health, such as at trap sites or during transport and captive phases of reintroduction efforts. Further research on using medetomidine-ketamine combinations in fishers should include carefully-regulated field trials in a variety of ambient conditions, examination of different medetomidine:ketamine ratios and doses to establish lower and upper bounds for appropriate use, formal examination of analgesic properties, and further evaluation of potential sex and species-specific differences among mustelids in cardiopulmonary responses.

Telazol and Flumazenil

Telazol is a 1:1 ratio by weight combination of the dissociative anesthetic tiletamine, and the tranquilizer zolazepam. Petrini (1992), Mitcheltree et al. (1999), Dzialak and Serfass (2002, 2003) evaluated Telazol for use on fishers. Generally, Telazol provided rapid induction (<6.0 minutes) and calm recovery (110.0–380.0 minutes) throughout a range of doses (Mitcheltree et al. 1999, Dzialak and Serfass 2002, in press; Tables 2, 3). In fishers, like other carnivores (e.g., Kreeger et al. 1990), the period of Telazol-immobilization lengthened as a function of increasing dose (Dzialak and Serfass 2002). At low doses (e.g., <5.0 mg/kg; Table 2), Telazol generally provided shallow immobilization combined with short recovery. For brief (ca. 60.0 minutes; Table 3) clinical or field procedures that involve physical palpation, Telazol at low doses would be more appropriate than ketamine because low doses of Telazol provided smooth respiratory patterns and complete muscle relaxation (Dzialak and Serfass 2002). Dzialak and Serfass (2002) reported that 1 of 4 fishers did not achieve induction at a mean ± SE dose of 2.9 ± 0.2 mg/kg. Greater doses (e.g., 5.0–11.0 mg/kg; Table 2) provided reliable chemical restraint and would be appropriate for most clinical procedures such as use of ultrasound or blood-collecting (Mitcheltree et al. 1999, Dzialak and Serfass 2002). Prolonged recovery (e.g., 350 minutes; Table 3) at doses ≥10.0 mg/kg likely would render Telazol impractical for field use where short recovery times are desirable, but appropriate for veterinary procedures such as tooth removal or surgery. Body temperature of fishers restrained with Telazol generally was 38.0–40.0 C (Table 3). Dzialak and Serfass (2002) observed slightly elevated respiratory rates at doses ≥10.0 mg/kg compared to fishers that received < 10.0 mg/kg (Table 3), but other vital signs including pulse rate, and blood-oxygen saturation, were consistent with known pharmacologic effects of Telazol (Lin et al. 1993).

Dzialak and Serfass (2003) examined the efficacy of flumazenil, administered 40 minutes post-Telazol injection at 0.02 mg/kg, for reducing recovery time associat-

ed with high doses of Telazol. Flumazenil was evaluated for reducing prolonged recovery in fishers restrained with Telazol because, although the tiletamine component of Telazol has no known antagonist (Table 1), flumazenil competitively excludes the specific binding of benzodiazepines (e.g., zolazepam; Table 1) at the receptor level. Additionally, for many species, plasma half-life of tiletamine is briefer than plasma half-life of zolazepam, indicating that recovery would be shortened by antagonizing zolazepam (Amrein et al. 1987, Lin et al. 1993). Fishers given flumazenil became alert sooner than fishers that did not receive flumazenil. However, antagonizing zolazepam enabled expression of residual tiletamine effects such as prolonged recovery (ca. 380 minutes) and profound ataxia. The flumazenil-induced alert condition was a potentially injurious situation because in attempting to regain coordinated mobility, ataxic fishers forcibly struck interiors of recovery cages. This condition may be unsafe in field settings because an uncoordinated, partially mobile fisher could be susceptible to injury, predation, or disrupted thermoregulatory function (Dzialak and Serfass 2003). In contrast to our results, Spelman et al. (1997) reported that in North American river otters *(Lutra canadensis)* immobilized with Telazol at 4.0 mg/kg, flumazenil at 0.08 mg/kg shortened recovery time considerably. Disparate results between Dzialak and Serfass (2003) and Spelman et al. (1997) demonstrate that interspecific variation in responses to Telazol and flumazenil can be considerable, and suggest that further research examining multiple dose regimens of Telazol and flumazenil should be undertaken.

The dose-related properties of Telazol associated with anesthetic duration conferred broad clinical and field utility of Telazol for use on fishers. Researchers using Telazol to restrain fishers would be able to manage duration of immobilization in accordance with requirements of a given procedure by manipulating the dose. Flumazenil was ineffective to reduce prolonged recovery in fishers restrained with high doses (e.g., $>$10.0 mg/kg) of Telazol. Thus, unlike medetomidine-ketamine combinations, use of Telazol at $>$10.0 mg/kg does not confer the benefit of reversibility. Researchers considering further evaluation of benzodiazepine antagonists or other drugs to reverse Telazol should anticipate the expression of residual tiletamine effects during recovery.

Conclusions

Based on our research and review of other studies, it is clear that several chemical restraints are appropriate for ruse on fishers. Managers and biologists conducting work that may require chemical restraint of fishers should base selection of a chemical restraint, and determination of appropriate dose, on clearly stated management or research objectives. Such objectives, considered together with attributes of the restraint event such as ambient conditions, physical condition of the fisher, and sex and age of the fisher govern the suitability of a given immobilization protocol. No single chemical restraint type or dose should be perceived as a panacea. Our experience with chemical restraint of fishers enables us to provide recommendations on drug type and intramuscular dose for immobilizing fishers. However, these recommenda-

tions should be considered within the context of each unique immobilization event and be viewed as a general guide. In fishers and other carnivores, ketamine and Telazol were safe and effective throughout a range of doses. Biologists considering chemically restraining fishers to facilitate brief, non-invasive procedures such as ear-tagging, radio-collaring, or collection of demographic data would find ketamine at 20.0 mg/kg or Telazol at 5.0 mg/kg appropriate. Ketamine administered to fishers generally was short acting, and provided shallow immobilization, regardless of dose. Accordingly, ketamine would not be appropriate for performing prolonged or invasive procedures on fishers. Further, ketamine at doses >25.0 mg/kg may be considered excessive because the period of chemical restraint provided did not lengthen as a function of increasing dose.

Telazol was more versatile than ketamine in 2 general ways. First, Telazol provided less muscle rigidity and smoother ventilation than ketamine. Consequently, Telazol would better facilitate a brief restraint event during which an external assessment involving palpation to detect pregnancy or injury, ultrasound, or collection of morphological data, were to be performed. Second, at greater doses, such as 10.0–11.0 mg/kg, Telazol would enable prolonged or invasive procedures including tooth-removal, blood-collection, or surgical repair of injury. Researchers considering further examination of bezodiazepine antagonism to shorten recovery in fishers restrained with high doses (10.0–11.0 mg/kg) of Telazol should anticipate residual tiletamine effects such as ataxia. For example, flumazenil enabled fishers to regain consciousness sooner than they would have otherwise, but flumazenil did not enhance practical utility of Telazol at 10.0g/kg because recovery remained prolonged and fishers were rendered ataxic and susceptible to injury.

Ketamine, ketamine-acepromazine, and Telazol generally were safe and useful to restrain fishers, but these chemical restraints lack specific antagonists. We considered medetomidine-ketamine and atipamezole a preferred alternative to other chemical restraints for most management and research objectives because they combined safety, broad clinical and field utility, and reversibility. Medetomidine-ketamine at 0.07–0.08 mg/kg medetomidine combined with 3.5–4.0 mg/kg ketamine provided prolonged recovery and a plane of anesthesia that may enable invasive procedures such as surgical repair of injury. Administration of atipamezole at approximately 0.35–0.40 mg/kg (upon completion of procedures) reversed the anesthetic effects of medetomidine-ketamine and remobilized fishers rapidly. Reversibility of medetomidine-ketamine with atipamezole would confer utility for brief procedures, or for situations in which release of fishers immediately post-anesthesia is desirable, such as field replacement of radio-collars. In warm ambient conditions, administration of atipamezole would enable field biologists to minimize the period of immobilization and, likely, reduce the risk of hyperthermia. Last, rapid induction, smooth ventilation, excellent myorelaxation, and rapid remobilization with atipamezole enabled reliable characterization and interpretation of anesthesia, conferring safety to researchers handling fishers. In contrast, ketamine-xylazine was the only drug or drug combination associated with clinical complications during immobilization. Ketamine-xylazine combinations are relatively well-studied in carnivores and, generally,

are safe and effective. However, given the safety and efficacy of newer ketamine-α_2-agonist combinations such as medetomidine-ketamine, practical applications of ketamine-xylazine combinations for use on fishers may be limited.

Typically, physiologic responses of fishers were consistent with known drug pharmacologies. Fishers may be prone to hyperthermia during immobilization with ketamine in warm ambient conditions, so biologists should be prepared to recognize and ameliorate this condition. Also, fishers appear to exhibit mild hyperventilation in response to α_2-agonism (i.e., xylazine or medetomidine). Accordingly, field biologists restraining fishers with medetomidine-ketamine should monitor respiration closely and be prepared to administer an α_2-anatgonist such as atipamezole, because a hyperventilative response coupled with high ambient temperatures could result in rapid elevation of body temperature. Research that would advance our understanding of chemical restraint in fishers includes deriving more reliable estimates of normal resting physiology, further examination of cardiopulmonary regulatory mechanisms mediated by $\alpha_2$receptors, and further examination of the conditions associated with thermoregulatory disruption during immobilization. More field research should be conducted to better develop field immobilization protocols. Finally, evaluation of new chemical restraints, particularly ketamine-α_2-agonist combinations (e.g., romifidine-ketamine), should be a new research priority.

Literature Cited

Amrein, R., B. Leishman, and C. Bentziger. 1987. Flumazenil in benzodiazepine antagonism. Actions and clinical use in intoxications and anesthesiology. Med. Toxicol. 2:411–429.

Arnemo, J.M., R.O. Moe, and N.E. Soli. 1994. Immobilization of captive pine martens *(Martes martes)* with medetomidine-ketamine and reversal with atipamezole. J. Zoo Wildl. Med. 25:548–554.

Arthur, S.M. 1988. An evaluation of techniques for capturing and radiocollaring fishers. Wildl. Soc. Bull. 16:417–421.

Belant, J.L. 1991. Immobilization of fishers *(Martes pennanti)* with ketamine hydrochloride and xylazine hydrochloride. J. Wildl. Diseases 27:328–330.

Berg, W.E. 1982. Reintroduction of fisher, pine marten, and river otter. Pages 159–173 *in* G.C. Sanderson, ed. Midwest furbearer management. Univ. Ill., Champaign.

Berne, R.M. and M.N. Levy. 1993. Physiology, third ed. Mosby, St. Louis, Mo. 1071pp.

Carroll, C., R.F. Noss, and P.C. Paquet. 2001. Carnivores as focal species for conservation planning in the Rocky Mountains region. Ecol. Appl. 11:961–980.

Clark, R.K. and D.A. Jessup. 1992. Wildlife restraint series. Internatl. Wildl. Vet. Serv., Salinas, Calif. 342pp.

Cottrell, W. 1978. The fisher *(Martes pennanti)* in Maryland. J. Mammal. 59:886.

Dzialak, M.R. and T.L. Serfass. 2002. Response of fishers to three different doses of Telazol. J. Pa. Acad. Sci. 76:3–6.

———, and ———. 2003. Effects of flumazenil on fishers *(Martes pennanti)* restrained with tiletamine-zolazepam. Wildl. Biol. 9(3):in press

———, ———, and T.L. Blankenship. 2001. Reversible chemical restraint of fishers with medetomidine-ketamine and atipamezole. J. Wildl. Manage. 65:157–163.

———, ———, D.L. Shumway, L.M. Hedge, and T.L. Blankenship. 2002. Chemical restraint

of fishers *(Martes pennanti)* with ketamine and medetomidine-ketamine. J. Zoo Wildl. Med. 33:45–51.

Frost, H.C. and W.B. Krohn. 1994. Capture, care, and handling of fishers *(Martes pennanti).* Maine Agric. For. Exp. Sta., Tech. Bull. No. 157, Univ. Maine, Orono. 38pp.

———, ———, and C.R. Wallace. 1997. Age-specific reproductive characteristics in fishers. J. Mammal. 78:598–612.

Griffin, K.A. and F.F. Gilbert. 1993. Heart rate of fishers *(Martes pennanti)* during exercise. J. Mammal. 74:285–290.

Haigh, J.C. 1982. Mammalian immobilizing drugs: their pharmacology and effects. Pages 46–62 *in* L. Nielsen, J.C. Haigh, and M.E. Fowler, eds. Chemical immobilization of North American wildlife. The Wisc. Humane Soc., Stevens Point. 447pp.

Irvine, G.W., L.T. Magnus, and B.J. Bradle. 1964. Restocking of the fisher in the lake state forests. North Am. Wildl. Nat. Resour. Conf. 29:307–315.

Jalanka, H.H. 1989. The use of medetomidine, medetomidine-ketamine combinations, and atipamezole at Helsinki Zoo-a review of 240 cases. Acta Vet. Scand. 85:193–197.

——— and B.O. Roeken. 1990. The use of medetomidine, medetomidine-ketamine combinations, and atipamezole in non-domestic animals: a review. J. Zoo Wildl. Med. 21:259–282.

Jessup, D.A. 1982. Restraint and chemical immobilization of carnivores and furbearers. Pages 227–244 *in* L. Nielsen, J.C. Haigh, and M.E. Fowler, eds. Chemical immobilization of North American wildlife. The Wisc. Humane Soc., Stevens Point. 447pp.

Kelly, G.M. 1977. Fisher *(Martes pennanti)* biology in the White Mountain National Forest and adjacent areas. Ph.D. Diss., Univ. Mass., Amherst. 178pp.

Kreeger, T.J., U.S. Seal, M. Callahan, and M. Beckel. 1990. Physiological and behavioral responses of gray wolves *(Canis lupus)* to immobilization with tiletamine and zolazepam. J. Wildl. Diseases 26:90–94.

Lheureux, P. and R. Askenasi. 1989. Agonism and antagonism at the benzodiazepine receptors: A new concept in common drug poisoning. Acta Anesth. Belgium 40:23–28.

Lin, H.C., J.C. Thurmon, G.J. Benson, and W.J. Tranquilli. 1993. Telazol—a review of its pharmacology and use in veterinary medicine. J. Vet. Pharm. Ther. 16:383–418.

Mitcheltree, D.H. 1996. Immobilization and captive management of fishers reintroduced in Pennsylvania. M.S. Thesis, Penn. State Univ., University Park. 122pp.

———, T.L. Serfass, M.T. Whary, W.M. Tzilkowski, R.P. Brooks, and R.P. Peper. 1997. Captive care and clinical evaluation of fishers during the first year of a reintroduction project. Pages 317–328 *in* G. Proulx, H.N. Bryant, and P.M. Woodard, eds. *Martes:* Taxonomy, Ecology, Techniques, and Management. The Provincial Mus. Alberta, Alberta, Can. 474pp.

———, ———, W.M. Tzilkowski, R.L. Peper, M.T. Whary, and R.P. Brooks. 1999. Physiological responses of fishers to immobilization with ketamine, ketamine-xylazine, or Telazol. Wildl. Soc. Bull. 27:582–591.

Nielsen, L. 1999. Chemical immobilization of wild and exotic animals. Iowa State Univ. Press, Ames. 342pp.

———, J.C. Haigh, and M.E. Fowler. 1982. Chemical immobilization of North American Wildlife. Wisc. Humane Soc., Stevens Point. 447pp.

Pack, J.C. and J.I. Cromer. 1981. Reintroduction of fisher in West Virginia. Pages 1431–1442 *in* Chapman, J.A., and D. Pursley, eds. Proc. World. Furbearer Conf., Frostburg, Md.

Petrini, K. 1992. The medical management and diseases of Mustelids. Proc. Joint Meet. Am. Assoc. Zoo Vet./Am. Assoc. Wildl. Vet. 1992:116–135.

Powell, R.A. 1993. The fisher: life history, ecology, and behavior. Univ. Minn., Minneapolis. 237pp.

Roy, K.D. 1991. Ecology of reintroduced fishers in the Cabinet Mountains of northwestern Montana. M.S. Thesis, Univ. Mont., Missoula. 94pp.

Seal, U.S., A.W. Erickson, and J.G. Mayo. 1970. Drug immobilization in the Carnivora. Internatl. Zoo Yearbook 10:157–170.

Serfass, T.L., R.P. Brooks, W.M. Tzilkowski, and D.H. Mitcheltree. 1994. Fisher reintroduction in Pennsylvania: feasibility and review. Penn. State Univ., Univ. Park. 28pp.

Spelman, L.H., P.W. Sumner, W.B. Karesh, and M.K. Stoskopf. 1997. Tiletamine-zolazepam anesthesia in North American river otters *(Lutra canadensis)* and its partial antagonism with flumazenil. J. Zoo Wildl. Med. 28:418–423.

———, ———, J.F. Levine, and M.K. Stoskopf. 1994. Anesthesia of North American river otters *(Lutra canadensis)* with medetomidine-ketamine and reversal by atipamezole. J. Zoo Wildl. Med. 25:214–223.

Stahl, W.R. 1967. Scaling of respiratory variables in mammals. J. Appl. Physiol. 22:453–460.

Tomson, F.N. 1987. Mink. Vet. Clin. North Am. 17:1145–1153.

Virtanen, R. 1989. Pharmacological profiles of medetomidine and its antagonist, atipamezole. Acta Vet. Scand. 85:29–37.

Wright, M. 1982. Pharmacological effects of ketamine and its uses in veterinary medicine. J. Am. Vet. Med. Assoc. 180:1462–1471.