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## FOCAL POINT

★ Because of their actions on specific receptors, the clinical actions of  $\alpha_2$ -adrenoceptor agonists can be antagonized by selective antagonists.

## KEY FACTS

- The  $\alpha_2$ -adrenoceptor agonists are potent analgesics that induce dose-related sedation, thereby decreasing the required dose of primary anesthetic, p. S11.
- Failure to achieve optimum sedation with  $\alpha_2$ -adrenoceptor agonists may be caused by preexisting stress, fear, excitement, or pain, p. S16.
- Tolazoline has been safely used to antagonize xylazine-induced sedation and initiate arousal; it produces strong peripheral vasodilation with sympathetic blocking and histamine-like actions, p. S17.
- Administration of an  $\alpha_2$ -adrenoceptor antagonist to reverse sedation is not without risk; deaths have occurred in animals receiving rapid intravenous overdoses of tolazoline or yohimbine, p. S17.

# Xylazine Sedation Antagonized with Tolazoline

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**Abstract:** Physiologic alterations induced by xylazine depend on the dose, rate, and route of administration and are influenced by the concomitant administration of other classes of drugs. When these factors are appropriately considered,  $\alpha_2$ -adrenoceptor agonists are safe drugs for inducing narcosis, analgesia, and muscle relaxation in healthy fasted ruminants. Tolazoline has proven to be a safe, effective antagonist for xylazine-induced sedation and other actions when the proper dose is administered.

The  $\alpha_2$ -adrenoceptor agonists, which are the most widely used drugs for immobilizing ruminants, have most of the desirable properties of opioids but induce few of their undesirable actions. Unlike opioids,  $\alpha_2$ -adrenoceptor agonists do not cause excitement and only induce minimal respiratory depression in ruminants. They are not FDA-controlled substances and therefore do not require extensive record keeping. In addition,  $\alpha_2$ -adrenoceptor agonists are potent analgesics that induce dose-related sedation, thereby decreasing the required dose of primary anesthetic. When the proper dose is administered, these agonists do not cause excitement or profound respiratory depression. Xylazine, the most notable  $\alpha_2$ -adrenoceptor agonist, induces analgesia, sedation, and muscle relaxation by activating centrally located  $\alpha_2$ -adrenoceptors.

The response of ruminants to xylazine is similar to that of other animals to opioids (e.g., dogs to morphine). Because of their actions on specific receptors, the clinical actions of  $\alpha_2$ -adrenoceptor agonists can be antagonized by selective antagonists (e.g., tolazoline, yohimbine, or atipamezole).<sup>1</sup>

## XYLAZINE

### History and Actions

Xylazine, the first  $\alpha_2$ -adrenoceptor agonist to be widely used in veterinary medicine, was synthesized in Germany in 1962 as an antihypertensive drug for humans. It was subsequently found to have potent sedative actions in animals. Although xylazine was not identified as an  $\alpha_2$ -adrenoceptor agonist when it was initially introduced for veterinary use, the drug had profound sedative-analgesic-muscle relaxant action in cattle and other ruminants. In the United States,



Figure 1A



Figure 1B



Figure 1C



Figure 1D



Figure 1E

**Figure 1**—A large bull weighing 1100 kg was (A and B) sedated by injecting xylazine into the tail vein and then (C) ketamine into the jugular vein. (D) A mouth wedge was inserted and an endotracheal tube placed to protect the airway in case the bull regurgitated. Finally, oxygen was supplied and surgery performed on (E) the injured foot.

xylazine is approved by the FDA for horses, dogs, cats, deer, and elk only.<sup>1</sup>

Xylazine's activation of  $\alpha_2$ -adrenoceptors located in the central nervous system (CNS) induces analgesia, sedation, muscle relaxation, anxiolysis, sympatholysis, and other responses. In addition to centrally located receptors, receptors are present in peripheral tissue (e.g., the gastrointestinal [GI] tract, uterus, kidney, and

platelets). Activation of the  $\alpha_2$ -adrenoceptors in the GI tract of ruminants results in ruminal hypomotility and increased GI fecal waste material.<sup>2</sup> The cardiovascular actions of  $\alpha_2$ -adrenoceptor agonists include increased blood pressure (BP) and decreased heart rate (HR), the latter being characterized by sinus bradycardia and/or atrioventricular blockade.<sup>1,3,12</sup>

If these actions are a response to an overdose of xylazine, they can be antagonized by administering tolazoline; however, tolazoline also antagonizes the sedation and analgesia produced by xylazine.<sup>1</sup> Drooling (probably from suppression of the swallowing reflex) and low bellowing are often observed in ruminants.<sup>1,3</sup> Because xylazine can depress the cyclic reticuloruminal motor function and thus result in fatal ruminal tympany in unfasted cattle, adult cattle should not receive food or

water for 24 hours before an immobilizing dose of xylazine is administered. If fasting is not possible, an  $\alpha_2$ -adrenoceptor antagonist (e.g., tolazoline) should always be available to alleviate ruminal depression and/or gut hypomotility and to relieve or alleviate tympany.<sup>4,5</sup>

### Use in Ruminants

Xylazine is a mixed  $\alpha_1$ -/ $\alpha_2$ -adrenoceptor agonist used in ruminants throughout the world. In 1991, estimates indicated that 10 million doses of  $\alpha_2$ -adrenoceptor agonists (of which 7 million were apparently xylazine) were administered annually to animals.<sup>6</sup> Xylazine is considered to be a reliable sedative with profound muscle relaxation, making it highly desirable for immobilizing large ruminants. Xylazine can be safely administered by the intramuscular, intravenous (Figure 1), and epidural routes.<sup>1</sup> Cattle are apparently one of the most sensitive species to the sedative and immobilizing actions of xylazine and therefore require a rather small dose. Clinical observations suggest that cattle are approximately 5 to 10 times more sensitive than horses to a given dose of xylazine. Sheep and goats are apparently slightly more sensitive than cattle or llamas.<sup>1,3</sup>

In cattle, the degree of sensitivity varies among breeds. Brahmins evidently are the most sensitive breed, followed by Herefords, Jerseys, holsteins, and Angus.<sup>1</sup> The peculiarity of US breeds of cattle can lead to dangerous overdosing, especially when a dose of xylazine intended for horses is accidentally injected—a strong argument for keeping a safe, effective antagonist, such as tolazoline, nearby.

### As an Anesthetic Adjunct

In the early 1970s, reports on the use of xylazine as an anesthetic adjunct were published in US and European veterinary literature.<sup>7-15</sup> These reports documented the effectiveness of xylazine in eliminating muscular hypertonicity in dogs and cats that had been anesthetized with ketamine<sup>7,9,10</sup> and the rapid onset of predictable sedation, analgesia, and muscle relaxation in horses and cattle after being injected with xylazine.<sup>8,11-16</sup> The onset of action for xylazine is approximately 3 to 5 minutes after intravenous injection and within 8 to 10 minutes after intramuscular injection. In cattle and sheep, peak plasma concentrations occur within 12 to 14 minutes.



**Figure 2**—Because the jugular vein is often difficult to catheterize in llamas, intravenous xylazine and ketamine are often given; recovery can be hastened by administering tolazoline.

The systemic half-life is approximately 23 minutes in sheep and 36 minutes in cattle.<sup>1,3</sup> In the United States, meat and milk withdrawal times for xylazine-treated cattle have not been established. In Canada, the United Kingdom, France, Germany, and Switzerland, however, withdrawal times have been determined.<sup>17,18</sup> In France and the United Kingdom, the meat withdrawal time ranges from 2 to 14 days; whereas the milk withdrawal time ranges from 0 to 72 hours in most countries.

When intramuscular xylazine is given in a dangerously high dose (i.e., 1.2 to 2.0 mg/kg), a 120-day withdrawal interval is imposed in Germany.<sup>17</sup>

After cattle have been injected with xylazine, a dose-dependent, sleeplike state occurs and often persists for 1 to 2 hours, although the duration of analgesia is much shorter (20 to 35 minutes) depending on the dose administered. In most domestic species, xylazine minimally affects respiratory function at recommended doses.<sup>1</sup> In contrast, caution is advised when administering xylazine or any other  $\alpha_2$ -adrenoceptor agonist to young ruminants in high singular or cumulative doses or combined with potent cardiorespiratory-depressant anesthetics (e.g., heavy doses of thiopental or pentobarbital).<sup>1</sup> Special precautions should be taken when mature ruminants receive xylazine before improper fasting because of the potential for developing life-threatening ruminal tympany.

### As a Sedative, Analgesic, and Muscle Relaxant

Xylazine is extensively used for sedation, analgesia, and muscle relaxation in cattle,<sup>18,19</sup> sheep,<sup>20-22</sup> goats,<sup>1</sup> and llamas<sup>1</sup> (Figure 2). In these animals, xylazine contributes to the safety and efficacy of general anesthesia by decreasing the required dose of anesthetic. It is a desirable adjunct when the appropriate dose is administered simultaneously with ketamine, telazol, guaifenesin-ketamine, or a thiobarbiturate (Table I) for inducing a short period of surgical anesthesia or when anesthesia is to be extended with an inhalant. After the onset of xylazine-induced sedation in large bulls (Figure 1), intravenous xylazine (0.11 mg/kg) followed by intravenous ketamine (2.0 mg/kg) can produce 20 to 40

<sup>a</sup>Personal communication; Mozier J, Animal Health Division, Chemagro Corporation, Stillwell, Kansas.

TABLE I  
Response of Mature Cattle and Llamas to Tolazoline<sup>a</sup>

Patient	Weight (kg)	Xylazine Dose (mg/kg)	Time Xylazine Given	Tolazoline Dose (mg/kg)	Elapsed Time Since		IV Supplement (mg/kg)	IV Supplement Administration	IV Induction Drugs	Maintenance Drugs	Response to Reversal Agent(s)
					Xylazine Administration	Supplement Administration					
Cow 1	555	0.17 IV	12:55 PM	1.1	3 hr, 53 min	—	None	—	Xylazine, ketamine	Halothane, 1:00–2:40 PM	Extubated 2 min after receiving tolazoline
Cow 2	884	0.17 IV	2:28 PM	1.1	1 hr, 41 min	—	None	—	Xylazine, ketamine	Halothane, 1:30–3:52 PM	Extubated 1 min after receiving tolazoline
Cow 3	591	0.12 IV	1:35 PM	0.99	1 hr, 50 min	—	None	—	Xylazine, ketamine	Halothane, 1:45–2:45 PM	Extubated and sternal 5 min after receiving tolazoline
Cow 4	682	0.11 IV	11:10 AM	0.15	2 hr, 10 min	—	None	—	Xylazine, ketamine	Triple drip (600–1200–60 mg), <sup>b</sup> 11:15 AM–12:02 PM; halothane, 12:02–1:10 PM	Extubated 4 min after receiving tolazoline
Cow 5	605	0.14 IV	3:20 PM	3.0	1 hr	—	None	—	Xylazine, ketamine	Triple drip (1000–2000–100 mg), <sup>b</sup> 3:25–4:10 PM	Extubated 5 min after receiving tolazoline
Cow 6	682	0.14 IV	1:15 PM	1.8	1 hr	—	None	—	Triple drip <sup>b</sup>	Halothane, 1:20–2:00 PM	Extubated before receiving tolazoline; sternal 5 min after receiving tolazoline
Cow 7	500	0.11 IV	1:30 PM	1.2	2 hr, 45 min	2 hr, 50 min	Doxapram, 0.12	—	Xylazine, ketamine	Halothane, 2.5%–3%, 1:40–4:00 PM; 10 mg IV torbugesic, 3:15 PM; 10 mg IV torbugesic 3:35 PM	Extubated 5 min and sternal 30 min after receiving tolazoline

TABLE 1 (continued)

Patient	Weight (kg)	Xylazine Dose (mg/kg)	Time Xylazine Given	Tolazoline Dose (mg/kg)	Elapsed Time Since		IV Supplement (mg/kg)	IV Supplement	Induction Drugs	Maintenance Drugs	Response to Reversal Agent(s)
					Xylazine Administration	Supplement Administration					
Cow 8	467	0.11 IV	2:35 PM	2.1	2 hr, 50 min	2 hr, 50 min	Doxapram, 0.13	—	Triple drip <sup>b</sup>	Halothane, 2:50-4:57 PM	Extubated 7 min after receiving tolazoline
Cow 9	671	0.10 IV	6:45 PM	1.5 1.5	3 hr, 34 min 3 hr, 46 min	3 hr, 28 min	Doxapram, 0.09	—	Xylazine, ketamine	Halothane, 6:50-10:07 PM	Extubated 1 min after receiving second tolazoline dose
Cow 10	1000	0.15 IV	10:20 AM	0.06	33 min	—	None	—	Xylazine, ketamine	Triple drip (560-1120-56 mg), <sup>b</sup> 10:25-10:46 AM	Standing 2 min after receiving tolazoline
Cow 11	395	0.11 IV	12:50 PM	1.8	1 hr, 20 min	—	None	—	Xylazine, ketamine	Halothane, 1:00-2:00 PM	Extubated 2 min after receiving tolazoline
Llama 1	49	0.55 IM	2:00 PM	1.0	1 hr, 30 min	—	None	—	Xylazine, ketamine	Halothane, 2:05-3:37 PM	Extubated 7 min after receiving tolazoline
Llama 2	118	0.05 IV	2:05 PM	2.5	30 min	30 min	Doxapram, 0.25	—	Triple drip <sup>b</sup>	Triple drip (60-120-3 mg), <sup>b</sup> 2:07-2:21 PM	Extubated 2:28 PM, sternal 1 min and standing 1 hr after receiving tolazoline

<sup>a</sup>Response after receiving xylazine in combination with ketamine, a triple-drip preparation, or halothane in oxygen to maintain anesthesia. In three cattle and one llama, doxapram was combined with tolazoline to enhance the arousal action of tolazoline.

<sup>b</sup>Triple drip is a drug combination of 5% guaifenesin glycerate, 2 mg/ml ketamine, and 0.1 mg/ml xylazine. When denoting maintenance amounts, the first number shows the milliliters of guaifenesin glycerate, the second the milligrams of ketamine, and the third the milligrams of xylazine.

IM = intramuscular; IV = intravenous.

minutes of surgical anesthesia that can be extended by administering an additional half dose of each drug.<sup>1</sup> Ketamine alone induces minimal muscle relaxation and poor visceral analgesia, and recovery is often accompanied by emergence excitement.<sup>1,19,20</sup> When xylazine is combined with ketamine, muscle relaxation, narcosis, and visceral analgesia are improved and emergence from anesthesia is uneventful (unless the patient is urged to its feet before completely recovering).<sup>1</sup>

A guaifenesin-ketamine-xylazine combination is an established anesthetic widely used in ruminants.<sup>1</sup> Guaifenesin acts centrally by inducing skeletal muscle relaxation and mild sedation without analgesia. Analgesia and narcosis are enhanced by combining ketamine and xylazine with guaifenesin. A triple-drip drug combination can be prepared by adding ketamine (2 mg/ml) and xylazine (0.1 mg/ml) to a 5% solution of guaifenesin (usually prepared in 5% glucose in water).<sup>1</sup> To induce anesthesia in patients weighing less than 250 kg (e.g., calves, llamas, sheep, and goats), the triple-drip preparation should be injected using a large syringe rather than by intravenous drip. The induction dose is 0.5 to 1.0 ml/kg, depending on the patient's size and the rate of injection.<sup>1</sup> Anesthesia can be maintained by a continuous infusion rate of 1.0 to 2.0 ml/kg/hr. Using a standard intravenous administration set (i.e., 15 drops is 1 ml), the maintenance infusion rate is calculated as follows:

$$30 \text{ Drops} \times \text{Body Weight (kg)} \div 60 = \text{Drops/min} \div 60 = \text{Drops/sec of Triple Drip}$$

Using a triple-drip preparation to maintain anesthesia in a 200-kg calf would require:

$$30 \text{ Drops} \times 200 \text{ kg} \div 60 = 100 \text{ Drops/min} \div 60 = 1.6 \text{ Drops/sec of Triple Drip}$$

Tolazoline can effectively relieve lingering sedation and promote early recovery after the triple-drip preparation has been administered (Table I).

## Dosing

The intramuscular dose of xylazine used to induce recumbency in docile beef cows and calves is approximately 0.22 mg/kg, and the intravenous dose is 0.11 mg/kg. In large bulls (e.g., weighing 900 kg or more), the intramuscular dose should be decreased to 0.18 mg/kg and the intravenous dose to 0.08 mg/kg.<sup>1</sup> When coadministered with xylazine, butorphanol apparently intensifies analgesia. This drug combination has been effectively used to sedate and apparently confer increased analgesia in horses and cattle.<sup>1,23</sup> When used to

supplement local or regional analgesia for surgery in standing cows, a total dose of 5 to 10 mg of xylazine administered concomitantly with butorphanol (total dose, 8 to 10 mg) provides satisfactory sedation and analgesia.

When a butorphanol-xylazine combination is administered to intensify analgesia and sedation in steers undergoing perineal urethrostomy for removal of urinary calculi, it must be remembered that urine output increases by several times within 2 hours after xylazine administration.<sup>24</sup> A major increase in urine output could easily cause the bladder to rupture if the blockage is not quickly relieved.

## Untoward Reactions

Failure to achieve optimum sedation with  $\alpha_2$ -adrenoceptor agonists may be caused by preexisting stress, fear, excitement, or pain because all of these signs are associated with increased endogenous concentrations of circulating catecholamines that can interfere with reductions in the release of excitatory neurotransmitters, a response induced by  $\alpha_2$ -adrenoceptor agonists. The most satisfactory use of xylazine or other  $\alpha_2$ -adrenoceptor agonists is achieved when given to calm, quiet patients in nonstressful surroundings with minimal environmental stimuli.<sup>1</sup>

Experimental and clinical evidence suggests that analgesia does not extend to the end of xylazine-induced sedation. Painful procedures should therefore be restricted to 15 to 30 minutes following xylazine injection, or a local and/or regional analgesic (e.g., lidocaine) should be used as a supplement.<sup>1</sup> Painful manipulations beyond this period can shorten sedation and could result in a hastened, excitatory recovery. Extremely apprehensive patients may prove refractory to xylazine-induced sedation and are more likely to experience untoward reactions than are calm patients.

Although increased myometrial tone and intrauterine pressure can occur in cattle that receive xylazine,<sup>25</sup> the drug has been administered during all stages of pregnancy but has not been definitively associated with an increased incidence of obstetric complications.<sup>1,3</sup> Nevertheless, it would seem prudent to refrain from indiscriminate use of large doses of xylazine in pregnant cows.

## Epidural Administration

In cattle, caudal epidural injection of xylazine produces analgesia that lasts 2 to 2.5 times longer than an equivalent dose of lidocaine.<sup>1,26</sup> Intravenous tolazoline (0.3 mg/kg) antagonizes the sedative actions of epidural xylazine. Analgesia caudal to the injection site of xylazine persists<sup>27</sup> because of the potent local anesthetic action of xylazine.<sup>1</sup>

## TOLAZOLINE

During the past three decades, the most significant advance in drugs designed to induce sedation, immobilization, and analgesia in ruminants has been the development of  $\alpha_2$ -adrenoceptor agonists alone and in combination with other major anesthetics (e.g., ketamine, telazol). Development of specific antagonists has extended the safe use of  $\alpha_2$ -adrenoceptor agonists in ruminants. The most notable antagonists are tolazoline, yohimbine, and atipamezole.

Tolazoline is an imidazoline derivative with  $\alpha_1$ - and  $\alpha_2$ -adrenoceptor antagonistic activity. This drug has been safely and extensively used to antagonize xylazine-induced sedation and initiate arousal in various species that are in a depressed state from anesthetic combinations that contain  $\alpha_2$ -adrenoceptor agonists.<sup>28-32</sup>

### Cattle

The  $\alpha_2$ -adrenoceptor antagonists are extremely valuable for anesthetic management of large domestic and wild animal species in the field and in veterinary hospitals. Tolazoline has the least specificity for  $\alpha_2$ -adrenoceptors of the antagonists ordinarily used by veterinarians.<sup>1</sup> In cattle, however, tolazoline is more effective than is yohimbine for antagonizing xylazine-induced CNS depression.<sup>31</sup> An intriguing question arises as to whether tolazoline, which has less specificity and selectivity for  $\alpha_2$ -adrenoceptors, has a more definitive pharmacodynamic profile for antagonism of mixed  $\alpha_2$ -adrenoceptor agonists (e.g., xylazine) than do more selective  $\alpha_2$ -antagonists (e.g., yohimbine or atipamezole).

Tolazoline produces strong peripheral vasodilation with sympathetic blocking and histamine-like actions, although these responses are relatively transient. Therapeutic doses cause a transient increase in the HR that is apparently more than a reflex response to peripheral vasodilation.<sup>34</sup> Conversely, massive overdoses can cause severe cardiac stimulation, increased gastric secretions, hyperperistalsis, and an explosive (although transient) diarrhea accompanied by abdominal stress. Less disturbing signs are piloerection, chilliness, and apprehension. These short-lived responses apparently result from the rapid renal excretion of tolazoline and can be blocked by administering atropine.<sup>1,34</sup> When the proper dose is given, tolazoline induces only a transient and incomplete  $\alpha_2$ -adrenergic blockade with mild hypotension.<sup>1</sup> Its direct action on peripheral vascular smooth muscle is responsible for vasodilation and an associated hypotension. The response is characterized by an increased cutaneous blood flow that results in bright red mucous membranes.

Administration of an  $\alpha_2$ -adrenoceptor antagonist to

reverse sedation is not without risk. Some animals have died after receiving rapid intravenous overdoses of yohimbine or tolazoline.<sup>28</sup> Conversely, the safety margin of tolazoline is apparently broad in calves.

In a study designed to examine the response of calves (weighing 65 to 88 kg) to intravenous tolazoline administered at a dose larger than that recommended, the calves were given intravenous saline (3 ml), yohimbine (0.22 mg/kg), or tolazoline (6.6 mg/kg) 15 minutes after receiving intravenous xylazine (0.11 mg/kg) to antagonize xylazine-induced sedation. Calves that received tolazoline were aroused in  $0.65 \pm 0.23$  minutes and walking unassisted in  $7 \pm 3$  minutes—a response similar to that of calves given 4 mg/kg of tolazoline. Calves that received yohimbine became sternal in  $22 \pm 12$  minutes and walked  $58 \pm 22$  minutes later. The saline control calves responded similarly to those treated with yohimbine by becoming sternal in  $21 \pm 11$  minutes and walking after  $58 \pm 13$  minutes. The high dose of intravenous tolazoline did not induce any evidence of excitement, serious hypotension, tachycardia, or diarrhea in any of the calves studied.<sup>31</sup>

When tolazoline is injected slowly and in an appropriate dose, unfavorable responses (e.g., hypotension, tachycardia) are rare. The recommended dose of intravenous tolazoline required to antagonize xylazine sedation and promote prompt arousal in cattle ranges from 1.1 to 2.2 mg/kg, depending on the elapsed time since xylazine was administered.<sup>27,35-37</sup> The highest recommended intravenous dose (2.2 mg/kg) should be reserved for treating a cow that was accidentally overdosed, is suffering from bloat, or requires drug reversal shortly after xylazine administration.

### Llamas

Because doxapram acts on the aortic and carotid chemoreceptors and the medullary respiratory center, cattle sedated with xylazine can become aroused<sup>1,39</sup>; but the drug is apparently less effective when used alone in llamas.<sup>39</sup> Our clinical experience has shown that the effectiveness of tolazoline as an initiator of arousal in xylazine-sedated cattle can be enhanced by concomitant administration of intravenous doxapram hydrochloride (1 to 2 mg/kg) and intravenous tolazoline (1.1 to 2.2 mg/kg).<sup>1,19</sup> The intensified arousal action initiated by doxapram is undoubtedly caused by its CNS-stimulating effect and not by the direct antagonistic action of xylazine at centrally located  $\alpha_2$ -adrenoceptors, which can occur with administration of tolazoline.

Llamas are apparently very sensitive to tolazoline.<sup>39</sup> Clinical experience suggests that the lowest effective dose should be used in llamas. Deaths have occurred in llamas after administration of the high recommended

dose for horses or cows; the cause of these deaths is unknown. After the llamas received tolazoline, they became aroused; and when the endotracheal tube was removed, they were unable to breathe.<sup>39</sup>

Because llamas are obligate nasal breathers, a large dose of tolazoline could cause nasal edema, which would close the nasal passages and result in suffocation.<sup>b</sup> Airway obstruction could also result from dorsal displacement of the soft palate. Because llamas start to chew the orotracheal tube before the airway has been protected, some practitioners use nasotracheal intubation.<sup>40</sup> The nasotracheal tube should remain in place until the llama has recovered and is walking. The size of nasotracheal tubes used for llamas ranges from 7-mm internal diameter for llamas weighing 30 kg to 12-mm internal diameter for llamas weighing 175 kg or more.<sup>40</sup>

## SUMMARY

Physiologic alterations induced by xylazine depend on the dose, rate, and route of administration and are influenced by the concomitant administration of other classes of drugs. When these factors are appropriately considered,  $\alpha_2$ -adrenoceptor agonists are safe drugs for inducing narcosis, analgesia, and muscle relaxation in healthy, fasted ruminants. The lowest possible dose required to achieve the desired depth and duration of action for a given procedure should be used.

Tolazoline has proven to be a safe, effective antagonist for xylazine-induced sedation and other actions (e.g., quelled ruminal motility) when the proper dose is administered. When a patient shows signs of pain and there is no definitive need to antagonize xylazine-induced CNS depression, the effects of xylazine should be allowed to wane, thereby preserving its analgesic action as long as possible. When butorphanol is combined with xylazine, its analgesic action may be increased in many species and extended into the post-operative period even after xylazine antagonism. Butorphanol has recently been categorized a schedule IV drug.<sup>41</sup>

<sup>b</sup>Personal communication: Riebold TW, College of Veterinary Medicine, Oregon State University, Corvallis, Oregon, 1998.

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### ARTICLE #6 CE TEST

The article you have read qualifies for 1.5 contact hours of Continuing Education Credit from the Auburn University College of Veterinary Medicine. Choose only the one best answer to each of the following questions; then mark your answers on the test form inserted in *Compendium*.

1. The first  $\alpha_2$ -adrenoceptor agonist to be widely used in veterinary medicine was
  - a. detomidine.
  - b. medetomidine.
  - c. xylazine.
  - d. yohimbine.
2. Xylazine is approved for use in
  - a. cattle, goats, and llamas.
  - b. horses, cats, dogs, deer, and cattle.
  - c. deer, elk, horses, dogs, and cats.
  - d. cattle, horses, cats, dogs, deer, and cats.
3. The best sedative-analgesic for cattle apparently is
  - a. yohimbine.
  - b. tolazoline.
  - c. xylazine.
  - d. detomidine.
4. When categorizing cattle for sensitivity to xylazine, which of the following reflects a ranking from most to least sensitive?
  - a. Brahmans, Herefords, Jerseys, holsteins, Angus
  - b. Brahmans, Angus, Herefords, Jerseys, holsteins
  - c. Brahmans, Jerseys, Herefords, Angus, holsteins
  - d. Brahmans, holsteins, Angus, Jerseys, Herefords
5. After xylazine is administered to cattle, a dose-dependent sleeplike state occurs. Which of the following statements accurately describes that state?
  - a. The sleeplike state may last 1 to 2 hours, but analgesia may only last 20 to 30 minutes.
  - b. Analgesia lasts longer than xylazine-induced sedation.
  - c. When epidural xylazine is administered, analgesia is short-lived and can be antagonized with yohimbine.
  - d. Sedation and analgesia should not be extended by administering ketamine or telazol.
6. The most widely used combination of drugs for maintaining anesthesia by intravenous drip is known as a triple drip, which includes
  - a. ketamine, xylazine, and telazol.
  - b. butorphanol, xylazine, and thiopental.
  - c. ketamine, xylazine, and guaifenesin.
  - d. telazol, yohimbine, and guaifenesin.